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ORIGINAL ARTICLE

Epidemiology of Contact Dermatitis: Prevalence of Sensitization to Different Allergens and Associated Factors

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Patch tests

Abstract

Background: In clinical practice, contact dermatitis is a relatively common skin complaint, whose prevalence has increased in recent years. Study by patch testing is essential for diagnosis of contact sensitization.

Objectives: To study the prevalence of sensitization to different allergens in a standard battery and observe the influence of different epidemiological and clinical variables on contact sensitization. A large number of allergens were included in our battery in order to detect new sensitizations whose prevalence might justify further study.

Material and methods: This was a retrospective, observational, epidemiological study of 1092 patients, conducted in our skin allergy unit between January 1, 2000 and December 31, 2005. All patients were studied with a battery of 51 allergens. We assessed the following variables: sex, age, type of referral, occupation, site and course of skin lesions, personal and family history of atopy, positive patch tests, clinical significance, diagnosis, source of sensitization, and occupational relationship.

Results: At least 1 positive result was found in 55% of the patients, and 55.7% presented contact dermatitis in one of its clinical variants: allergic contact dermatitis (28.2%), irritant contact dermatitis (20.1%), photoallergic contact dermatitis (2.2%), and phototoxic contact dermatitis (1.2%). The most prevalent allergens were nickel sulfate (29.3%), palladium chloride (11.7%), cobalt chloride (10.8%), potassium dichromate (7.5%), fragrance blends (6.3%), and p-phenylenediamine (6.1%).

A positive occupational relationship was found in 41.1%, and 21.3% of the patients studied were diagnosed with occupational contact dermatitis. Metalworkers, construction workers, and professional hairdressers were the most strongly represented groups. The most common source of sensitization was contact with metallic objects, followed by drugs, cosmetics, and rubber items. Female sex was the only independent variable that had a significant influence on the risk of contact sensitization in general.

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Conclusion: Women became sensitized at a younger age than men, and the frequency of positive results in the patch tests increased with age, reaching a maximum at between 60 and 69 years of age, when the greatest rate of sensitization occurred. Comparison of our results with other Spanish data showed a progressive and constant increase in sensitization to nickel sulfate, fragrance blends, balsam of Peru, and Colophonium, and a decrease in sensitization to potassium dichromate. The inclusion of new allergens such as palladium chloride, diallyl disulfide, and p-toluene sulfonamide formaldehyde improved the sensitivity of the standard battery in the detection of contact sensitization. We therefore recommend further studies of these allergens.

PALABRAS CLAVE
Eccema de contacto;
Dermatitis alérgica de contacto;
Alérgenos de contacto;
Epidemiología;
Serie de pruebas estándar;
Pruebas epicutáneas

Epidemiología de la dermatitis de contacto: prevalencia de sensibilización a diferentes alérgenos y factores asociados

Resumen

Introducción: El eccema de contacto (EC) constituye una enfermedad cutánea relativamente frecuente en la práctica clínica, cuya prevalencia ha aumentado en los últimos años. El estudio mediante pruebas epicutáneas (PE) es fundamental e imprescindible en el diagnóstico de la sensibilización de contacto.

Objetivos: Estudiar la prevalencia de sensibilización a diferentes alérgenos de la serie de pruebas estándar y observar la influencia de diferentes variables epidemiológicas y clínicas en la sensibilización de contacto. Introducimos un amplio número de alérgenos en nuestra serie de pruebas con la finalidad de detectar nuevas sensibilizaciones, cuya prevalencia justifique un estudio más detallado de éstos.

Material y métodos: Se realizó un estudio epidemiológico, observacional y retrospectivo de 1.092 pacientes, llevado a cabo en nuestra unidad de alergia cutánea desde el 1 de enero de 2000 hasta el 31 de diciembre de 2005. Se estudió a todos los pacientes con una serie de pruebas compuesta por 51 alérgenos. Valoramos las siguientes variables: sexo, edad, procedencia, profesión, localización y evolución de las lesiones cutáneas, antecedentes personales y familiares de atopia, positividad de las PE, relevancia clínica, diagnóstico, origen de la sensibilización y su relación profesional.

Resultados: El 55% de los pacientes estudiados tuvo alguna positividad y el 55,7% presentó EC en alguna de sus variedades clínicas: eccema alérgico de contacto (28,2%), eccema irritativo de contacto (20,1%), fotodermatitis alérgica de contacto (2,2%) y fotodermatitis tóxica de contacto (1,2%). Los alérgenos más prevalentes fueron sulfato de níquel (29,3%), cloruro de paladio (11,7%), cloruro de cobalto (10,8%), dicromato potásico (7,5%), mezcla de perfumes (6,3%) y parafenilendiamina (6,1%). El 41,1% de los pacientes con EC tuvo una relación profesional positiva y el 21,3% del total de los pacientes estudiados se diagnosticó de dermatitis de contacto profesional; los metalúrgicos, los trabajadores de la construcción y los peluqueros fueron los profesionales más representativos.

