

Bulb dermatitis

Dermatological problems in the flower bulb industries

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The irritant and allergenic properties of the most important flower bulbs are described, as well as the clinical symptoms they cause. The tulip contains the allergen tulipalin A; sensitization and irritation are responsible for the development of tulip fingers. The same clinical picture can be caused by *Alliums* like the onion and garlic. The narcissus causes lily rash, a dermatitis rarely caused by sensitization. The hyacinth evokes itching in practically everyone: an irritant reaction caused by calcium oxalate crystals. Patch testing is complicated as the allergens are not all identified.

Key words: plants; bulbs; irritant contact dermatitis; allergic contact dermatitis; occupational; tulip; narcissus; hyacinth; garlic; onion. © Munksgaard, 1997.

Accepted for publication 18 March 1997

There are some 250 genera that contain bulbous plants. Many of these are not really important from a commercial point, as they are rare and only found in the wild. But within the available genera there are thousands of species of bulbs and cultivars (1, 2). Bulbous plants are divided in true bulbs, e.g., onions and daffodils, corms, e.g., *Crocus* and *Gladiolus*, rhizomes, e.g., *Iris*, and plants with tubers, e.g., dahlia.

The interest in and the introduction of bulbs in the western world dates back from the 16th century. The history of the tulip is in this aspect interesting. The introduction of the, at that time rare, *Tulipa* in Holland by Carolus Clusius 4 centuries ago, in 1593, was the start of an unforeseen development: the bulb trade. Nowadays the bulb and bulb-flower trade is an economically important part of the Dutch agriculture export. In 1993 about 2 billion bulbs and 800 million flowers stems are exported. The most important bulbs are the *Tulipa*, *Narcissus* and the *Hyacinthus*, others like lilies and the gladiolus are also important. Many other bulbs are grown: *Allium*, *Crocus*, *Muscari*, *Scilla*, etc., often referred to as "secondary crop" ("bijgoed").

For the cultivation of these bulbs, large amounts of pesticides are a necessity but recent, much stricter, environmental regulations will limit the use of these products.

In this review, the dermatological problems re-

lated to the most important crops will be discussed. The dermatological problems which we can expect are contact dermatitis, irritant as well as allergic, contact urticaria and pruritus. The problem is usually caused by the sap of the plant but some times by the pesticides. It should not be forgotten that these growers are often involved in the maintenance of their machinery and buildings. This will bring them into numerous contact situations that could cause dermatitis. A good history and sometimes an investigation at the work site, is a must for the detection of the cause.

Tulip

The *Tulipa*, belonging to the Liliaceae, is native to Southwest central Asia (2). Most cultivars seem to be derived from *Tulipa gesneriana* L. The tulips grown on a large scale in Holland nowadays came originally from Turkey and might have been already cultivars from *Tulipa gesneriana* L (3). The plants were brought in 1593 to the medical garden of the University in Leiden by Carolus Clusius. This was the start of an unforeseen rapidly expanding bulb trade. The number of cultivars at this moment is approximately 2500, according to the register of the Bulb Research Centre in the Netherlands.

Medical use of the plant is not known, yet it is mentioned in 1673 in a book on herbal medicine,

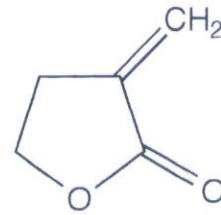


Fig. 1. Tulip fingers.

saying that it might be an aphrodisiac (4). Tulip bulbs have been used as food in Holland at the end of the Second World War.

