Contact Dermatitis in California Nursery Workers:
Part II. Pilot Field Study

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Abstract

Among the subgroups of agricultural workers, nursery workers have previously been identified as a group at high risk for occupational skin disease. Review of available surveillance information on nursery skin illnesses has also demonstrated that provocation patch testing is performed in less than 1% of the reported cases. We tested reactions to a battery of pesticides, plants, and the standard European patch antigens among a sample of nursery workers. From a pool of 896 workers' compensation records (441 skin and 455 non-skin (eye, systemic/respiratory or musculoskeletal)) injuries or illnesses, 467 (52.1%) were contacted by mail and 349 (38.9%) had valid addresses or phone numbers. Of this group 29 workers (8.3%) agreed to participate. Eleven additional subjects were identified from among their coworkers, and one agricultural extension specialist who worked extensively in the nursery industry also participated. Demographically participants and non-participants were similar, but we could not ascertain whether they were similar or dissimilar with regard to history of skin disease. In the 39 subjects who underwent testing to the complete battery of plant, pesticide, and standard series antigens, we observed reactions to one or more test substances in 18 (46.2%). This included 8 subjects (20.5%) reacting to either nickel, chromium, fragrance mix, wool, or thiuram (an ingredient in many rubber formulations that is also used as a fungicide) in the standard environmental antigen series, 5 (12.2%) reacting to either carnations or primrose in the plant series, and 10 (25.6%) reacting to either sulfur, PCNB, captafol, difolatan or chlorpyrifos in the pesticide series. Reactions to pesticides and to sulfur, in particular, appeared to be correlated with a history of mixing, loading, or applying pesticides. Because the study was hampered by a low participation rate, the findings can not appropriately be generalized to the entire population of interest. However, the reactions to sulfur, PCNB, chlorpyrifos, and to carnation extracts were unexpected based upon prior published literature and deserve additional study.

Among the subgroups of California agricultural workers, nursery workers have previously been identified as a group at high risk for occupational skin disease (O'Malley and Mathias, 1988). This report describes the results of a pilot study to evaluate the proportion of cases due to delayed hypersensitivity reactions among nursery workers and the specific agents most frequently responsible. A preliminary report describing the novel pesticide patch tests developed for this project has been published previously. (O'Malley, Rodriguez, and Maibach, 1995).

Methods

Case review - Potential cases were identified from the Doctor's First Reports (DFRs) filed with the California Department of Industrial Relations (CDIR) as part of routine data collection by the Pesticide Illness Surveillance Program (PISP) operated by the California Environmental Protection Agency, Department of Pesticide Regulation (DPR) between 1989 and 1992. Although the DPR surveillance program focuses on pesticide-related illnesses, all nursery illness DFRs are collected at CDIR. Those not relevant to pesticide exposures are routinely discarded at a later date. For purposes of this study all nursery illness DFRs collected between 1990 and 1992 were reviewed to evaluate the occurrence of contact dermatitis in nursery workers according to the 9th revision of the International Classification of Diseases (ICD9).

Skin-cases were defined as subjects with one or more skin diagnoses including contact dermatitis - plants (ICD 692.6), dermatitis due to unspecified causes (ICD 692.9), contact dermatitis due to chemicals (ICD 692.4), urticaria (ICD 708.9), tinea (ICD 110) and numerous miscellaneous skin diagnoses. **Non-skin cases** were defined as subjects with eye injuries or systemic/respiratory illnesses. ICDs for **eye injuries** included conjunctivitis without specified cause (ICD 372), chemical conjunctivitis (ICD 372.05), foreign bodies in the eye (ICD 930.9), corneal abrasions (ICD 918.3), keratitis (ICD - 370.9), corneal ulcers (ICD 370.03), eye contusions (ICD 921.3), pterygium (ICD 372.4), and iritis (ICD 364.3). For **systemic/respiratory illnesses**, ICDs included exposures to pesticides (ICD 989.4, ICD 989.3), exposures to fertilizers (ICD 989.8), and hay fever (ICD 477.5). Other diagnoses included chest pain, pharyngitis, asthma, abdominal pain, epistaxis, and gastroenteritis.

Case contacts - Cases were contacted by mail at the address listed on the DFR to solicit participation in a follow-up study. Additional contacts were made by telephone where possible. However, no attempt was made to contact cases received after active field work began and no attempt was made to contact the scattered cases missed during initial sorting. For 1989, only pesticide illness cases were available, because non-pesticide cases had been discarded prior to initiation of the project. Because of the limited number of subjects who agreed to the dermal patch testing and questionnaire following the initial contact, co-workers of cases contacted by mail were also enrolled in the follow-up study.

Patch test techniques and patch test selection

Patch testing of study subjects was conducted at regional sites in the counties of Butte, Humboldt, Los Angeles, Monterey, Orange, San Diego, San Francisco, San Mateo, and Ventura between June and November, 1992. All patch test materials were applied to subjects using a Finn Chamber dosed with approximately 30 μl of test solution, measured with a volumetric pipette, applied to the upper back, secured with paper tape, and read at 48 and 96 hours. The International Contact Dermatitis Research Group (ICDRG) system (Adams, 1990) was utilized for the readings. Briefly, reactions were scored as 1+ (weak reaction, macular erythema), 2+ (strong reaction, edematous or vesicular), or 3+ (extreme reaction, spreading, bulbous, ulcerative). Equivocal reactions were designated as 0.5+ or +/-.

Pesticides for patch testing were selected from an analysis of nursery dermatitis cases reported to PISP from 1982-1989 (O'Malley, Rodriguez, and Maibach, 1995). Compounds with at least 10 reported cases were included in the patch test battery, excluding the compound propargite, known to be an extremely potent irritant. Two frequently reported compounds, dodemorph and metalaxyl, were not tested because no source of technical material was available. All materials were formulated in butanol at 1% concentration except chlorothalonil (formulated at 0.01%), malathion (0.5%), and fenbutatin-oxide (0.1%).

Three additional materials were tested that were not on the list of materials most frequently reported in nursery workers. Inorganic sulfur was tested because of its frequent use as a fungicide/miticide on ornamental nursery crops and its overall frequency as a reported source of skin disease in California agricultural workers (O'Malley, Mathias, and Coye, 1989). Two additional nursery fungicides, dichloronitroaniline (DCNA) and pentachloronitrobenzene (PCNB), were also included because of their structural similarity to other nitrobenzene sensitizers. Additional pesticides tested included those in the European Patch Test series (TroLab antigens, obtained from the Pharmascience company of Toronto, Canada) - captan, folpet, zineb, maneb, pyrethrum, benomyl, and ziram.

