Parthenium: A wide angle view

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INTRODUCTION

Parthenium hysterophorus L. (congress grass, congress weed, carrot weed, wild feverfew, the “Scourge of India”) is an exotic weed that was accidentally introduced in India in 1956 through imported food grains.[1] It has become a common weed causing dermatitis of epidemic proportions.[2] The epithet “congress weed” refers to the US congress (who allocated the shipment for Pune, India).[3] In Pune, it found an ecological niche without natural enemies and spread rapidly along the canal banks, roads and railway tracks to become a major field weed.[4] Both rural and urban areas have been invaded by this weed. It is the leading cause of plant induced air-borne contact dermatitis in India[5] and has achieved major weed status in India and Australia within the past few decades.[6] The weed can affect human health, animal husbandry, crop production and biodiversity.[6]

DISTRIBUTION

Parthenium hysterophorus is a native of the West Indies and North East Mexico.[7] During the last hundred years, it has spread worldwide [Table 1].[8-10] It is thought to have originated as a result of natural hybridization between Parthenium confertum and P. bipinnatifidum.[11]

BOTANICAL ASPECTS OF P. HYSTEROPHORUS

It belongs to the family Asteraceae/Compositae (Daisy family), which is one of the largest and most important families in the plant kingdom. The family includes troublesome weeds, ornamental annuals, herbaceous perennials, medicinal and food plants [Table 2].[12,13] Fifteen species of Parthenium L. occur in America and the West Indies. One species, Parthenium hysterophorus L. was introduced to the Indian subcontinent.

All contain allergenic sesquiterpene lactones (SQLs).

In South America, P. hysterophorus does not contain parthenin, but instead has hymenin, which is a diastereomer. However, in India, the plant contains large amounts of parthenin and ambrosin. No cross reaction between parthenin and hymenin exists in humans and guinea pigs.[14,15]

The plants of Compositae family have many tiny flowers

Figure 1: Composite head vertical section

Table 1: Distribution of P. hysterophorus L. worldwide

<table>
<thead>
<tr>
<th>Continent</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>Madagascar, Mozambique, South Africa</td>
</tr>
<tr>
<td>America (North)</td>
<td>Bahamas, Bermuda, Cuba, Haiti, Jamaica, Rico, USA</td>
</tr>
<tr>
<td>America (South)</td>
<td>Argentina, Bermuda, Belize, Bolivia, Dominica, Guatemala, Guyana, Honduras, Paraguay, Tahiti, Trinidad, Tobago, Venezuela</td>
</tr>
<tr>
<td>Asia</td>
<td>China, India, Nepal, Pakistan, Taiwan, Vietnam</td>
</tr>
<tr>
<td>Australia</td>
<td>Australia</td>
</tr>
<tr>
<td>Europe</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
(florets) clustered to form a flower head (capitulum). This flower head is surrounded by bracts (modified leaves) that form an involucre beneath or around a flower cluster [Figure 1].

P. hysterophorus has two life cycles,
1. Juvenile or rosette stage
2. Mature or adult stage

Juvenile stage
It has a rosette with large, dark green, simple, radicle, pinnetisect small leaves and flowering is absent. The large lower leaves are spread on the ground like a carpet, without allowing any vegetation underneath it.

Adult stage
It is procumbent (trailing along the ground but not rooting), profusely branched, leafy herb resembling a bush or shrub because of its height (1-2.5 m). The stem becomes tough and woody as the plant matures into a hardy bush. Enormous number of pollen grains (624 millions per plant) are produced by anemophilous (by wind) pollination. It is an extremely prolific seed producer with upto 25,000 seeds (achenes) per plant. The plant is thermo- and photo–insensitive; hence, it grows round the year except in severe winters; in other words, it survives environmental extremes. It is a rapid colonizer and competes out other vegetation in its vicinity within two growing seasons. It grows in almost all types of soil except near the seashore as the saline soil is not conducive to parthenium flowering.

Allergenicity
The allergens in Asteraceae are SQLs and thus the patients with contact dermatitis to Compositae can react to many other non-Compositae SQL containing plants [Table 2]. The SQLs are found in the leaves, stems, flowers, and some pollens. The highest concentrations are found in trichomes which are present on stems, the underside of leaves and in the flowering heads.