Exposure

The tulip is known to cause dermatitis in many who work with these plants, most notorious are "tulip fingers" (Fig. 1). Tulip fingers were described in the twenties by Overton (5) and Schouten (6, 7). Contact dermatitis can be expected in those who have contact with plant sap and the hard skin of the bulb: the tecta. This will mainly be in professional growers and their personnel but it is also possible in those who handle flowers, like florists. Contact is extensive by handling the bulbs for peeling off the bulblets from the main bulb, by sorting bulbs and preparing them for shipping, and as far as this is done by hand, cutting or picking flowers and harvesting bulbs. In some specialised companies the bulbs are sometimes handled and prepared in a special way: the bottom part of the tecta is peeled off to promote an early and synchronised growth. Many of those who are involved in this work do so on temporary base as most of these activities are seasonal. The period for peeling is usual in the school holidays and so attracts temporary labourers. The phenomenon of tulip fingers is known to all of them. They know the cause and will only go to the doctor when they are severely affected. They just stop working. This means also that they are hardly seen by dermatologists. When the grower/owner of the farm is suffering of this type of eczema, the situation is different. If it is not possible for him to avoid extensive contact with tulip sap he may suffer at periods from severe hand eczema which will make work very difficult for him. Sometimes they decide to change crops.



Tulipalin A

Fig. 2. Tulipalin A: α -methylene- γ -butyrolactone.

Tulip fingers

The clinical picture of tulip fingers ranges from dry fissured, hyperkeratotic finger tips, pulpitis, paronychia and nail changes to an extensive eczema, sometimes with pustules of the fingers or the whole hand. Spreading of the eczema to the face, the neck, the arms or the ano-genital region does occur. The finger tip and dystrophic nail changes are characteristic; the hyperkeratotic and pustular lesions under the nail are painful. Often it starts with erythema, severe burning and itching. Contact urticaria and respiratory symptoms can occur also (8). There are few figures on the prevalence of eczema due to tulips. Bertwistle (9) noted that 85% of the workers at risk suffered of tulip fingers. Other figures in the literature are 5 out of 9 (56%) bulb handlers (9) and 8 out of 12 (67%) nursery workers who were affected (11) and Van der Werff (12) estimates this as 40%. Our own investigations among 103 growers indicated that 14% had skin complaints (13). Hjorth (14) considered the % of tulip sensitivity in Denmark as 4%. Such figures are not reliable as many affected persons do not visit a doctor.

Tulipalin A

Originally it was thought that this dermatitis was caused by mechanical traumata by the skin of the bulb. The brown outer layer of the bulb, the tecta, is dry and hard. It is not unlikely that indeed small particles of tecta cause skin damage, especially under the nails. The effect will be stronger in combination with sap from the plant. The tulip does not contain significant amounts of calcium oxalate crystals, which are responsible for skin complaints from some other bulbs.

The sap of the tulip contains an allergen: tulipalin A (Fig. 2). This allergen was found responsible for tulip fingers by Verspyck Mijnsen (15). Important work was done by the chemists who isolated and determinate the structure of this allergen (16, 17). The bulb contains several glucosides of

which tuliposide A and B are the most interesting. The tuliposides hydrolyse easily to tulipalin A and B (16, 17). Tulipalin A is the main if not the only sensitizer in man but tulipalin B seems to have a weakly sensitising capacity also (15, 18). The extraction of the allergen can be done in different ways. The method described in refs (19–21) yields tuliposides. The method with ether described by Verspyck Mijnsen (15) and Beijersbergen (22) gives an extract containing tulipalin A. This allergen is stable in a slightly acid environment if the concentration is not too high. Such an extract with tulipalin A (0.1%) in vials, more than 6 years old, still contained 60% of the allergen. The material is to date suitable for patch-test purposes (23). A related chemical 3-methyl-2-oxotetrahydrofuran (α -methyl- γ -butyrolactone) was also isolated in these vials, it is a non-sensitising degradation product. Tulipalin A is found throughout the whole plant but especially high amounts are present in the bulbs and the pistils (22, 24, 25). The corresponding tuliposide A could very well cause allergic reactions because it rapidly hydrolyses to tulipalin A (22, 26).

Not all tulips cause the same amount of problems; in the literature, some varieties, Preludium, Rose Copeland, Clara Butt, Le Nôtre are indicated as more problematic (7, 9, 12). The history of the patient is probably not very reliable on this point. Investigations with patch tests and even better tulipalin A quantification in several varieties, showed differences but these are small (11, 15, 24). One wonders if a patient could notice the differences, once sensitized. The cultivar "Apeldoorn" is often recommended for making extracts.