Plant materials associated with nursery dermatitis were analyzed from cases reported to PISP from 1982-1989.[a] Plant antigens were selected from this list, if available. Test material from the European patch test series included primin (the antigen from *Primula obconica*), geraniol, and eucalyptus. Material kindly supplied by Doctor B.M. Hausen of the University of Hamburg included carnation, primin, chrysanthemum, ivy, sunflower, tulips and daffodils. Plant exposures for which no antigens could be identified included poinsettias, azaleas and redwood. Sunflowers and *Anthemis cotula* (Mayweed) were not reported in the PISP series, but were included in the patch test series because of their availability in the Hausen series (Table 1).

Results

Preliminary testing for new patch materials

The initial phase of the study involved preliminary testing for novel patch test materials with 21 volunteers at a dermatology research foundation affiliated with UC San Francisco. The novel materials tested included acephate, chlorothalonil, DCNA (dichloronitroaniline), diazinon, dienochlor, chlorpyrifos, fenbutatin oxide, malathion, permethrin, fluvalinate, vinclozolin, pentachloronitrobenzene, and inorganic sulfur. This test group differed substantially in demographics from the nursery study subjects as described below (see section on *Demographics of study population*).

The initial testing demonstrated 1-2+ reactions to 0.01% chlorothalonil in 4/10 subjects. In the remaining 11 subjects, no reactions were seen to 0.001% chlorothalonil; 1 control subject who reacted to chlorothalonil also had a 1+ reaction to sulfur at 1%. No other tests were positive. The 0.001% concentration of chlorothalonil was used for all subsequent testing conducted. Concentrations of other test materials were not altered.

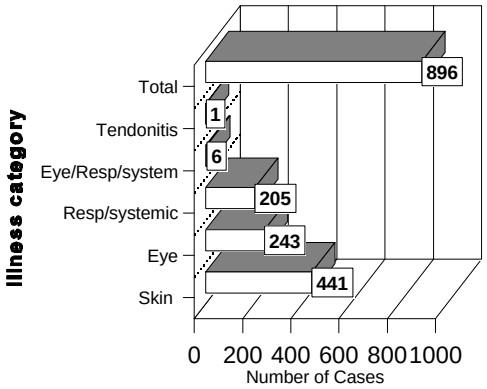

Figure 1 - Distribution of Doctor's First Reports (DFRs) reviewed by category of illness

Skin DFRs

Four hundred forty-one cases of skin disease were reported in the study period including 55 cases in 1989, 127 in 1990, 122 in 1991, and 137 in 1992. The cases in 1989 were confined to reports of suspected pesticide illness or injury, since non-pesticide illnesses were not collected for that year. By demographics, 275 (62.4%) were male, and 398 (90.2%) had Hispanic surnames. The mean age was 33.9 years old. The most frequent diagnoses included contact dermatitis - plants (ICD 692.6 - 141 cases - 32.0%), dermatitis due to unspecified causes (ICD 692.9 - 134 cases -

[a] There were 295 nursery cases reported to PISP 1982-1989; the specific plant involved was not specified in 147. The most frequently reported among the remaining 148 included: roses (27[18.2%]), carnations (26 [17.6%]), chrysanthemums (14 [4.7%]), poinsettia (14[4.7%]), mushroom (13 [8.8%]), geranium (7[4.7%]), alstroemeria (3[2.0%]), and lily or lily bulbs (3[2.0%)] . Plants in the European series or Hausen series for which only single cases were identified included eucalyptus, ivy and daffodils.

30.4%), contact dermatitis due to chemicals (ICD 692.4 - 98 cases - 22.2%), urticaria (ICD 708.9 - 26 cases - 5.5%), and tinea (ICD 110 - 16 cases - 2.5 % of the total). Miscellaneous skin diagnoses represented by more than one case included cellulitis of the hands, skin burns, skin callouses, lacerations of the hand, dyshidrosis, and porphyria cutanea tarda. Other conditions represented by only single cases include non-traumatic skin blisters, insect bites, thumb wounds, scabies, zoster, measles, seborrhea, folliculitis, photo contact dermatitis, and heat rash.

Non-Skin DFRs

In addition to the DFRs involving dermatitis described above, the patch test study included comparison subjects selected from 455 workers with non-skin injuries or illnesses. The 249 workers with eye injuries included subjects with (in order of descending frequency) conjunctivitis (ICD 372.0 or 372.05), corneal or conjunctival foreign bodies (ICD 930.9), corneal abrasions (ICD 918.3), keratitis (ICD 370.9), corneal ulcers (ICD 370.03), ocular contusions (ICD 921.3), pterygium (ICD 372.4), and iritis (ICD 364.3). The 205 workers with isolated systemic or respiratory illnesses included subjects with exposure to pesticides and fertilizers (ICDs 989.4, 989.3 and 989.8), hay fever (ICD 477.5), chest pain (ICD 786.5), pharyngitis (ICD 462.0), asthma (ICD 493.9), abdominal pain (ICD 799.0), epistaxis (ICD 787.4), and gastroenteritis (ICD 558.9). Six cases had combined eye injuries and systemic/respiratory illnesses. One of the non-skin DFRs had tendinitis (ICD 726.9).

Demographics of study population

Combining the skin and non-skin groups, a total of 896 DFRs involving nursery workers were reviewed by DPR during the study period, including 132 (14.7%) in 1989, 239 (26.7%) in 1990, 270 (30.1%) in 1991, and 255 (28.4%) in 1992. Skin illnesses and injuries accounted for 441 (49.1%) and non-skin illnesses and injuries for 455 (50.8%) of the reports.