Cross-reactivity between SQLs does not follow any rules. No single SQL nor the commonly used “SQL mix” of three common SQLs (alantolactone, dehydrocostus lactone and costunolide) serves as a reliable screen for SQL allergy. Therefore, the samples of the suspect plant should always be used while patch testing a patient. Over 200 skeletal types and 1350 individual types of SQLs have been described, and each of these may have multiple functional groups attached to them.

SQLs are characterized by the presence of a \( \gamma \)-butyrolactone ring bearing an exocyclic \( \gamma \)-methylene group [Figure 2].

Human health
Around three decades ago, serious human health risks from P. hysterophorus were reported from Pune. Several thousands of cases of allergic contact dermatitis with some fatalities have been reported. An outbreak of epidemic proportion followed a dam burst. “After 1-10 years of exposure to the weed, 10-20% of the population will develop severe allergic reactions. There may be hay fever, asthma or dermatitis and can be caused by dust and debris from the plant as well as pollen.” The severity of dermatitis in India is greater in comparison to America because the plant grows more vigorously in India and contains large amounts of the sesquiterpene lactone, parthenin, which is absent in the plants in South America.

It clinically involves the adult males in both USA and India. Studies have estimated a ratio of 20 : 1 between men and women. This cannot be explained in terms of degree of exposure since Indian women and children also work in fields. Possibly women and children are less frequently sensitized. However, the studies on plant dermatitis from India have shown a male-to-female ratio of 1 : 1 and 5 : 5 : 1. In a study from Minnesota, the large male preponderance appeared to change with the male-to-female ratio of 1.4 : 1. Initially, the exposed sites of the face, neck and flexures are affected with erythema, blistering and intense pruritus resulting later in skin thickening, hyperpigmentation and development of a leonine facies. Unexposed sites may get involved late in the course of the disease. A seasonal variation is initially observed with the dermatitis flaring in the summers corresponding to the growing season and disappearing in winters. After several years, persistent pruritic lichenified dermatitis develops.
without seasonal variation. Winter exacerbation is seen in the months of September, October and November and may be due to the increased growth of Parthenium following the North-East monsoon showers.[26]

Various patterns of dermatitis have been described;[1,12,25,27–32] a typically airborne contact dermatitis (ABCD) involving the eyelids and nasolabial folds, photodermatitis (essentially a pseudo-photodermatitis) involving the eyelids, nasolabial folds, areas under the chin and behind the ears, atopic dermatitis, seborrheic dermatitis, exfoliative dermatitis and photosensitive lichenoid dermatitis. Hand dermatitis is observed in gardeners after contact with the weed.[12] Vitiliginous skin appears to be spared perhaps due to the vacuolization of Langerhans cells in these areas.[33]

Air borne contact dermatitis is not always due to Parthenium hysterophorus. Xanthium strumarium, another weed belonging to Compositae, is reported to be a causative agent in North India with patch test positive to xanthium but negative to parthenium.[34] Other members of the Compositae family causing ABCD in North India include Chrysanthemum morifolium (chrysanthemums), Dahlia pinnata (dahlia) and Tagetes indic (marigold). [35] Since the allergens of Compositae

Table 2: Allergenic Compositae and non-Compositae with sesquiterpene lactones[12,13]