Tulipalin A also occurs in *Erythronium* (dog tooth violet, fawn-lily), a pretty little flower bulb belonging to the Liliaceae (24, 27). Furthermore, it is found in the economically much more important *Alstroemeria* spp (Peruvian lily) (24). They belong to the Alstroemeriaceae, a genus formerly classified with the Amaryllidaceae (28). This plant causes the same complaints as the tulip (26, 29, 30, 33). The growers of these plants and the florists are exposed to the allergen by cutting the flowers and stripping the leaves.

Prevention

The prevention of tulip fingers can be very difficult if the work with the tulip bulb is not done very carefully. Opinions differ on latex gloves giving any protection. According to Marks (33) the allergen penetrates polyvinyl but not nitrile gloves; experiments with latex and neoprene gloves showed that it penetrates at least to some of these materials. Nitril and 4H® gloves give the best protection (33,

34). Although, in practice patients mention that depending on how hygienically they work and treat the gloves, ordinary rubber fingers and household gloves do give protection and can prevent skin complaints. The allergen can also be found in dust collected from workplaces and can even cause airborne contact dermatitis (24).

Patch tests

Patch tests can be performed with parts of the tulip or the *Alstroemeria*. There is a slight risk that patients become sensitised in this way; irritant reactions can occur (26). It is possible to make one's own extracts, but it is easier to obtain α -methylene- γ -butyrolactone from a chemical company (e.g., Sigma) (15, 20, 26). The test concentration is 0.01%, but it might be better to start with 0.001% in water. The undiluted product supplied by Sigma contains 2% of 2,6-di-tertiary-butyl-para-cresol; hence, a control test with this material is advisable. Currently, the allergen is available commercially as a patch test substance. Patch-test reactions may give depigmentation (35). Contact allergy to tulipalin A is very long lasting (12, 36); in one person a positive reaction was obtained about 30 years after he last had contact with tulips (13).

Narcissus

Most cultivated daffodils or narcissus stem from *Narcissus pseudonarcissus* L. They belong to the family of the Amaryllidaceae. The narcissus is native to Europe, mainly the Mediterranean region, north Africa, Southwest Asia and cultivated in many other parts of the world. Narcissus have been grown as garden plants since the Middle Ages. There are many varieties, the main cultivars are derived from *N. pseudonarcissus* L. (wild daffodil), *N. jonquilla* L. (jonquil), *N. poeticus* L. (pheasant's eye), *N. tazetta* L. (tazetta) and *N. triandrus* L. (angel's tears). The flowers have a strong scent.

For the flower trade in wintertime, narcissus are grown in greenhouses. Oil derived from *N. jonquilla* L., Jonquil oil, sometimes seems to be used in the fragrance industry (37). The plant is used in Chinese folk medicine and homeopathy; it has an emetic effect among many other properties (38).

Exposure

During the growth period, the bulbs form small bulbs which are attached to the main bulb. The stem of the plant is hollow and contains large quantities of mucus. This mucus and the sap from the bulbs contain calcium oxalate crystals, which

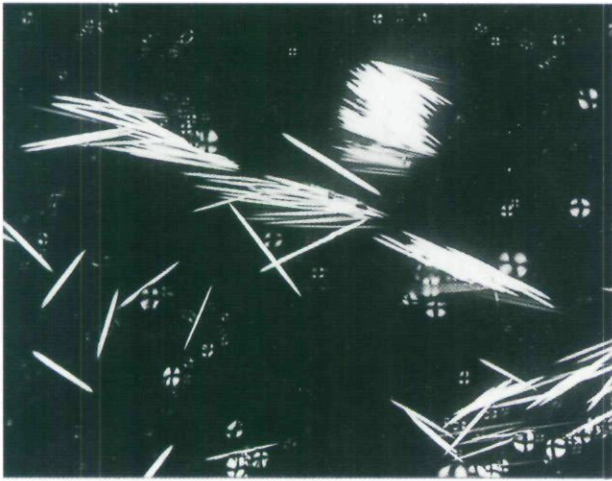


Fig. 3. Needle-shaped calcium oxalate crystals; a bundle of needles is falling apart.

can be rhomboid or needle-shaped (6, 7, 39) (Fig. 3).

