# PHYTO-PHOTO-DERMATITIS

BY

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Phyto-photo-dermatitis is a bullous eruption appearing on parts of the body which have been in contact with certain plants and simultaneously exposed to sunlight some 48 hours previously. Until recently (Roxburgh, 1947) standard text-books on skin diseases have paid little attention to this relatively common dermatitis. We owe the term phyto-photo-dermatitis to Klaber (1942). It is an adequate name which describes the aetiology of an eruption caused by a variety of plants. The term phyto-photo-dermatitis includes dermatitis bullosa striata pratensis (Oppenheim), Oppenheim's disease, meadow dermatitis, parsnip dermatitis, and berloque dermatitis.

The incident described below is recorded because of the large number of cases occurring within a few days, and because of a surprising lack of familiarity with the condition shown by many practitioners and the patients and their relatives.

The disease is by no means unknown to country folk. However, many inquiries made over the past eight years in Wiltshire, Somersetshire, Devonshire, and Lincolnshire revealed that none of the people with whom discussions have been held realized the true causes of the dermatitis. In the country, children running bare-legged through long grass in the summer months are quite often affected, but as the parents are familiar with the signs and symptoms the doctor is seldom consulted. It is not common for adults to be afflicted in such circumstances. Whether this can be attributed to the style of clothing or whether some degree of desensitization occurs during childhood has not been ascertained. Another point of interest is that it seems to be more prevalent in districts where heath-land and moors exist.

Oppenheim (1926) gave the first clear and detailed description of the condition, which had affected a number of his patients sunbathing on the grass in the Viennese suburb of Ottakring. Two years later he realized the significance of contact with plants in the production of dermatitis, when he thought that siliceous compounds in the plants might be the important factor (Oppenheim and Fessler, 1928). From this time various plants in many different countries have been incriminated. Although Philadelphy (1931) seemed to have recognized that sunlight might be a factor in the production of the dermatitis, it was not until Kitchevatz (1934a), in France, carried out experiments with ultra-violet rays that the dermatitis was known to be due to a photosensitization arising from contact with the juices of certain plants. He later (1936b) ingeniously utilized the advent of an eclipse of the sun to strengthen his arguments.

## Botanical Aspects

As further cases are published it is possible that many more plants possessing photodynamic properties will be recorded, but the following list of those involved in phyto-photo-dermatitis may be of value. References are also given as an aid to more detailed study.

The wild parsnip, *Pastinaca sativa,* appears to have been the plant first, and most commonly, associated with photosensitivity (Stowers, 1897; Hartmann and Briel, 1927; Heye, 1929; Hirschberger and Fuchs, 1936; McKinlay, 1938; Jensen and Hansen, 1939; Klaber, 1942). Cultivated parsnips have been reported by Whittle, Hellier, and Lee (1946) as being responsible for the dermatitis in some instances. Other plants accused are yarrow or milfoil, *Achillea millefolium* (Philadelphy, 1928; Gans, 1929; Spillman and Weiss, 1931); angelica, *Angelica sylvestris* (Bogdanovitch *et al.,* 1935), buttercup, *Ranunculus bulbosus,* and mustard, *Sinapis arvensis* (Spillman and Weiss, 1931); bindweed, *Convolvulus arvensis* (Klaber, 1942); common rue, *Ruta graveolens* (Oppenheim, 1932); the allied fraxinella, *Dictamnus fraxinella* (Baronovysky, 1929), and gas-plant, *D. albus* (Cummer and Dexter, 1937); cow-parsnip, *Heracleum sphondylium,* and its cultivated relatives, *H. giganteum* (Straton, 1912) and *H. mantegazzianum* (Miescher and Burckhardt, 1937; Kuske, 1938); figs, *Ficus carica* (Straton, 1912; Legge, 1921; Kitchevatz, 1934c; Behcet *et al.,* 1939; Klaber, 1942); meadow grass, not identified specifically (Oppenheim, 1926; Hartmann and Briel, 1927; Corsi, 1933; Corson, 1935; Kitchevatz, 1936a); Persian or Tahitian lime (Sams, 1941); agrimony, *Agrimonia eupatoria* (O'Donovan, 1942).