<table>
<thead>
<tr>
<th>Compositae</th>
<th>Binomial name</th>
<th>Common name</th>
<th>Allergenic sesquiterpene lactones[14]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild flowers and weeds</td>
<td>Ambrosia spp.</td>
<td>American rag weeds</td>
<td>Artemisiiifolin, isabelin</td>
</tr>
<tr>
<td>*Artemisia vulgaris L.</td>
<td></td>
<td>Mugwort</td>
<td>Ludovicins A, B and C, Artegasin-A</td>
</tr>
<tr>
<td>*Achillea millefolium</td>
<td></td>
<td>Yarrow, milfoil</td>
<td>Oleoresin - helanalin, helanalin acetate</td>
</tr>
<tr>
<td>Arnica montana</td>
<td></td>
<td>Arnica, mountain tobacco</td>
<td>Oleoresin - helanalin, helanalin acetate</td>
</tr>
<tr>
<td>Helium autumnale L.</td>
<td></td>
<td>Sneezeweed</td>
<td></td>
</tr>
<tr>
<td>*Parthenium hysterophorus L.</td>
<td></td>
<td>Congres grass</td>
<td>Parthenin, ambrosin, bymenin coronopilin</td>
</tr>
<tr>
<td>Tanacetum cinerantherifolium</td>
<td></td>
<td>Pyrethrum</td>
<td>SQGs present; pyrethrin is not an SQL</td>
</tr>
<tr>
<td>*Tanacetum vulgare</td>
<td></td>
<td>Tansy</td>
<td>ArbusculinA, tanacetin, parthenolid</td>
</tr>
<tr>
<td>*Taraxacum officinale</td>
<td></td>
<td>Dandelion</td>
<td>Glucopyranoside of taraxin acid</td>
</tr>
<tr>
<td></td>
<td>Anthems arvensis L.</td>
<td>Field chamomile</td>
<td></td>
</tr>
<tr>
<td>*Xanthium strumarium L.</td>
<td></td>
<td>Cocklebur</td>
<td>SQGs present</td>
</tr>
<tr>
<td>Dahlia spp.</td>
<td></td>
<td>Dahlia</td>
<td>SQG present</td>
</tr>
<tr>
<td>*Dendrathaemum cultivars</td>
<td></td>
<td>Chrysanthemum</td>
<td>Artegasin-A, ?alantolactone, ?parthenolide</td>
</tr>
<tr>
<td>*Helianthus annuus</td>
<td></td>
<td>Sunflower</td>
<td>1-0 methyl 1,4,5-dihydro neveusin A,</td>
</tr>
<tr>
<td>Rudbeckia hirta</td>
<td></td>
<td>Black-eyed susan</td>
<td></td>
</tr>
<tr>
<td>Tagetes spp.</td>
<td></td>
<td>Marigold</td>
<td>No SQL, ACD rare</td>
</tr>
<tr>
<td>In herbal medicine</td>
<td>Achillea millefolium</td>
<td>Yarrow, milfoil</td>
<td>*-thertienyl, bithienyl – roots (phototoxic)</td>
</tr>
<tr>
<td>*Arnica montana</td>
<td></td>
<td>Arnica, mountain tobacco</td>
<td>Carabron, helanalin, helanalin acetate</td>
</tr>
<tr>
<td>Cardenelmum officinale</td>
<td></td>
<td>Pot marigold</td>
<td>ACD to ointments; no SQL</td>
</tr>
<tr>
<td>Helianthus annuus</td>
<td></td>
<td>Sunflower</td>
<td>1-0 methyl 4,5-dihydro neveusin A,</td>
</tr>
<tr>
<td>*Inula helenii L.</td>
<td></td>
<td>Elecampane</td>
<td>(Trichomes major, pollen minor)</td>
</tr>
<tr>
<td>*Tanacetum parthenium</td>
<td></td>
<td>Feverfew</td>
<td>Parthenolide (water soluble)</td>
</tr>
<tr>
<td>Tanacetum vulgare L.</td>
<td></td>
<td>Tansy</td>
<td>Arbusculin A, tanacetin, parthenolid</td>
</tr>
<tr>
<td>*Taraxacum officinale</td>
<td></td>
<td>Dandelion</td>
<td>Glucopyranoside of taraxin acid</td>
</tr>
<tr>
<td></td>
<td>Saussurea costus (Falc.)</td>
<td>Costus</td>
<td>Dandelion allergen</td>
</tr>
<tr>
<td>Food plants</td>
<td>Cichorium endiva</td>
<td>Endive</td>
<td>Lactucin, lactucopicrin</td>
</tr>
<tr>
<td>*Cichorium intybus</td>
<td></td>
<td>Chicory</td>
<td>Lactucin, lactucopicrin</td>
</tr>
<tr>
<td>Cynara scolymus</td>
<td></td>
<td>Globe artichoke</td>
<td>Cynaropicrin</td>
</tr>
<tr>
<td>*Lactuca sativa L.</td>
<td></td>
<td>Lettuce</td>
<td>Lactucinopicrin</td>
</tr>
<tr>
<td>*Helianthus annuus L.</td>
<td></td>
<td>Sunflower seeds (oil)</td>
<td>1-0 methyl 1,4,5-dihydro neveusin A,</td>
</tr>
<tr>
<td>Carthamus tinctorius</td>
<td></td>
<td>Saflower</td>
<td>(Trichomes major, pollen minor)</td>
</tr>
<tr>
<td>Tragopogon</td>
<td></td>
<td>Vegetable oyster or salsify</td>
<td>(Trichomes major, pollen minor)</td>
</tr>
</tbody>
</table>

ACD - Allergic contact dermatitis, *Cause air borne contact dermatitis, * are not SQLs; is a natural phototoxic thiophene

without seasonal variation. Winter exacerbation is seen in the months of September, October and November and may be due to the increased growth of parthenium following the North-East monsoon showers.[26]
are sesquiterpene lactones (SQLs), cross reactions may occur. Parthenium hysterophorus and X. strumarium have shown a high rate of cross-sensitivity in Indian patients, whereas the prevalence of cross reaction with chrysanthemum is generally low. It is also important to distinguish between true cross sensitization and polysensitivity. If a patient develops independent allergies to more than one agent that do not share any chemical groups (antigenic determinants), then such a situation is called polysensitivity and not cross-sensitivity.