El origen más frecuente de las sensibilizaciones fue el contacto con objetos metálicos, seguido de los medicamentos, los cosméticos y los objetos de goma.

El sexo femenino fue la única variable independiente que influyó de forma significativa en la sensibilización de contacto en general.

Conclusiones: Las mujeres se sensibilizaron más precozmente que los hombres, y la prevalencia de positividad de las PE aumentó con la edad, y alcanzó el máximo a los 60-69 años, intervalo en el que también se encontró el mayor índice de sensibilización. Al comparar nuestros resultados con los nacionales, observamos un aumento progresivo y constante de la sensibilización al sulfato de níquel, a la mezcla de perfumes, al bálsamo del Perú y a la colofonia y un descenso en la sensibilización al dicromato potásico.

La introducción de nuevos alérgenos, como el cloruro de paladio, el dialil disulfuro y la resina de paratolueno sulfonamida formaldehído, mejoró la sensibilidad de la serie de pruebas estándar en la detección de la sensibilización de contacto. Por esto, aconsejamos más estudios sobre estos alérgenos.

Introduction

The skin is a large, complex, and vitally important organ that is actively involved in immune surveillance[1] as it receives a wide range of physical, chemical, thermal, and biologic aggressions. Failure of this first line of defense may lead to various diseases, including contact dermatitis.

Contact dermatitis is a common condition that consists of an inflammatory skin reaction essentially marked by 2 distinct processes: *a)* irritant contact dermatitis, which is a nonimmune inflammatory reaction that develops following exposure to an irritant and is characterized by a wide range of clinical manifestations that vary with type of irritant, temperature, moisture level, body site, and a range of individual characteristics such as age, sex, ethnic background, and previous skin diseases[2,3]; and *b)* allergic contact dermatitis, which is an immune reaction to a sensitizing agent that enters the body through the skin.[4] According to the Gell and Coombs classification,[5] contact dermatitis is considered to be the clinical expression of a type IV delayed-type hypersensitivity reaction, and this has been shown to be T-cell mediated.[6] A distinction between irritant and allergic contact dermatitis is not always made in routine practice as the 2 conditions often have identical clinical features and both irritants and allergens have been implicated in their pathogenesis.

Contact dermatitis is diagnosed on the basis of careful questioning, which should include investigation of previous skin disease, occupation, working environment, use of personal items, causes of exacerbations and improvement (if these exist), time since onset, and lesion severity. Patch tests should be performed when an allergic mechanism is suspected. These tests, which are the gold standard in such cases, consist of re-exposing the patient to suspect allergens under controlled conditions. Although patch tests were first described by Jadassohn,[7] it was Bloch[8] who described a method for performing the tests, established a system for analyzing skin reactions to an allergen, and highlighted the differences between healthy and sensitized individuals.

Numerous working groups, including the International Contact Dermatitis Research Group (ICDRG) and the Spanish Contact Dermatitis Research Group[9] (abbreviated in Spanish to GEIDAC), were set up to resolve problems caused by the enormous differences in the materials and methods used in skin patch testing and to promote the study of new allergens and report on new occupational skin diseases.

The work of these groups has led to the establishment of a standard test series consisting of a determined number of allergens[10] (which differ slightly between countries)[11-13] that cause sensitization in a large proportion of the general population. This series serves a general screening purpose and is reassessed periodically to improve its ability to detect new types of sensitization. Allergens are supplied by various manufacturers, such as Almiral-Hermal, Chemotechnique Diagnostics, and Martí Tor, who provide updated lists of their allergens. Patch-test results are classified according to whether they are positive or negative, in line with the method proposed by the ICDRG,[14] and positive results are then quantified using a progressive scale. The interpretation of results requires a thorough examination of clinical manifestations and history of exposure to the allergen.[15] Results should, therefore, be analyzed by a dermatology specialist to ensure correct diagnosis, appropriate treatment, and successful implementation of strategies to prevent recurrence. The association between an allergen and disease is called clinical relevance.

The epidemiology of contact dermatitis has been analyzed by numerous studies in recent years, with the majority of studies using standard updated series accepted by the different working groups[11-13,16-37] (Table 1). These studies are helpful in that they not only describe disease distribution in the general population, but also shed light on associated risk factors. Results are often difficult to compare between groups as the composition of standard series varies from one place to the next because of geographic and cultural differences in allergen exposure. There is no question, however, that contact dermatitis is a common disease in daily clinical practice, with an estimated prevalence, in all its clinical forms, of between 1% and 10% in the general population.[28,38] An analysis of the above studies shows that nickel sulfate is the most common contact allergen, attributable to the fact that there has been a predominance of women in all the series studied.