Growers come into close contact with the plant by picking flowers and handling bulbs during harvesting, peeling, selecting and preparing bulbs for the trade. Contact with the sap or mucus of the plant will be most intensive by picking the flowers. Florists may have contact with the cut flowers but usually the flowers are already bunched when they arrive from the auction floor.

Lily rash

Dermatological problems caused by narcissus were described, as early as 1910, by Walsh (40), among lily-pickers in the Scilly islands: "daffodil itch" or "lily rash". In the spring of 1910, Walsh went to the Scilly islands to investigate a dermatitis that attacked both those who picked and those who packed daffodils. The description by Walsh (40) is very exact and is comparable with recent experience (13). The rash or eczema is seen in places where sap from the plant is in contact with the skin. This will usually be the hands and the arms and regions touched by the hands like the face and the anogenital area, and sometimes the legs, depending on the efficiency of the protection of the trousers. The clinical picture is usually mild: erythema, papules, partly urticarial, but it may become more eczema-like with vesicles and even pustules. Sometimes, it becomes more chronic and in rare instances generalised (12). Lüders (41) describes eczema with rhagades on the first and second finger in gardeners who cut the foliage when harvesting the bulbs. A clinical picture like in tulip fingers is also seen. On abraded skin and in wet conditions, the skin reaction is more severe. Palmer

(42) made the same observations, and noticed that there is a great variety in individual susceptibility. He suspected, based on positive skin tests with pollen and extracts of daffodil leaves, that the eczema was caused by sensitisation.

In a recent survey, practically all narcissus growers admitted to experience lily rash to a certain extent (13). About 50% had considerable skin complaints. The complaints were usually of short duration. Some growers had urethritis-like symptoms. The most severe dermatitis reactions were seen in damaged skin. Wound healing is said to be delayed. Hardening of the skin has been observed (12, 40, 43). Generally the dermatitis disappears at the end of the season.

Flushing of the face is mentioned by Palmer (42). Walsh (40) noticed that some workers experienced eye irritation and headache from the scent of the flowers. It is not clear whether the eye and nose irritation are caused by narcissus pollen, and what the rôle of the scent is. Gonçalo (44) described a patient with skin symptoms and conjunctivitis, stiffness of the nose and dyspnea by narcissus flowers. The patient tolerated handling of bulbs well (44). Patients with mucosal symptoms are also described by Van der Werff (12).

The urticarial properties of narcissus sap have been experimentally proven by Lahti (8) in an animal model for contact urticaria.

According to the literature, growers think that some cultivars are more irritant than others, the cultivars *Camponella*, *Ornatus*, *Gloriosa*, *Scilly White*, *Grand Monarque*, *Actaea* and *Princeps*, the *Poetas*-group, being the worst (12, 30, 40). The growers interviewed by us had never noticed a difference in irritant potential (13).

Pathogenesis

The compounds responsible for the irritation are not really known, but alkaloids are thought to be involved. More than 15 alkaloids have been isolated; some of these have skin-irritant properties (43). 4 groups of alkaloids have been isolated, which seem characteristic for *Amaryllidaceae*: galanthamin, homolycorin, lycorin and tazettin. Lycorin is quoted as having cytostatic properties (41, 43). It is most likely that the calcium oxalate crystals are important in the irritation by evoking micro-trauma to the skin and facilitating the penetration of other irritant substances like alkaloids (5, 37, 41). The sap of the narcissus bulb is rather irritant as was shown with patch tests in volunteers (41). Probably over 90% of the dermatitis cases reported in the literature are not allergic, but of irritant origin; contact allergy to narcissus is rare (43). The allergens are not exactly known. Gude et al.