The degree of contact hypersensitivity to an agent can be determined by the titer of contact hypersensitivity (TCH). Increased dilutions of the causative antigen in addition to the standard concentration recommended for the antigen are applied on the sensitized patient. The highest dilution (or the lowest concentration of the antigen that still produced a distinct positive patch test reaction was labeled as the titer of contact hypersensitivity (TCH) in that patient. The TCH was found to be a reliable indicator of the degree of contact hypersensitivity, and the results have been shown to be reproducible. However, other reports have found that the TCH does not correlate with the clinical severity of contact dermatitis or response to treatment.

The severity of dermatitis in a parthenium sensitive patient depends on the degree of contact hypersensitivity in the patient at that time and the quantity of antigen in contact with the patient. Inhalation of pollens can cause allergic rhinitis that can develop into bronchitis or asthma if the pollens enter the respiratory tract during breathing.

Parthenin has enhanced toxicity due to the presence of a cyclopentene group that can cause chromosomal damage in animal cells, uncouple phosphorylation and inhibit the key cellular enzymes. Aeropollen sampling in Bangalore (Southern India) over a 6-year period revealed that 40-60% of the total pollen count was from P. hysterophorus. Allergenicity to P. hysterophorus pollen extracts was recorded in 34% allergic rhinitis and 12% bronchial asthma patients from Bangalore.

Parthenin pollen is now a major cause of allergic rhinitis in Bangalore with 7% of the population affected and 40% sensitive to the pollen. Such a high incidence of allergic rhinitis to a specific pollen has not been reported from any other place in the world. Subsequent studies in Northern India (Punjab) showed that a significant proportion of bronchial asthma patients is sensitized to P. hysterophorus. In New Delhi, out of 63 patients with airborne contact dermatitis, 62 showed a positive reaction to the parthenium weed.

Studies on cross-reactivity between ragweed (Ambrosia) and parthenium pollen suggest that individuals sensitized to parthenium may develop type-I hypersensitivity reactions to ragweed and vice versa when they travel to regions infested with the weed, to which they have not been previously exposed. Parthenium weed may have a more sinister effect on human health since it has been hypothesized that parthenium-contaminated animal feed leads to tainted milk and that the hepatotoxic parthenin reacts synergistically with copper in causing Indian childhood cirrhosis (ICC).

**PHOTOSENSITIVITY AND PARTHENIUM (COMPOSITAE) DERMATITIS**

The relationship between photosensitivity and parthenium dermatitis has been a mystery. SQLs are not photo sensitizers, they have neither phototoxic nor photoallergic properties. There is only one well-documented case of photocontact dermatitis. The reduction in the minimal erythema dose (MED) to UVB and minimal phototoxic dose to UVA has been reported. The photo aggravation of parthenium dermatitis has been reported, but improvement is observed in patients after avoiding further exposure to plant even if they move to a sunny area.

**PATHOGENESIS OF PARTHENIUM DERMATITIS**

Delayed hypersensitivity alone does not explain the varying clinical patterns and photoaggravation. The combined type IV and type I hypersensitivity to parthenium has been recently postulated. Type I hypersensitivity mediated by IgE, particularly in the sensitized atopic individual with parthenium dermatitis could be initiating and perpetuating the dermatitis. P. hysterophorus may be precipitating or exacerbating the atopic dermatitis. Photoaggravation, heat intolerance and flexural involvement are the features of atopic dermatitis. Various clinical patterns of parthenium dermatitis such as flexural eczema, prurigo nodularis, chronic actinic dermatitis can be observed in patients with an atopic diathesis. Although a combination of type III and type IV hypersensitivity had also been postulated, this has been questioned since IgG antibodies that mediate type III hypersensitivity have not been detected.