It will be noticed that, although a considerable number of species are involved, they belong to a few families only: Umbelliferae (wild parsnip, cultivated parsnip, cow-parsnip, yarrow, angelica); Rutaceae (common rue, gas-plant, limes); Rosaceae (agrimony); Moraceae (figs); Ranunculaceae (buttercup); Cruciferae (mustard). The majority of these plants belong to the families Umbelliferae and Rutaceae.

## Geographical Distribution

Phyto-photo-dermatitis has a wide geographical distribution. Following on Oppenheim's first communication in Austria in 1926, cases were soon reported from Germany and France. In the latter country Jacowski collected seven cases from the airfield at Étampes and its neighbourhood. Five were French airmen who, between June 23 and 29, 1935, sunbathed or walked bare-legged in the grass. Two further cases were children belonging to French Air Force families living on the same station, exposed to the sunlight and grass at the same time. A number of other people so exposed were not affected (Jausion and Jacowski, 1936b). Cases were also reported from Italy, Yugoslavia, Russia, Switzerland, Denmark, Spain, and the United States of America.

From the time of Stowers (1897) no cases were recorded in Great Britain until Straton (1912) reported a case in Wiltshire following contact with figs. Corsi (1933) described the typical skin eruption in a student who indulged in sunbathing after a swim near Tunbridge Wells. McKinlay (1938) described several similar cases from Salisbury Plain, where, later, O'Donovan (1942) reported some dozen more. Until O'Donovan's cases occurred in the hot summer of 1940 no importance had been attached to the disease. Public interest at this time had been aroused to the dangers of noxious war gases, and the appearance of blisters on the skins of unsuspecting people—Service and civilian—gave concern to the local public authorities, who at first had the impression that the victims had come into contact with mustard gas. At that time I attended eight cases amongst Army personnel who were doing airfield guard duties in the heart of the Plain. These soldiers were undergoing intensive field training, stripped to the waist in the hot sunshine. They had thus come into contact with patches of cow-parsnip, which they used for concealment and cover. Within forty-eight hours the affected men's chests and bellies were covered with the characteristic striate, criss-cross weals and blisters. Whittle *et al.,* quoted above, have also mentioned some cases occurring in France in 1944 among A.T.S. girls peeling cultivated parsnips in bright sunshine. Klaber (1942) recorded two cases due to contact with wild parsnip in 1940, and another in 1941 in which bindweed appeared to be involved.

## Biochemical and Biophysical Aspects

The nature of the photosensitizing substance in these plants which causes the dermatitis has not yet been fully elucidated. Kitchevatz (1936a) showed that it is not chlorophyll, but that alcoholic extracts from figs had this property. Jausion and Jacowski (1936b) suggested that sweating as well as exposure to strong sunlight was required before

erythema and vesiculation followed an application of watery extract of grass. Obvious sweating was not found to be essential in the experiments detailed below. Following the production of bullae some forty-eight hours after the application of the undiluted juices of rue, wild parsnip, and figs in bright sunlight, Kuske (1938) began to investigate the photodynamic properties of a group of ketonic compounds known as furo-cumarins. Chemically pure compounds were obtained from oil of bergamot to produce bergapten, oxy-peucedoin from masterwort (*Peucedanum ostruthium*), and ficusin from figs, while others have been isolated from a number of essential oils as well as from dill and parsley. All these substances when applied to the skin in sunlight produced bullae or erythema after forty-eight hours, followed by prolonged pigmentation. It would be interesting if these complex ketones could be isolated from all the plants producing phyto-photo-dermatitis, but that is beyond the resources of most clinical workers in this field.

Jensen and Hansen (1939) have elucidated the biophysical aspects of the problem in a series of carefully conducted experiments. They showed that the active range of the solar spectrum required to produce the dermatitis lies between 320 and 366 millimicrons in the long-wavelength end of the ultra-violet section, with a less active band between 264 and 280 millimicrons. These findings probably account for the incidence of the disease at the height of summer, when these rays are able to penetrate the atmosphere, and also explain the failure of a number of workers to reproduce the photodynamic effects with ordinary artificial ultra-violet rays. Jensen and Hansen further demonstrated that irradiation of alcoholic extracts of wild parsnip did not render the extract active of itself. Individual susceptibility to the plant was found to be unlikely in that all the subjects tested gave similar results.