(43) isolated several compounds which showed allergenic properties in guinea pigs. Ether extract of the bulbs of *N. pseudonarcissus* L. contained 2 sensitizing alkaloids, homolycorin and masonin. They were classified as weak sensitizers. The stem and leaves did not contain these alkaloids. They therefore conclude that it is understandable that sensitization will take place in those who handle bulbs rather than flowers. Homolycorin had already been isolated from *Leucojum vernum* L. (spring snowflake) and *N. poeticus* L. in 1954, and masonin from *N. jonquilla* L. and *Nerine masonorum* L., all belonging to the Amaryllidaceae (43). An interesting finding is reported by Bleumink & Nater, they described a gardener who developed contact eczema from daffodils (45). Positive patch-tests were obtained with leaves and flower extracts, but also with extracts of snowdrop leaves, *Galanthus nivalis* L., also belonging to the Amaryllidaceae. Gonçalo et al. (44) also had positive test reactions with a (different) extract in their patient. This suggests that there might be more allergens involved and that there could be a species difference (12, 13).

Patch tests

Patch testing is possible with leaves and other parts of the plant, but the results have to be interpreted very cautiously as irritant reactions are likely to occur. Hausen (37) advises to use extracts or the alkaloids, but because of their irritancy, only in diluted form: short-ether extracts 1% and alkaloids 0.1%, both in pet. It is very important to perform tests in controls.

Hyacinth

The hyacinth originates from the eastern part of the Mediterranean, but is widely distributed as cultivated plant and is extensively grown in Holland where it was introduced in 1562. It is not exactly sure from which wild species most contemporary cultivars stem, but probably from *Hyacinthus orientalis* L. (Liliaceae). There are many cultivars. Oil from the hyacinth is used in the fragrance industry and has caused allergic contact dermatitis (46, 47).

Exposure

The brown outer layer, the tecta, is just as in the tulip a dead and hard skin which is formed in the last weeks of the growth. In the tulip, the tecta is only one layer thick in contrast to the hyacinth where it is composed of several, loose, layers (12, 15). The broken particles of the tecta may cause

damage to the human skin. The bulb contains high amounts of calcium oxalate crystals (6%) (7). These needle-like crystals do not dissolve in water but in weak acid solutions, hence such solutions were recommended for cleaning the skin to prevent severe hyacinth-itch. In the plant-cell, the crystals form bundles and are encapsulated by mucus: raphides. When these cells are damaged, the raphides are released and fall apart in separate crystals (Fig. 3). It is assumed that due to the mechanical microtrauma evoked by crystals, skin irritation and itching are elicited.

By handling the bulbs the tecta is effortlessly damaged resulting in numerous small, sharp particles and the release of calcium oxalate crystals. The particles will become mixed with dust and readily become airborne, resulting in spreading to other regions than the hands. In the end, it will also be found on covered skin. This extensive contact will especially take place by sorting and packing up bulbs.

Hyacinth itch

Skin irritation caused by handling hyacinth bulbs was discussed by Freeman (48). He refers to Henslow and Morris who already explained this condition as due to oxalate crystals adhering to the scales of bulbs penetrating the skin. He also put forward the possible rôle of a parasite, found on the bulbs, resembling scabies mites. In Dutch, the condition is some times called "bulbscabies" ("bolleschurft") (6). The theory of mite infestation has been abandoned. Eczematous eruptions in persons sorting hyacinth bulbs were described by Laporte in 1903 (49).

Hyacinth itch is known to all who work with these bulbs, nearly everyone experiences the itching but there are large individual differences (12). The phenomenon of hardening seems to occur. Schouten (6) mentions that about 10% have no complaints. In a recent survey, 27 out of 103 bulb growers experienced severe pruritus, 4 probably had real eczema, while only a few had hardly any complaints (13). Care in working with these bulbs together with hygienic measures are indicated as important factors to decrease the severity of the complaints. In the literature, it is mentioned that some cultivars cause more inconvenience: Marconi, Carnegie, City of Harlem and most of all Innocence (12). In our own investigation, none of the growers made such a distinction (13).

Clinical picture

Dry circumstances, in combination with a humid skin, by perspiring, favours the complaints: the air-

borne material will easily stick to the skin. Places where clothing grates on to the skin are often involved. The complaints are usually itching with urticarial lesions, associated in some cases with papules and vesicles. Sites of predilection are the volar side of the forearms, the face, the thighs and inguinal and ano-genital region (12). As a rule, work can be continued.