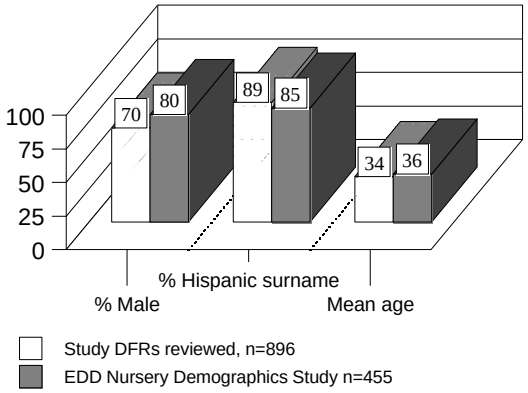

Figure 2 - Demographics of study DFRs versus California Employment Development Department's nursery demographic study

The DFRs reviewed involved 864 separate individuals employed in 327 separate enterprises located in 44 different counties. The 11 counties with the most frequent claims - San Diego, San Mateo, Monterey, Los Angeles, Humboldt, Orange, Santa Cruz, Santa Barbara, Ventura, Sonoma and Sacramento - accounted for 78.0% of the reports. The 40 businesses associated with 5 or more cases accounted for 54.4% of the reports. Analysis of demographic variables showed that 601 (69.6%) of the 864 affected workers were male and 771 (89.2%) had Hispanic surnames. The 832 workers with a reported age or birth date had an average age of 34.1 years. The study population thus had a demographic profile similar to that reported in a study published by the California Employment Development Department (EDD) in 1992.[b]

[b] Demographic survey information published by California Employment Development Department (California Agricultural Studies 92-3, California Nursery Workers and the Nursery Industry) indicate that the industry employs 30,000 workers annually, employed by 1,226 separate businesses. The industry is spread throughout the state, but businesses in Los Angeles, San Diego, San Mateo, Orange, Ventura, Monterey, Santa Barbara, Santa Cruz, Santa Clara, and Alameda counties account for 66.9% of the statewide employment. In the survey interviews, approximately 85% of the workers reported being born in Mexico; no identification was made specifically on percentage with Hispanic surname. Of the workers surveyed, 80% were male, and the average age was 36 years old. About 10% of the workers reported working seasonally, the remainder working full time - an average of 46 hours/week.

Pesticide vs. non-pesticide illnesses

The DFRs reviewed included 464 (51.8%) associated with pesticide exposures. Lost-work-time information available for 417 (89.9%) of the pesticide cases, indicated that 86 (20.7%) had one or more days of disability. The reports reviewed also included 432 reports (48.2%) involving non-pesticidal illnesses and injuries (principally exposures to plants or non-pesticidal nursery chemicals). No lost work time information was available on these cases.

Contacts with study subjects and study participation

Of the 896 DFR's received and reviewed during the study period, 491 (54.8%) were contacted by mail; the remaining cases were received after active field work began or missed during initial sorting of cases. One hundred eleven (25.5%) were sent only one letter because the address identified from the DFR proved to be invalid and no valid phone number was identified. Of the remaining 380 workers, 29 (7.6%) agreed to participate in the study, including one subject who completed the study questionnaire but did not participate in the patch testing. Eleven coworkers of the DFR subjects were also recruited for the study (non-DFR patch subjects). One additional participating subject was an agricultural extension agent involved in the nursery industry (tested only to chlorothalonil because of a history of a prior reaction to that compound).

Demographic characteristics of participants (DFR patch subjects), non-participants, and non-DFR patch subjects

The 29 subjects identified from DFR's (DFR patch subjects) differed somewhat from non-participating DFR subjects with respect to ethnicity and gender. Twenty-two (75.9%) of the DFR patch subjects had Hispanic surnames compared to 774 (89.3%) of the 867 non-participating DFR subjects (p=0.034 by Fisher's exact test). Fifteen (51.7%) were men, compared to 625 (68.1%) of the 867 non-participating subjects (p=0.05 by Yates' corrected chi-square). The DFR study subjects had a mean age of 36.4 years compared to 34.1 for non-participating DFR subjects (p>0.05 by Student's t-test). The proportion of skin DFR's among the participants was 48.3% compared to 49.8% in the non-participants (p>0.05).

The 12 non-DFR patch subjects had demographic characteristics similar to those of the 29 DFR patch subjects. Their mean age was 36.4 years; 7 (58.3%) were male; 10 (83.3%) had Hispanic surnames. None of the differences between the DFR patch subjects and non-DFR patch subjects achieved statistical significance.

When both non-DFR and DFR subjects were included in the analysis, the patch test group as a whole still differed from the non-participating DFR subjects with respect to gender (22 [53.7%] were male compared to 70.4% of the non-participants)) and with respect to ethnicity (32 [78.5%] vs 89.3% of the non-participants) had Hispanic surnames), but not with respect to age (mean age=36.5 years vs. 34.1 years for the non-participants.

The diagnoses recorded for the 29 DFR patch test subjects resembled those recorded for the non-patch test DFR study subjects (n=868), including **14 cases of skin disease** (Contact dermatitis [CD], chemicals 692.400 - 1, CD, plants 692.600 - 4, CD, non-specified cause 692.900 - 8, and finger/thumb cellulitis 681.000 - 1), **8 eye injuries** (Conjunctivitis, not specified 372.000- 5, Chemical conjunctivitis - 372.050-1, Corneal Abrasion - 918.300 - 1, Foreign Body, Eye - 930.900 - 1) and **7 case of systemic/respiratory illness** (Otitis Media - 382.900 - 1, Hay Fever - 477.900 -1, Asthma - 493.900 - 1, Epistaxis -784.700/Pesticide exposure, not

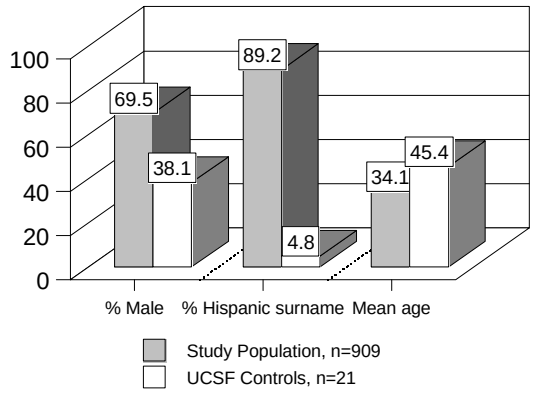

Figure 3 - demographic characteristics of study population versus UCSF controls

elsewhere classified [PestNEC] - 989.400 - 1, OP/Carbamate exposure - 989.300 -1, PestNEC - 989.400 - 1, Viral Syndrome - 999.500/PestNEC - 989.400 - 1).

All study subjects versus UCSF controls

The entire study group (n = 908, including coworkers of the DFR patch subjects) differed from the UCSF control subjects (n=21) in several respects. One (4.8%) of the UCSF volunteers had a Hispanic surname compared to 807 (88.8%) of the study group. Eight (38.1%) were male, compared to 632 (69.5%) of the nursery workers. The mean age of the UCSF volunteers was 45.4 years compared to 34.2 for all 908 nursery study subjects. These differences were all highly statistically significant (by Fisher's exact test, chi-square, or Student's t-test).