**Animal husbandry**

The impact of Parthenium weed on livestock production is diverse (both direct and indirect) affecting grazing land, animal health, milk and meat quality, and marketing of...
pasture seeds and grain. This weed can be a serious problem in grasslands in India and can reduce the pasture-carrying capacity by 90%.\[63\] The most comprehensive analysis of its economic impact on livestock production has been made from Australia.\[64,65\]

Serious health hazards to livestock in parthenium-invaded areas have been reported.\[66\] While cattle and buffalo sparingly feed on parthenium weed, goats readily graze it. In artificial feeding tests, buffalo bull calves accepted the weed alone or in mixtures with green fodder with severe consequences. The majority (11 out of 16) developed severe dermatitis and toxic symptoms and died within 8-30 days. Alopecia, loss of skin pigmentation, dermatitis, and diarrhea have been reported.\[66\] Degenerative changes in both the liver and kidneys and inhibition of liver dehydrogenases have been reported in buffalo\[67\] and sheep.\[68\] The milk and meat of cattle, buffalo and sheep becomes tainted by parthenium.\[45,69\] The practical impact of the presence of antigens in meat and milk must be studied.

**Crop production**

The impact of parthenium on crop production system may be direct and indirect.\[6\] Allelopathogenicity (direct toxicity) due to release of phytotoxic substances such as caffeic, vanillic, chlorogenic, p-hydroxybenzoic acids, parthenin, ambrosin and coronopilin inhibit several crop plants and multi-purpose arable crops, thus decreasing the crop yields.\[70\] Indirect effects include poor fruiting of leguminous crops in Southern India; in parthenium-infested fields, parthenium pollen was found on Crotalaria and Desmodium.\[71\] Parthenium pollen was found to reduce the chlorophyll content probably by interference with porphyrin biosynthesis.\[71\]

Another indirect effect is its potential role as an alternate host for crop pests functioning as an inter season reservoir or inoculum source, as for example, in the case of scarab beetle, which is a pest of sunflower (Pseudoheteronyx sp.) in central Queensland.\[72\] The agromyzid, Liriomyza trifolii – a pest of bell pepper (Capsicum annuum, Solanaceae) – prefers to feed and oviposit on P. hysterophorus that grows along the roadsides in the pepper growing regions of Texas.\[73\] In addition, P. hysterophorus may act as a secondary host for plant diseases. The bacterial pathogen, Xanthomonas campestris pv. phaseoli, could be transmitted from the weed to Phaseolus vulgaris (Leguminosae) with reciprocal infection, at the preflowering and pod-formation stages.\[74\] The bacterial wilt pathogen has been recorded on P. hysterophorus in India.\[75\] A number of crop viruses have been detected from Tamil Nadu and Karnataka in India and from Cuba.\[61\]

**Biodiversity**

The invasive capacity and allelopathic properties have rendered P. hysterophorus with the potential to disrupt the natural ecosystems. It has been reported to be causing a total habitat change in native Australian grasslands, open woodlands, river banks and flood plains.\[64,65\] Similar invasions of national wild life parks have been observed recently in Southern India.\[61\]

**INVESTIGATIONS IN PARTHENIUM DERMATITIS**

The confirmation of the diagnosis of parthenium dermatitis requires a few investigations:

1. **Patch tests:** It is always important to carry out tests with the plant material "as is."
2. **Prick tests:** Performed with the parthenium antigen included in the Indian Standard Series (ISS) and with leaf "as is." Plant materials can be crushed and diluted with saline (for example, 1 : 9 parts) in order to obtain a solution that can be easily pricked. Both the immediate reaction at 15 min and the late phase reaction (LPR) at 24-48 h should be recorded.\[57\]
3. **RAST for parthenium specific antibodies but RAST is less sensitive than prick testing.**\[74,77\]
4. **A detailed history of atopy and Serum Ig E estimation.**\[57\]
5. **Clinical severity scoring (CSS) is as described by Verma et al.**\[78\]

**Plant extracts**

Plant allergens are low molecular weight secondary plant metabolites and are usually soluble in acetone, ethanol or ether. A filtered acetone or ethanol extract of dried plant material or a short ether extract of fresh material produces a solution suitable for patch testing. Aqueous extracts degrade rapidly and lose their sensitizing power within a month.\[79\] Acetone extracts of P. hysterophorus are reported to be more sensitive than water extracts, with good sensitivity to 1% acetone extract.\[80\] Although extracts in organic solvents are more stable, with time, evaporation of the solvent may increase the concentration and the sensitizing effect of the allergen(s).\[81\] Incorporating an evaporated extract into petrolatum represents a standard means of retaining material for patch testing.