## Present Series

The cases occurred at a Royal Air Force station in Lincolnshire during the summer of 1947. Two different squads, with forty airmen in each, were sent by their physical-training instructors on a twelve-mile race—the first on July 15 and the second on the 16th. The first mile or two was across fields and then over an assault course thickly overgrown with wild parsley (*Anthriscus sylvestris*) and yarrow, while the remainder of the run was along roads where an occasional patch of cow-parsnip was found in an immature stage of growth. The race on both days was held in brilliant sunshine, and the airmen ran in short trousers, many without vests or stockings. On the morning of the 17th an airman who had taken part in the first run reported sick, complaining of intense irritation and weals on the legs the previous evening, some thirty-six hours after exposure. By the morning large blisters had developed. During the next two days twenty-three more airmen were found to be suffering from the same symptoms with varying degrees of severity. At the same time four officers' children and seven children from the married airmen's quarters, some of whom had been reported as having contracted chicken-pox, were found to be suffering from minor degrees of phyto-photo-dermatitis. Subsequent inquiries from the parents elicited the information that three of these children had been diagnosed as suffering from varicella in the same month a year previously, and that the skin eruption was identical with that of the present outbreak.

The clinical features of this series of cases were a sudden onset of itching or burning in areas of the skin exposed to the plants and sunlight simultaneously twenty-four to forty-eight hours previously. Within six hours of the onset long linear weals with a bordering zone of erythema appeared, followed in a few hours by bullae. The bullae varied in size from dew-drops to large wrinkled blisters 5 in. (12.5 cm.) in diameter. The blisters were surrounded by an areola of bright-red erythema ½ in. (1.25 cm.) wide, merging imperceptibly into the surrounding skin. The smaller bullae tended to be strung along straight weals like necklaces on a cushion, while the larger ones were oval or linear in shape and 4 to 10 in. (10 to 25 cm.) long. The largest blister completely encircled the left lower leg, and had a length of 5 in. above the ankle and a depth of 3 in. (7.5 cm.) Seven ounces (200 ml.) of straw-coloured fluid were removed by aspiration. The same airman also had numerous weals and smaller blisters on both legs, extending half-way up the thighs, and on the chest and abdomen down to the waistline. A pattern of scarlet stripes and long blisters criss-crossing one another, or with a tendency for several adjacent ones to run in parallel lines, was the characteristic picture. The skin between the lesions and the parts not exposed appeared to be normal. There was no associated conjunctivitis or rhinorrhoea. Seven severe cases required treatment in hospital, but within ten days the largest blisters had healed. Minor cases did not seem to be troubled for more than two or three days. A deep-purple pigmentation remained at the site of the lesions for the several weeks it was possible to keep most of the victims under observation. Four cases still showed faint but easily discernible pigmentation, faded to a violet hue, six months later.

Patch-tests were carried out on two hospital patients and two unaffected volunteers. The flowers, leaves, and stalks of wild parsley, yarrow, and cow-parsnip were applied to the arms; control areas were protected from sunlight by adhesive plaster and test areas were exposed to the sunlight. Only the wild parsley exposed to sunlight gave positive results to the flowers, leaves, and stalks in all four subjects. Erythema appeared in twenty-four hours, followed by small vesicles in forty-eight to seventy-two hours. The patches were left on for six hours, and the subjects under observation spent most of that time in bright sunlight. For the remainder of the time under observation they remained covered. The tests were repeated on four more volunteers in much the same manner, but the flowers, leaves, and stalks were only rubbed on to the normal skin. All four gave much stronger positive results with wild parsley than did those in the previous test on exposure to sunlight. This time, in one person, cow-parsnip produced erythema in seventy-two hours, followed in a few days by desquamation and faint residual pigmentation. Aqueous and alcoholic extracts of the same plants were then painted on the arms of four subjects, one arm exposed to sunlight and the other covered. All four again produced erythema followed by slight vesiculation with both extracts of the wild parsley but not with other plants. One of the volunteers on to whose skin the plants had been rubbed still, after eight months, has pigmentation of the areas which gave positive results with wild parsley.