The itching disappears when the crystals are removed from the skin. Showering can have a favourable effect, although Schouten (6) did not see much effect of washing with water and soap but advised diluted acid. A good ventilation system and vacuum-cleaning are important in the prevention of hyacinth itch; wetting of the bulbs, before handling, can also be helpful. When working with hyacinth bulbs, contact with the face, arms and the neck has to be avoided.

Eczema and hyperkeratosis and fissuring of the finger tips, as in tulip fingers, is seen also. In very sporadic cases, hyacinths seem to cause bronchial asthma (12). Cases of possible allergic contact dermatitis from hyacinths have been sporadically described in the literature; most publications are on irritant contact dermatitis (50, 51). According to Van der Werff (12) approximately 1 in 60 growers develops allergic contact dermatitis.

Patch test

Patch tests with plant material can be difficult to interpret because of irritant properties. There were no positive patch-test reactions to hyacinth extract in our recent survey (13). To date no allergen has been isolated and identified. Compounds like phenylacetaldehyde, benzyl benzoate, cinnamic alcohol, benzyl alcohol, and eugenol might be involved as they are all found in hyacinth oil (37).

Alliaceae

The Alliaceae are an interesting group. The most important genus is *Allium*, including garlic (*Allium sativa* L.), chives (*A. schoenoprasum* L.) and the onion (*A. cepa* L.). All kinds of cultivars are grown world-wide and used in the kitchen and the garden, but garlic, e.g., is also important in folk medicine. Many bulbs of this genus contain irritant sulphur compounds like benzyl- and isothiocyanates. Although growers sometimes do have skin complaints, usually this happens in cooks, housewives and others involved in the food industries, as they are most exposed to the sap of these plants. Typical is dermatitis of the fingertips of the 1st 3 fingers of the non-dominant hand, the hand holding the vegetable for cutting. The clinical picture can be exactly the same as seen in tulip fingers. The

lesions may be less characteristic and may spread, sometimes even resembling psoriasis (39).

The possible irritants and allergens are not all isolated and identified, nor are they probably the same in all *Alliums*. A problem is that some of the allergens are irritants as well, complicating patch testing. The allergens in the onion are not yet identified, but suspect are alliin and propanthiol-S-oxide (37).

Tuliposide A has been thought to be involved but this is not supported by more recent reports (24, 37, 52). Allergic contact eczema by onions seems to be not common; most publications indicate an irritant origin. Patch tests can be performed with a water, ethanol, or an ether extract. Tests can be done with the sap of the bulb, but careful interpretation is necessary. Major allergens in garlic are diallyldisulfide, allylpropyldisulfide and allicin (37, 39). Cross-reactions between garlic and onions have been noticed, but this does not seem to happen all the time (39, 52, 53). If diallyldisulfide is not readily available as test material, patch tests with extracts are indicated, as for onions. The method of Cronin (54) using juice of onion and garlic diluted to 50% in arachis oil, might be the most practical way of proceeding. Mitchell (55) is in doubt as to whether it is useful to do patch tests with these irritant substances.

Immediate-type reactions to garlic, chives and onion are sometimes noticed (37, 56–58).

Other Bulbs

There are many more bulbs grown but not to such an extent as those described above. Skin complaints can of course also happen with all the other bulbs; usually irritation is involved. Occasionally, cases are described of patients with complaints in relation to other bulbous plants, e.g., *Iris*, *Ranunculaceae*, *Scilla*, and *Ornithogalum* (59, 60), but the importance is probably, apart from for the individual patient, not so great. Most valid information can be found in the encyclopaedic work of Mitchell & Rook (28).

Other Contactants

Although not really belonging to this subject, contact eczema due to other sources in bulb growers should be considered. They have many contacts with irritants and potential allergens, e.g., pesticides. Large amounts of pesticides are used in the bulb industry, and contact can be rather intensive, dependent on the way they are used. Patch testing with plant parts such as leaves may be complicated by pesticide residues on these parts. Control tests with unsprayed plants can be necessary. Tests with extracts or the allergens can solve these problems.

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