**TREATMENT OF PARTHENIUM DERMATITIS**

Oral hyposensitization has been successfully attempted in several small studies; patch test reactions decreased or
became negative and the patients clinically improved.\textsuperscript{[12,52]} This result is acceptable on the basis of the fact that while chrysanthemum allergy is the commonest Compositae allergy in Europe, it is extremely rare in Japan where chrysanthemum leaves and flowers are eaten with sushi, salad and soups.\textsuperscript{[12]}

The results of oral hyposensitization with parthenium leaf are not consistent and continued therapy appears to be necessary.\textsuperscript{[82,83]} It is thought to cause the depletion of memory T-cells.\textsuperscript{[83]} As with Toxicodendron, the hyposensitization side effects include pruritus ani, a widespread urticarial or eczematous eruption, and dyspepsia.\textsuperscript{[83]} The risk of the toxic side effects should also be considered.\textsuperscript{[84]}

Acute dermatitis has to be treated immediately. Once daily application of potent topical steroids is as effective as twice daily.\textsuperscript{[85]} Potent topical steroids and oral prednisone are relatively ineffective unless employed early and if the further exposure to SQIs is prevented.\textsuperscript{[12,48,86]} Antihistamines suppress only the immediate reaction of type I hypersensitivity; the LPR remains unaffected.\textsuperscript{[87]} Systemic corticosteroids have been the mainstay of treatment in the acute phase. Long-term use may lead to adrenocortical axis suppression with attendant complications.\textsuperscript{[88]} A trial with dexamethasone-cyclophosphamide pulse (DCP) therapy was unsuccessful.\textsuperscript{[89]}

The combined type IV and type I hypersensitivity has been recently postulated in parthenium dermatitis.\textsuperscript{[57]} Corticosteroids are not usually thought of being capable of protecting against immediate allergic reactions.\textsuperscript{[90]} Corticosteroids have both immunosuppressive and anti-inflammatory actions. They suppress delayed hypersensitivity and also the LPR of the type I hypersensitivity reaction.\textsuperscript{[26]} However, it has been observed that even the brief application of a corticosteroid could diminish the immediate reaction.\textsuperscript{[92]}

Similarly, the preventive application of corticosteroid to the nasal mucosa of an allergic patient is capable of diminishing the symptoms produced by an antigen challenge.\textsuperscript{[92]} The protective effect of corticosteroids extends to the immediate reaction when continuously administered.\textsuperscript{[93]} The application of corticosteroid topically for several days depletes the mast cells in the skin and thus reduces the response to histamine-releasing agents.\textsuperscript{[94]}

Azathioprine has immunosuppressive, anti-inflammatory and steroid-sparing properties and is effective in the treatment of parthenium dermatitis at the dose of 1-2 mg/kg/day.\textsuperscript{[78, 95]} A weekly pulse dose of 300 mg is also reported to be effective with better compliance and reduced cost of therapy.\textsuperscript{[78]} The safety of a bolus dose has been questioned.\textsuperscript{[200]} Its limitation is the slow onset of action taking 2-3 months to achieve a clinical effect.\textsuperscript{[26]}

Cyclosporine, an immunosuppressive with potent anti-inflammatory actions, has been reported to be effective in the acute phase of parthenium dermatitis as a crisis intervention measure.\textsuperscript{[26]} It also overcomes the side effects of systemic corticosteroid usage. It suppresses the delayed hypersensitivity reaction as well as the LPR.\textsuperscript{[26]} The histopathology of the LPR following prick testing with parthenium allergen is reported to show leukocytoclastic vasculitis, which was absent following the initiation of cyclosporine.\textsuperscript{[26]}

Methotrexate has also been reported to be effective at a dose of 15 mg/week along with topical corticosteroids and sunscreens.\textsuperscript{[101]}

Chloroquine 200 mg TID for one week, ethinyl estradiol 0.5 mg for 3 weeks have also been used;\textsuperscript{[86]} however, they are not currently advised. PUVA therapy has reportedly helped Compositae dermatitis. A protocol developed by Storrs et al. combines PUVA with oral prednisone.\textsuperscript{[12]}