The results obtained from these patch-tests seem to confirm the observation made in the field that wild parsley was the offending plant in this series of cases. It would also appear that the photo-sensitizing substance is present in alcoholic and watery extracts. Support is given to Jensen and Hansen's suggestion that phyto-photo-dermatitis is not due to individual susceptibility to the particular plants giving rise to it. The fact that yarrow and cow-parsnip, both of which have been found by other workers to possess photodynamic properties, did not produce any result, or in the latter case produced only a weak one, is difficult to explain. It suggests that the same species of plants may possess photodynamic properties in one location and not in another, or that they possess these properties at a certain stage of maturity or at different periods of the summer. Further work is required to solve these problems.

## Differential Diagnosis and Treatment

Since the effects of noxious gas warfare have become more widely known phyto-photo-dermatitis has more than once given rise to the belief that the patients have come into contact with mustard gas. It is, however, easily distinguished by the absence of erythema in the axillae and groins, of conjunctivitis, or of respiratory and other systemic symptoms. The blisters of phyto-photo-dermatitis, though sometimes very large, are wrinkled like the folds of a slack tent and not tense and dome-shaped as with mustard gas.

Phyto-photo-dermatitis is sometimes confused with varicella, especially when children have one or two small bullae on the hands and legs. The characteristic mixture of fresh lesions, crusting, and healing vesicles of varicella is absent, while the distribution of phyto-photo-dermatitis is on the exposed parts only.

Treatment consisted of aseptic aspiration of the large blisters and the application of sedative lotions such as calamine or calamine and lead, which tend to dry up the lesions. Liniment of calamine or zinc cream is useful in the late stages to keep the skin soothed yet supple.

## Summary

Thirty-six cases of phyto-photo-dermatitis are recorded. A further eight cases are noted.

Wild parsley (*Anthriscus sylvestris*) was found to be the plant responsible for the outbreak. This was confirmed by patch-tests.

The history, the geographical distribution, and the biochemical and biophysical factors of the disease are briefly discussed, along with the species of plants indicated as causing it.

Differential diagnosis and treatment are also mentioned.

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**Addendum.**—Since this article was prepared for publication three more cases have occurred on the same Royal Air Force station. Three aircraft apprentices, lying with rolled-up shirt-sleeves on the grass watching athletics on May 19, 1948, in bright sunshine, developed typical vesicles on the forearms on May 21. Investigation has not been completed in these cases.

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# THE PROGNOSIS AND TREATMENT OF SPRUE IN INDIA

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In a clinical survey of 600 cases of sprue during the last war it was noted that only 31% had reached complete remission of the disease before evacuation from India, and it was believed that the relapse rate in England was high. The object of this paper is to assess the prognosis and results of treatment in a further series of 62 cases treated by me in India in 1945–6 and followed up for a period of two years in England. Their fate may be representative of that of the 1,073 cases sent back to England between 1943 and 1946. The value of the methods of treatment used in these cases can now be judged in perspective: and since these cases are likely to be the last treated without folic acid they may provide a basis for assessing the results of folic acid or other treatment.

## Scheme of Treatment

Cases were treated on admission by diet alone or by diet with parenteral liver and other substances, according to the severity of the symptoms of relapse. Whenever possible, cases were treated by diet alone (Group 1). If diet failed and symptoms of relapse persisted, the patient was given for a preliminary period an "investigation diet," from which such therapeutic substances as liver were omitted (Group 2). With this diet the effect of parenteral liver, nicotinic acid, and riboflavin was assessed, particular attention being paid to clinical features such as weight, stools, and blood count, as well as to fat-balance, glucose tolerance, and, in 10 cases, nitrogen balance. Ten cases showed such severe signs of relapse that no preliminary control period was possible and parenteral therapy was begun immediately (Group 3).

This grouping demonstrated the value of dietetic treatment alone. Cases which responded satisfactorily were classified as mild sprue. Those which failed to respond to a trial of dietetic therapy, or were so ill on admission that it could not be considered, were given parenteral liver and classified as severe sprue. It was therefore justifiable to attribute any improvement that occurred in severe sprue as due to parenteral therapy and not to dietetic measures alone. At this stage various remedies were tried in order to obtain preliminary assessment of their potency and/or mode of action. It was intended to do further trials of apparently active substances alone under controlled conditions in an adequate number of cases, but this proved to be impracticable.

These observations form the basis of the brief remarks in this paper on the value of various therapeutic methods used. Further details may be found in the report on sprue submitted to G.H.Q. India (in press).