Employment

The patch test subjects (n=41) reported an average of 8.2 years employment in the nursery industry and 8.9 years in agriculture. At the time of testing, two members of the control group worked in blue collar occupations (construction and painting), eight in white collar occupations (assistant hotel manager, travel consultant, computer programmer, retail sales, and medical personnel). The remaining 11 were unemployed, disabled, retired, or employed in the home. Twenty-six (63.4%) of the patch test subjects were employed in the nursery industry at the time of their participation in the study, nine (22.%) were unemployed, and the remaining subjects were variously employed in agricultural extension, landscape gardening, restaurant work, home repair, and spa manufacturing. Three of the UCSF volunteers had worked previously in agriculture (1 year, 5 years and 20 years of employment, respectively) and there was an average of 1.2 years agricultural employment for the UCSF control group as a whole; median number of years in agricultural employment was 0. Two (9.5%) of the UCSF control group were employed in blue collar occupations and the remainder were employed in white collar occupations at the time of testing; this compared to 31(75.6%) of the nursery subjects employed in blue collar occupations at the time of testing. The demographic differences between the nursery workers and the UCSF volunteers were all statistically significant.

Nursery work tasks

Specific work tasks performed by study participants were ascertained from questionnaire responses. Twenty-three (56.1%) of the 41 subjects reported having applied pesticides, but only ten of these reported pesticide application or pest-control as a principal work task. Twenty-five (61.0%) worked some part of the time in planting, picking, or harvesting; nine (22.0%) worked in shipping or packing operations (Figure 4). Four (9.8%) reported working part of the time as supervisors and four as irrigators, three worked in maintenance and cleaning, and 2 reported working as laboratory analysts or technicians. Other work tasks carried out by at least one subject included sales/customer service, forklift operator, and painter. As noted above, one non-DFR subject was employed as a farm advisor in a county with a large nursery industry.

Figure 4 - packing and sorting roses in a Northern California nursery

Rash history

Thirty (73.2%) of the forty-one patch test subjects reported a rash between 1988 and 1992 and nineteen (46.3%) had a rash in the year prior to testing. The proportion of cases with a prior rash history by study subgroup is shown in Figure 5. Of 15 study subjects with **skin illnesses or injuries** identified from compensation reports, 13 (86.7%) affirmed the history of skin rash on questionnaire. (One of the subjects who responded negatively to this question [subject 63] had an eye injury with a secondary skin eruption on the eyelids in February 1992. The other [subject 23] had a rash above the eyes for 7-8 months during 1991 reportedly associated with exposures to nursery plants and the negative response was unexplained.) Of the 14 **non-skin illnesses**, 10 (71.4%) had a history of skin rash during the study period, and 6 (42.9%) of the 14 had a history of skin rash in the year immediately prior to testing. Of the **12 non-DFR subjects**, 9 (75.0%) had a history of skin rash in the study period, 5 (41.7%) had a history of skin rash in the preceding year, and 3 (25.0%) had dermatitis at the time of their patch testing. Nine (75%) of the twelve non-DFR subjects reported a skin

rash during the study period and 5 (41.7%) reported a rash in the year prior to participating in the patch test study. None of the UCSF control subjects reported a case of rash suspected to be contact dermatitis, but one reported a case of mild seborrhea.

History of atopy (allergy)

The patch test subjects (25/41) did not differ from UCSF controls study subjects (10/21) with respect to history of atopy, with the distribution of atopy by study subgroups as shown in Figure 5. There was no difference in the history of specific allergies including hay fever (21/41 vs 9/21), childhood eczema (8/41 vs.3/21), allergy to penicillin or other medication, food allergy, or composite allergy index (25/41 vs 10/21). Of the nursery patch test subjects, 22 (53.7%) reported suspected allergy to one or more plants, compared to 7 (33%) of the UCSF controls (p>0.05). [One of the UCSF controls who did not respond to this item on the questionnaire was assumed to be negative.] Specific plants suspected of causing allergy among the study subjects included poison oak (6), poinsettias (6), daffodils (4), primula (3), and pollen, tulips, "tumble weed", rhododendron, succulents, eucalyptus, sycamore, aloe vera, citrus, ivies, oakleaf, geranium, and grape ivy. Among UCSF controls, reported plant allergies included poison oak (4), pollen (3), daisies, grass, ragweed, rose thorn, and weeds.

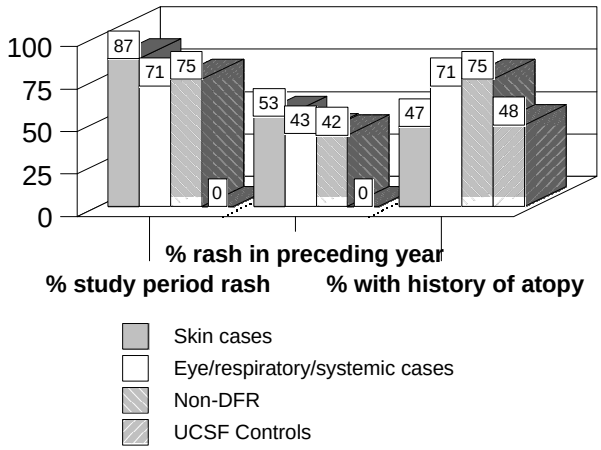

Figure 5 - Rash history and history of atopy by study group

Examination and Patch test results

Cases with positive patch test reactions and cases with noteworthy skin conditions at the time of testing are discussed below. The remaining cases are discussed in appendix 1.

DFR subjects with skin disease (n=15 including 1 subject who refused patch testing)

Subject 23 worked sorting, packing, and shipping flowers in a nursery that produced roses and primroses. On 12/29/89, she developed a pruritic rash on right hand, then on the arms and neck that was suspected of being related to an allergy to primula. The subject was treated with prednisone. No active dermatitis was present at the time of examination, but the subject had cuts on the forearms from handling roses. Positive patch test reactions included **primula (2.0+) and carnations (2.0+)**.

Subject 28 worked as a pesticide applicator at a nursery producing landscape and fruit trees, landscape shrubs, oleanders, pansies, petunias and other ornamentals. He had dermatitis reported on a compensation claim 7/5/91, felt to be secondary to chemical exposures at work. The examination reported on the claim described a confluent erythematous, papulo-vesicular rash on the forearms bilaterally; a similar rash was noted in a "V" shaped distribution on the chest. Test results showed reaction to **sulfur (0.5+)** and to **carnations (2.0+)**. No specific information was contained in the questionnaire about either sulfur or carnations.