\textbf{PREVENTION OF PARTHENIUM DERMATITIS}

The most effective treatment (if possible) is prevention by avoiding the weed. However, the attempts at eradication of the weed have been unsuccessful. One of us (CRS) has burned the leaf and patch tested with the residue; however, the result was a positive patch test. Since it has no economic value, efforts have been made to utilize parthenium as a green leaf manure, biopesticide, compost for agricultural purposes and additive with cattle manure in biogas production.\textsuperscript{[102]} Patch testing with the compost in a sensitive patient yielded positive result, thereby confirming that the allergenicity is retained.\textsuperscript{[103]} “Parth” in the Sanskrit language is another name for Arjuna, an invincible or indestructible character in the Indian epic Mahabharata. Parthenium hysterophorus is thus inadvertently and aptly named.\textsuperscript{[103]}

\textbf{Measures of prevention and protection}

Since P. hysterophorus is ubiquitous, a change of residence or job is not a suitable option. This would also lead to social and economic consequences. Hence, prevention is aimed at the reduction in the quantity of the antigen to which the patient is exposed. These measures include the following:\textsuperscript{[95]}
Lakshmi C, et al.: Parthenium

1. To remove as much of the causative plant as possible from the immediate environment of the patient.
2. To cover as much of the skin as possible by clothing.
3. To wash the uncovered areas of the skin with soap and water as frequently as possible (preferably every 2-3 h) in order to wash off the antigen before it penetrates the skin.
4. To frequently use a barrier cream to slow down the penetration of the antigen into the skin and to wash each time before the reapplication of the barrier cream.
5. To avoid the exposure to sunlight; sunscreen lotions may serve as barrier creams.
6. Drying of clothes indoors also helps in reducing the quantity of antigen. Clothes dried outdoors gather the airborne parthenium allergen. Pieces of cloth dried outside are reported to elicit a positive patch test in a sensitive patient.[104]
7. Gloves may not offer protection since the sesquiterpene lactone permeates vinyl, polyethylene and latex gloves.[105]

CONTROL OF P. HYSTEROPHORUS

Prevention of parthenium dermatitis can be attempted by biological or chemical control of the weed, P. hysterophorus.

Biological control[6]
P. hysterophorus is essentially a ruderal (grows in rubbish, poor land or waste land) plant in the New World and only occasionally achieves a weed status in the fields or pastures. Biotic factors suppress the plant within its native range compared to its increased fitness or vigor in their absence, as in Australia and India, and therefore, the biological control may offer the best long-term solution for the management of this weed. However, there is skepticism surrounding the introduction of exotic biocontrol agents, which include the following.
1. Arthropods
In the 1980s, after preliminary screening in Mexico and final evaluation in quarantine in Australia, six oligophagous or monophagous species were released in quarantine in Queensland:
   1. A defoliating beetle, Zygogramma bicolorata Pallister (Chrysomelidae),
   2. A seed-feeding weevil, Smirnicyx lutulentaus Dietz (Curculionidae),
   3. A stem galling moth, Epiblema strenuana (Walker) (Tortricidae),
   4. A leaf mining moth Bucculatrix parthenica Bradley (Lyoniitidae),
   5. A sap-feeding planthopper, Stobaera concinna (Stal) (Delphacidae),
   6. A stem boring curculionid weevil, Listronotus setosipennis (Hustache)

Despite the release of Z. bicolorata over 17 years ago in Australia in the areas of massive sunflower cultivation, there have been no reported instances of beetle attack on the crop. Beetle defoliation is reported to cause up to 99.5% decline in weed population and replacement by up to 40 different plant species in the fallow land.

Z. bicolorata proved to be an effective control agent in Bangalore. Beetle attacks were reported on sunflowers from Karnataka. However despite the widespread cultivation of sunflower as a crop in Karnataka, Maharashtra, Tamil Nadu, Andhra Pradesh and Kerala, there have been no further reports of beetle feeding on sunflower in field situations.

2. Pathogens
Mainly fungal and include exotic agents such as classical biocontrol agents as well as adapted or opportunistic pathogens such as mycoherbicides [Table 3].

3. Antagonistic plants and bioherbicides
Cassia uniflora (Leguminosae) moved into areas that were previously (“traditionally”) occupied by parthenium weed in Maharashtra, India.