Figure 6 - Lichenified hand dermatitis subject 31

Subject 31 worked packing and shipping flowers at a nursery producing carnations, violets, cactus, primula, roses, chrysanthemums, and "ornamentals". She was treated 4/8/91 for a rash above the eyes that began 7-8 months earlier. It was suspected that the rash was due to plant exposures at work. The examination reported on the compensation claim described an excoriated, erythematous dermatitis above both eyebrows. At the time of testing, the subject had a lichenified hand dermatitis (Figure 6) that she suspected was caused by primula. There was no reaction to primin on testing, but she did have a positive reaction to elemental **sulfur (1.0+)**.

Subject 38 worked as a pest control assistant at a nursery producing azaleas, chrysanthemums, poinsettias, and carnations. She had a facial rash suspected to be a work-related contact dermatitis on 04/26/89. On testing, she proved to have a positive reaction to **fragrance mix (1.0+).** She had no reactions to other test antigens, suggesting her dermatitis may have been related to a cosmetics product, rather than to an antigen in the work place.

Subject 42 worked in a cactus nursery as a harvester and soil mixer. On 3/21/91, he sought treatment for a scaly, itchy rash on the dorsum of his right wrist. His questionnaire responses indicated that he had a dermatitis of the shoulders in July 1992 but did not seek medical treatment, in addition to the rash reported on the DFR. He also had a history of an unspecified allergy associated with harvesting peaches. Positive patch tests included **carnation (1.0+), primin (0.5+), captafol (0.5+), and folpet (0.5+)**. His questionnaire did not indicate a history of either spraying pesticides or handling carnations.

Subject 44 worked at a nursery producing impatiens, begonias, carnations, urn plants, capsicum, and unspecified "ornamentals". On 3/1/91 she had a case of dermatitis attributed to unspecified flowers. (She listed eucalyptus as a possible allergen on the study questionnaire). On testing, no reaction occurred with eucalyptus or other plant antigens, but the subject had a strong reaction (Figure 7) to **neomycin (2.0+)**. It was not known whether she had ever used a topical medication containing neomycin either at home or at work.

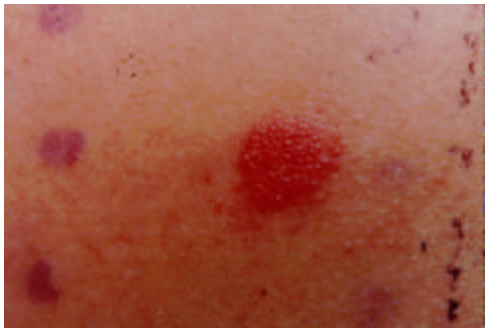

Figure 7 - 2 + reaction to neomycin - subject 44

Subject 46 worked in a poinsettia nursery. While cutting plants for transplantation, sap contaminated his hands and face, and he developed a corresponding pruritic rash. Examination at the time of treatment showed a macular rash on the face, eyelids, neck and ears. The rash had resolved at time of patch testing, but he had a large ulcerative lesion (Figure 8) on his hand from reported self-administration of battery acid to remove a wart. On testing, he had **no reaction** to any of the patch test antigens.

Subjects with non-skin conditions

Subject 25 worked planting and irrigating at a nursery that produced petunias, poinsettias, geraniums, and "ornamentals". He also did pesticide application work. After getting dust in his eyes while loading plants onto a truck 12/3/91, he developed conjunctivitis. On the study questionnaire, he reported having a skin eruption on the feet, hands, arms, and neck in January 1991, but never sought medical treatment. At the time of testing, he had a minimal dermatitis and post-inflammatory changes in web spaces of hands. He had a reaction to **sulfur (2.5+).** His questionnaire responses did not specify the names of pesticides that he had previously handled.

Figure 8 - self-inflicted battery acid burn - subject 46

Subject 29 worked as a pesticide applicator for a nursery producing multiple ornamental plants. He sought treatment for an episode of possible systemic pesticide poisoning in June

1992, but proved to have a non-work related condition. On patch testing, he had a **reaction to wool extract (2.0+)**, but no reactions to any other test antigens.

Subject 34 was an irrigator working for a nursery producing stone fruit trees and conifers (pines). He had an episode of conjunctivitis after getting an unspecified chemical product into his eye on 8/1/91. He also had a dermatitis of the abdomen (reported on the study questionnaire, but not on the DFR) on the same date. Patch testing showed a positive reaction to **chlorpyrifos (1.0+)**. He did not recall the specific chemicals he handled at work.

Subject 36 worked planting and harvesting, and also as a pesticide applicator, at a nursery producing ornamental flowers and cactus (*Echinopsis*). He developed conjunctivitis on 8/8/91 while transplanting cuttings, but did not report having any skin problems during the study period. On testing, he had a reaction to **nickel (2.0+)** and also to **elemental sulfur (1+)**.

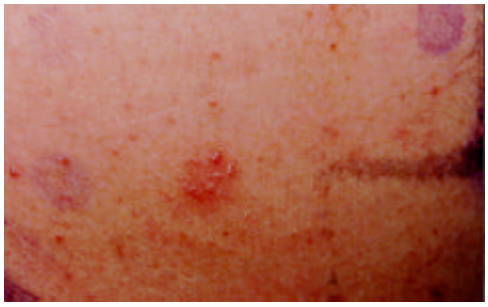

Figure 9 - 1+ reaction to sulfur - Subject 43

Subject 43 worked as a pesticide applicator in a nursery producing pine trees, pear trees, and ficus. He sought treatment during November, 1989 for an episode of allergic rhinitis that he felt was related to a pesticide. On the study questionnaire, he also indicated a history of allergy to sycamore trees. Patch test reactions included **chromium (1.0+)** and **sulfur (1.0+)**.

Subject 53 worked as a harvester at a nursery producing iris, daffodils, alstroemeria, and tulips. He had a worker's compensation claim for conjunctivitis (2/13/90), but no claim for dermatitis. On the questionnaire, he reported having an unspecified rash during the year prior to participating in the study, but did not seek medical treatment. On testing, he had a positive reaction to **benzocaine (1.5+).** It was unknown whether he had a previous history of exposure to a benzocaine-containing topical medication.

Subject 55 worked as a sales and customer service representative for a wholesale nursery producing oleanders, boxwoods, albaceas, pine, birch, and landscape ornamentals. On 9/6/91, she sought medical treatment after being exposed to fumes from a broken bottle of malathion. She had no history of dermatitis between 1988 and 1992, but had a positive reaction to **primin (1.0+)**. There was no specific questionnaire response indicating exposure to primula.

Subject 56 worked harvesting and transplanting cuttings for a nursery producing daisies, poinsettias, jasmine, spider plants, chrysanthemum, and "ornamentals". On 6/13/91, he sought treatment for an episode of allergic rhinitis: stinging and sneezing, associated with cutting flowers. He had a positive reaction to **PCNB (1.0+)**. There was no information on the questionnaire specifically indicating a history of handling this compound.

Non-DFR subjects

Subject 40 worked at a rose nursery as a pesticide applicator. He reported having a transient episode of dermatitis in August 1992, but did not file a workers' compensation claim. On testing, he had a weak reaction to **thiuram (scored 0.5+, with a "ring" or "edge" effect present, indicating an irritant effect)**, a rubber additive in the standard series. It is sometimes used as a fungicide, and is s also an analogue of several thiocarbamate compounds.

Subject 45 transplanted poinsettias one or two days a week in a Southern California nursery during July 1992. During the questionnaire and interview, she commented that skin problems associated with this activity were common among her coworkers. She developed an eczematous dermatitis over her hands that had only partially resolved at the time of patch testing (9/92). **Patch tests were negative**. It was not possible to perform a KOH preparation at field site and she did not seek medical treatment for her condition.

Subject 47 worked as a pesticide applicator at a nursery producing a wide variety of ornamental plants. He reported that he used an acid as a paint remover on the skylight/roof of the nursery where he worked. He suffered a full thickness burn (9/92) on the end of his thumb through a hole in the end of his glove (Figure 10). No DFR on this case was received and the specific acid involved was not identified. Attending physicians from the university hospital burn service, where he was treated, inferred from the degree of tissue necrosis that the paint remover may have been hydrofluoric acid.

Figure 10 - full thickness burn from unknown acid - subject 47

Subject 54 worked as a harvester and occasionally as a pesticide applicator at a nursery producing alstroemeria, iris and daffodils. Positive reactions included **carnation (1.0+)** and **sulfur (2.0+)**. The questionnaire indicated a history of dermatitis, but not the specific pesticides the subject handled, nor whether there was a history of working with carnations.

Subject 57 worked shipping, packing, and sorting plants in a nursery that handled multiple varieties of ornamentals (poinsettias, chrysanthemums, daisies, spider plants, white button, yellow button, star jasmine, and others). On the study questionnaire, she reported having dermatitis of her eyelids in 1991, for which she did not seek medical treatment. Although she reported a history of suspected allergies to certain types of plants, she had a reaction to **nickel (2+),** and was negative to all of the plant antigens tested.

Subject 59 worked as a harvester at a southern California nursery and had no history of skin problems during the study period. He had never worked as a pesticide applicator. On testing, he had reaction to **PCNB (1.5+)**, but none to other test antigens.

Statistical associations

Eight study subjects had reactions to one or more antigens in the standard series, including 2 DFR subjects with dermatitis, 4 DFR subjects with non-skin conditions and 2 non-DFR subjects. The number of cases studied provided relatively little opportunity for identifying statistical associations, but odds ratios were calculated to identify possible trends among the largest subgroups of cases (Table 3). There was a non-significant association between atopy and reactions to plant antigens (OR =3.16*[c]). Another positive, non-significant association was observed between a history of work as a pesticide applicator and reactions to elemental sulfur (OR=3.6*) and all pesticide antigens combined (OR=2.18*). Reaction to plant and pesticide antigens also appeared to be correlated (OR=5.8*), but was not of statistical significance. No apparent associations were observed between history of skin disease during the study period and reactions to antigens in the standard series (OR = 0.58*), pesticides (OR=0.35*), or plants (OR=0.86*).

Discussion

Six (42.9%) of the 14 DFR skin cases had patch reactions to one or more test materials, including 2 to standard series antigens, 3 to pesticides and 3 to plant test materials. The relevance of the reactions was positive in one patient (subject 23) and more ambiguous in the remaining cases. For example, the finding of reaction to standard series fragrance mix suggests that the facial dermatitis in subject 38 was secondary to non-occupational exposures. Subject 44 had a case of dermatitis thought to be related to eucalyptus or flowers (carnations, impatiens, and capsicum [peppers]), but was negative to eucalyptus and the other plant antigens tested. Although first aid ointments containing neomycin are sometimes a source of workplace contact dermatitis (Adams, 1990), there was no documented history of such exposure in this case.

[c] * p>0.05 by Fisher's exact test

The study subjects with non-skin injuries and those for whom no DFR was received had positive patch test reactions with approximately the same frequencies as the subjects with dermatitis. Although this might seem to indicate that the positive tests had no clinical relevance, both groups had a cumulative incidence of skin disease during the study period of greater than 70% and more than 40% reported skin problems in the year prior to testing (Figure 5). (These figures compare to 12% prevalence of subjects in the NHANES study population who reported skin conditions of concern [NHANES, 1979].)

A typical case in the group who did not have skin disease reported through workers' compensation was subject 25. He had mild hand dermatitis at the time of testing, a history of spraying pesticides, and a 2+ reaction to sulfur. Other materials producing reactions in this group included the pesticides chlorpyrifos, pentachloronitrobenzene, and the plants materials primin and carnation extract. However, neither reactions had definite relevance comparable to the reaction to these materials seen in subject 23. Significant non-allergic conditions included the poinsettia transplant dermatitis in subject 45 and the acid burn suffered by subject 47.

The incidence of skin disease in the group without skin DFRs raises the question of under-reporting of this condition among the nursery population. However, the low rate of participation in our study prevents any generalization from the results. Although the patch-test participants in the study were demographically similar to non-participants and to the California nursery workforce as a whole, it seems unlikely that they were representative in terms of skin disease history. Rather, they were likely to have been motivated to participate because of a personal history of skin problems. Alternative approaches to enrolling participants should be considered in future studies, including contacting potential participants at the time of initial medical treatment or directly in the work place.

The frequency of reactions to sulfur observed in our study was unexpected. Responses to sulfur were infrequent (1/21) in our unexposed control population, and no reaction was greater than 1+. However, the difference in the frequency of reaction could represent a variation in susceptibility related to the differences in ethnicity, age, gender and occupation, between the nursery workers and the UCSF controls. It is likely, for example, that active employment in nurseries and other manual labor occupations at the time of testing may have been associated with a higher rate of sweating under the patches. It is possible that this factor could have increased the likelihood of irritant reactions. Morphologically, the reactions to sulfur ranged from 1+ with edema and erythema to 2+ with erythema, edema, and blistering observed. Most were observed at 96 but not at 48 hours. Although these clinical/morphological features suggest allergy, it was not possible to biopsy the lesions during the field testing to confirm the mechanism of the reactions. The reactions to sulfur occurred principally in subjects reporting having worked as pesticide sprayers (OR=3.6, Table 2).