Cassia sericea had the ability to smother or overgrow P. hysterophorus in North-East India and it has also been reported that it reduces the vigor of parthenium weeds. The wholesale propagation of C. uniflora for biological control was aborted when it was found to be a major host of Bemisia whiteflies and the reservoir of tomato leaf curl virus. Marigold (Tagetes erecta) can outgrow P. hysterophorus in field trials.[6]

Aqueous foliar extracts of Azadirachta indica, Aegle marmelos and Eucalyptus tereticomis totally inhibit the seed germination of parthenium and are cheap effective bioherbicides.[106]

Chemical control (herbicides)
Well known herbicides such paraquat, trifluralin, diphenamid, napropamide and propachlor fail to control parthenium weed.[107] Timing of chemical control is critical. They should be treated when plants are small and have not produced seed and when grasses are actively growing to recolonize the infested area (early summer).[108] Maintaining competition...
Table 3: Fungal pathogens for biological control of *P. hysterophorus*

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Neotropics</th>
<th>Palaeotropics</th>
<th>Effects</th>
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</thead>
<tbody>
<tr>
<td>Classical biocontrol agents</td>
<td></td>
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<tr>
<td>Basidiomycotina, Uredinales (Rust Fungi)</td>
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<tr>
<td>Puccinia abrupta diet and Holw. var.</td>
<td>Argentina, Bolivia, Brazil</td>
<td>Kenya, Mauritius</td>
<td>Hastened leaf senescence, decreased life span and dry weight.</td>
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<tr>
<td>Partheniicola (Jackson) Parmelel</td>
<td>Central America, Mexico</td>
<td></td>
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<tr>
<td>Puccinia melampodi diet and Holw.</td>
<td>Central America, Mexico</td>
<td></td>
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<tr>
<td>Basidiomycotina, Ustilaginales (White smut)</td>
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<tr>
<td>Entyloma partheni sydow (= <em>E. compositarum</em>)</td>
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<tr>
<td>Mycoherbicides</td>
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<tr>
<td>Ascomycotina, Erysiphaenes</td>
<td>Mexico</td>
<td></td>
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<tr>
<td>Erysiphe cichoracearum DC var. cichoracearum Braun</td>
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<td></td>
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<tr>
<td>Sphaerotheca fulginea (Schlecht). Poll</td>
<td>Central America, Mexico</td>
<td></td>
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<tr>
<td>Mitosporic fungi (= fungi Imperfecti)</td>
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<tr>
<td>Alternaria spp.</td>
<td>Mexico</td>
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<tr>
<td><em>A. protenta</em> (E. G. Simmons)</td>
<td>Cuba, Mexico</td>
<td>India</td>
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<tr>
<td><em>A. zinniae</em> (M. B. Ellis)</td>
<td>-</td>
<td>India</td>
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<tr>
<td>Cercospora partheniphila</td>
<td>-</td>
<td>India</td>
<td></td>
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<td>Colletotrichum capsici</td>
<td>-</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td><em>C. gloeosporoides</em> (Penz.) Sacc.</td>
<td>-</td>
<td>India</td>
<td></td>
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<tr>
<td>Curvularia lunata (Walker) Boedijn</td>
<td>-</td>
<td>India</td>
<td>Leaf spot disease.</td>
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<td>Fusarium spp.</td>
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<tr>
<td>Myrothecium roridum Tode ex Fr.</td>
<td>-</td>
<td>India</td>
<td>Kills mature plants</td>
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<tr>
<td>Oidium partheni (Satyaprasad and Usharani)</td>
<td>-</td>
<td></td>
<td>Suppresses seed germination</td>
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<tr>
<td>Rhizoctonia solani Kuhn</td>
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<tr>
<td>Sclerotium rolfsii Sacc collar rot disease</td>
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</tbody>
</table>

Neotropic - The tropical areas of the “New World,” Central America and the Northern part of South America, Paleotropic - The tropical areas of the “Old World,” Africa, SE Asia and the Western Pacific.

is important for control of parthenium weed; therefore, spraying with a selective herbicide that will not kill other species is recommended.

Selective chemical herbicides include,[109] Ametryne, Ametryne + simazine, Atrazine, Fomesafen, Metribuzin, Linuron, Prometryne, Metobromuron, 2, 4-D, Oxadiazon

*P. hysterophorus* poses a serious health risk in Australia and India as it invades new areas and retains the established ones. This review has highlighted the dermatological aspects, current views on pathogenesis, other health hazards and its impact on agricultural as well as the natural ecosystems. Since its avoidance is not possible due to various reasons, preventive, therapeutic and control options are presented.

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