The large number of cases associated with elemental sulfur in California agriculture is striking and would seem to imply that sulfur is a potent skin irritant. However, standard skin irritation studies for most agricultural formulations have shown just the opposite.[d] Other work, using guinea pigs (Matsushita *et al*, 1980), has shown that a 25% concentration of wettable sulfur powder produces a 2+ irritant reaction. The guinea pig maximization test, conducted with a 5% topical concentration of sulfur, has shown that elemental sulfur is a moderately strong experimental allergen (Matsushita *et al*, 1980). Two case reports implicate elemental sulfur as a human contact allergen. Schneider (1978) reported two cases of contact allergy in patients who used medications containing elemental sulfur to treat superficial fungal dermatoses. Both patients had positive patch test reactions to 5% elemental sulfur in various vehicles. A control series was not reported. Our findings suggest that allergic reactions to sulfur should be studied in other populations.

In addition to sulfur, we observed reactions to PCNB, chlorpyrifos, folpet, and captafol. Captafol has been reported previously as an irritant and sensitizer from Japan (Matsushita *et al*, 1980), Korea (Lee *et al*, 1981), the United States (Cottel, 1972; Camarasa, 1975), New Zealand (Stoke, 1979) , Kenya (Verhagen, 1974), and England (Groundwater, 1977). Folpet is a thiophthalimide compound structurally analogous to captafol and cross reactions to these compounds are common (Lisi *et al*, 1986; Lisi *et al*, 1987). The reaction to this compound in occurred in the same subject 42 who reacted to captafol (Table 2). PCNB has some structural elements similar to the experimental sensitizer

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[d] Unpublished DPR data

dinitrochlorobenzene and an allergic reaction to PCNB in a pesticide formulator has previously been described (Cronin, 1980). Allergic reactions to chlorpyrifos have not been reported previously, but deserve evaluation in future research.

Although reactions to plants appeared to be somewhat less frequent than reactions to pesticides, this could have been due to lack of test antigens for the nearly endless variety of plants handled by nursery workers. Reactions to poinsettias, lily bulbs and other common plant pathogens may have been due to irritant rather allergic mechanisms. As described above, some cases of persistent eczema may due to fungal infections (Subject 45), although this could not be confirmed by tests available at the field sites.

We did not observe reactions in our pilot study to some well known nursery plant sensitizers including tuliposide A (alstroemeria, lily bulbs, and tulips)and chrysanthemums. We observed reactions to primin, another common sensitizer, in 2 subjects (Benezra *et al*, 1985; Mitchell and Rook, 1979). Unexpectedly, the plant antigen producing the most frequent reaction was carnation extract (5 subjects). No reports on carnations have been published in recent years, but several reports from the older literature are summarized by Mitchell and Rook (1979).

Conclusion

Our study described skin injuries and illnesses in California nursery workers, including documented cases of contact dermatitis to plants and pesticides. Non-pesticidal chemicals also produced serious morbidity, illustrated by a third degree acid burn in one subject. Although the study was hampered by a low participation rate, some observations deserve follow-up. These include further study of the allergenic potential of PCNB, chlorpyrifos and elemental sulfur.

References

Adams RM (1990): **Occupational Skin Disease**, 2nd Edition. 1990, Philadelphia WB Saunders

Benezra C, Foussereau J, Ducombs G, Sell Y, and Foussereau J (1985): **Plant Contact Dermatitis** St. Louis, Mo

Camarasa G (1975): Difolatan dermatitis. **Contact Dermatitis** 1:127

Cottel WI (1972): Difolatan. **Contact Dermatitis Newsletter** 11:252

Cronin E (1980): **Contact Dermatitis** Churchill Livingstone; Edinburgh, London and New York, 1980 p. 400

Groundwater JR (1977): Difolatan dermatitis in a welder; non-agricultural exposure. **Contact Dermatitis** 3:104

Lee SL, Chin YW, Chang WH, and Kim JS (1981): A study on hypersensitivity of Korean farmers to various agrochemicals. Determination of concentration for patch test of fruit-tree agrochemicals and hypersensitivity of orange orchard farmers in Che-ju Do. Korea. **Seoul Medical Journal** 22:137-42

Lisi P, Caraffini S, and Assalve D (1987): Irritation and sensitization potential of pesticides. **Contact Dermatitis** 17:212-8.

Lisi P, Caraffini S, and Assalve D (1986): A test series for pesticide dermatitis. **Contact Dermatitis** 15:266-269

Matsushita T, Yoshioka M, Aoyama K, Arimatsu Y, and Nomura S (1977): Experimental study on contact dermatitis caused by fungicides benomyl and thiophanate-methyl. **Industrial Health** 18:141-147

Matsushita T, Nomura S, and Wakatsuki T (1980): Epidemiology of contact dermatitis from pesticides in Japan. **Contact Dermatitis** 6:255-9

Mitchell J and Rook A (1979): **Botanical Dermatology** Vancouver Greengrass

National Center for Health Statistics (1979). NHANES: Skin conditions in persons 1-91 years of age in the United States

O'Malley MA and Mathias CG (1988): Distribution of lost-work-time claims for skin disease in California agriculture: 1978-83. **Am J Ind Med** 14:715-720

O'Malley M, Mathias CGT, and Coye MJ (1989): Pesticide associated skin disease in California: 1978-1983; in **Principles of Health and Safety in Agriculture**, J.A. Dosman and D.W. Cockroft, eds. CRC Press; Boca Raton, 1989. pp. 301-304

O'Malley M, Rodriguez P, and Maibach HI (1995): Pesticide patch testing: California nursery workers and controls. **Contact Dermatitis** 32:61-63

Schneider HG (1978): Schwefelallergie. **Hautartz** 29:340

Stoke JC (1979): Captafol Dermatitis in the timber industry. **Contact Dermatitis** 5:284-92

Verhagen ARHB (1974): Contact Dermatitis in Kenya. **Trans St John's Hosp Dermc Soc** 60:86-90

Table 1 - Patch Test Materials

European Standard Series	Plants	Pesticides
Potassium dichromate	Geraniol 1%	Acephate 1%
Neomycin sulfate	Eucalyptus oil 2%	Benomyl 0.1%
Thiuram	Tuliposide A (0.1%) - tulips, lilies, alstroemeria	Captan 0.1%
Paraphenylenediamine	Chrysanthemum 1%	Chlorothalonil 0.001%
Cobalt dichloride	Sunflowers 2.5%	Chlorpyrifos 1%
Benzocaine	Anthemis cotula 1%	Diazinon 1%
Formaldehyde	Hedera (ivy)	Dienochlor 1%
Colophony	Daffodil 1%	Fenbutatin-oxide 0.1%
Quinonline	Carnations 1%	Fluvalinate 1%
Balsam of peru		Malathion 1%
PPD		Permethrin 1%
Wool alcohols		Vinclozolin 1%
Mercapto mix		PCNB 1%
Epoxy		DCNA 1%
Parabens		Sulfur 1%
PTBP		Folpet 0.1%
Fragrance mix		Maneb 1%
Ethylene diamine		Zineb 1%
Quaternium 15		Ziram 1%
5-chloro-2-methyl-isothiazolone		
MBT		
Primin		

Table 2 - Summary of Positive Patch Test Reactions by Study Group

Material	DFR Skin	Other DFR	NonDFR
Sulfur	(28, 31)	(25, 36, 43)	(54)
PCNB		(56)	(59)
Chlorpyrifos	(34)		
Captafol	(42)		
Folpet	(42)		
Primula	(23, 42)		(55)
Carnation	(23, 28)		(54)
Wool		(29)	
Neomycin	(44)		
Nickel		(36)	(57)
Fragrance mix	(38)		
Thiuram			(40)
Chromium		(43)	
Benzocaine		(53)	

Table 3 - Statistical Associations for Patch Test Reactions

Exposure Factor	**Outcome**		**Total**	**Odds Ratio**
	All antigens combined +	_		
Atopy +	10	13	23	0.77
-	8	8	16	
	Standard series antigens +	-		
Atopy +	4	19	23	0.63
-	4	12	16	
	Pesticides +	-		
Atopy +	6		23	1.06
-	4		16	
	Plant +	-		
Atopy +	4		23	3.16
-	1		16	
	Standard series antigens +	-		
History of Skin disease	6	26	32	0.58
-	2	5	7	
	Standard series antigens +			
Pesticides +	2	8	10	0.96
-	6	23	29	
	Pesticides +	-		
History of Skin disease	7	25	32	0.37
-	3	4	7	
History of spraying +	7	15	22	2.18
-	3	14	17	
	Sulfur +	-		
History of spraying +	4	18	22	3.6
-	1	16	17	
	Plants +	-		
History of Skin disease	4	28	32	0.86
-	1	6	7	
Pesticides +	3	7	10	5.8
-	2	27	29	

Appendix - Listing of study participants who had negative patch tests

Study Id	Comment
22	The subject spent 2 hours watering plants inside an area sprayed the previous day 'M-Pede', a insecticidal soap. He sought treatment for symptoms of dizziness, leg weakness, and diarrhea. The condition was reported as a viral syndrome.
24	This subject worked planting, shipping, packing, and sorting in a nursery that produced ivy and ferns. He developed a case of conjunctivitis case 12-7-91. She was also noted to have a lichenified dermatitis on the back of her hands and forearms. She felt the rash was due to unspecified pesticides used on ivy.
26	The subject was a farm advisor who worked extensively with the nursery industry and reported having an episode of conjunctivitis following contact with chlorothalonil in 1977. Patch test to chlorothalonil was negative and other materials were not tested.
27	The subject worked as assistant manager and pesticide applicator at a nursery producing stone fruit trees, nut trees, chestnuts, and ornamental plants. While at work the patient had sudden onset of dizziness, lightheadedness, nausea, paleness at work, but normal physical examination. Symptoms were attributed to exposure to unspecified chemical.
30	The subject worked at a nursery producing numerous ornamental plants. He had a foreign body and conjunctivitis in the right eye from a foreign body on 8/31/90. At the time of testing, the subject had hand dermatitis from a job as a dish washer.
32	The subject worked as an assistant manager at a nursery producing orchids, roses, eucalyptus and gardenias. On 2/6/89 he had a metallic foreign body in the left eye. He had a history of an unspecified dermatitis during the study period..
33	The subject worked as a harvester on a bulb farm that produced daffodils and iris. She developed erythema and vesicular lesions on face on 6/27/88 (the case was received at DPR in 1989) that she attributed to a chemical exposure.
35	The subject worked packing and sorting in a nursery producing strawberry plants. She developed itching while sorting strawberries on 11/4/91.
37	The subject worked as a harvester at a nursery producing a variety of ornamental flowers. While harvesting poinsettias, she noticed a rash on the skin both arms. She didn't want to participate in the patch testing and only completed the questionnaire.
39	The subject worked doing soil analysis in the laboratory at a nursery producing ornamental plants. On 9/12/89, she developed skin irritation (itching, burning, and dry skin) primarily on face and forearms, possibly due to exposure to plant materials or to pesticides.
41	The subject worked planting and harvesting at a nursery producing roses and chrysanthemums and other ornamental crops. On 8/2/91, he developed severe burning with a numbing sensation to the inside of his mouth and his face. He also had a history of asthma and urticaria since 1977, he associated with exposure to chemical sprays used on the plants.
48	This non-DFR subject worked as a pesticide sprayer at a landscape nursery producing mahonias, nidularia, laurel, rhododendron, fuschia, and Japanese maple. He had no history of a skin rash during the study period.
49	This subject worked in shipping, packing and sorting operations at a bulb farm producing iris, daffodils, monkshood, alstroemeria, and tulips. On 1/17/91, while working with flowers she developed a finger dermatitis with 1-2 mm papules and ulcers.
50	This subject worked as a forklift driver and laborer at a bulb farm (see subject 49). On 3/13/92, she developed a skin infection (felon) in the right thumb, that she characterized as “daffodil poisoning”.
51	This subject worked as a supervisor on a bulb farm (see subject 49). On 11/7/90, she had a corneal abrasion when material from wet bulbs splashed into her eye.
52	This subject worked on the bulb farm described above. On 2/14/92, she had mild edema of the right upper eyelid without scleral injection. The condition was recorded as an allergic reaction to daffodils.
58	This non-DFR subject worked shipping packing and sorting at a nursery producing ornamentals (chrysanthemum, star jasmine, poinsettias, spider plants, and others).
60	This non-DFR subject worked as a planter, harvester, and maintenance worker at the same nursery as subject 58. He had a history of rash during the year before participating in the study , for which he received treatment by a doctor in Mexico.
61	This non-DFR subject had worked as a planter, harvester and laboratory assistant at the same nursery as subject 58. She reported temporarily being unable to work because of an unreported exposure to pesticides at the nursery the previous year, but didn’t know specific product involved.
62	This non-DFR subject had worked as a irrigator planter, and harvester at the same nursery as subject 58. He had a history of unspecified rash during the study period, but not in the 12 months prior to the interview.