The main aim of this study was to perform an epidemiological analysis of contact dermatitis in the health care area covered by our hospital in order to determine the most common allergens in our setting.

We believe that this study is justified not only because of the current relevance of contact dermatitis in the Spanish health system but also because of the unquestionable impact it has on health-related quality of life. Furthermore, contact dermatitis is a common occupational disease that generates considerable health care costs and has important medicolegal ramifications.[39] Only by analyzing the current situation and improving our knowledge of the epidemiological characteristics of contact dermatitis, will we be able to begin to implement adequate measures to prevent the disease.

Material and Methods

We performed a retrospective, epidemiological, observational study of all the patients studied at the skin allergy and occupational skin disease unit in the dermatology department of Hospital Clínico Universitario in Valladolid, Spain between January 1, 2000 and December 31, 2005. We included 1092 patients, all of whom underwent a complete study, ie, with all the patch tests needed to reach a definitive diagnosis. In all cases, the patch tests were performed and analyzed at our unit by 2 dermatologists experienced in contact dermatitis. The ethical principles governing biomedical research promoted by the Declaration of Helsinki[40] were applied throughout the study, and patient confidentiality was maintained in accordance with the provisions of the Spanish organic law 15/1999 of 13 December on data protection and law 41/2002 of 14 December regulating patient autonomy and rights and obligations in matters of information and clinical documentation. Written informed consent was obtained from all participants (Appendix 1).

Table 1 Current Epidemiological Situation of Contact Dermatitis: Key National and International Studies

Geographical Area	Year of Study	Year of Publication	Patients, No. (%)	PT+, %	Most Common Allergen	Second Most Common Allergen	Third Most Common Allergen
Australia							
Ciconte et al[16]	1988-1993	2001	817 (63)	53	Nickel sulfate	Fragrance mix	Cobalt chloride
United Kingdom							
Britton et al[11]	2000	2003	3062 (68)	—	Nickel sulfate	Fragrance mix	Balsam of Peru
Austria							
Wöhrl et al[19]	1997-2000	2003	2766 (76.5)	48,9	Nickel sulfate	Mercury	Thiomersal
USA							
NACDG[23]	2001-2002	2004	4913 (61.3)	69	Nickel sulfate	Neomycin sulfate	Balsam of Peru
Europe							
Uter et al[25]	2002-2003	2005	10 511 (62.9)	—	Nickel sulfate	Cobalt chloride	Fragrance mix
Portugal							
GPEDC[30]	2004	2005	2806 (69.6)	58.4	Nickel sulfate	Potassium dichromate	Cobalt chloride
Czech Republic							
Machovcova et al[27]	1997-2001	2005	12 058 (55.9)	63.5	Nickel sulfate	Balsam of Peru	Fragrance mix
Israel							
Lazarov[12]	1998-2004	2006	2156 (68.7)	43.5	Nickel sulfate	Fragrance mix	Potassium dichromate
Spain							
Giménez Camarasa[9]	1977	1979	2806 (55.2)	60	Nickel sulfate	Potassium dichromate	Cobalt chloride
Miranda et al[31]	2000	2001	4310 (62.1)	49.6	Nickel sulfate	Cobalt chloride	Potassium dichromate
García Bravo[32]	2001	2004	3.832 (60)	55.1	Nickel sulfate	Cobalt chloride	Potassium dichromate
Santiago de Compostela[33]	1990	1995	1.015 (61.2)	57.4	Nickel sulfate	Cobalt chloride	PPD
Barcelona[34]	1994	1995	800 (76.2)	57.7	Nickel sulfate	PPD	Cobalt chloride

Abbreviations: GPEDC, Portugues Contact Dermatitis Research Group; NACDG, North American Contact Dermatitis Group (patch test results); PPD, paraphenylenediamine; PT+, patch test positivity.

Clinical histories were taken according to an established protocol, with recording of the following epidemiological variables: age, sex, skin patch test date, place of residence, profession, and clinical variables (time since onset, lesion site, and personal or family history of atopy). We used an extended series of 51 allergens, with additional, specific tests performed in accordance with the patients' occupations or leisure activities. All positive results were recorded, and clinical reactions indicating an irritative reaction were excluded. Clinical relevance was established on the basis of clinical history and physical findings. Patch test results were interpreted following the recommendations of the ICDRG[14] using standardized allergens supplied by Almirall-Hermal or Chemotechnique Diagnostics. The allergens were placed on Curatest patch test strips and attached to the upper part of the patient's back using Omnifix hypoallergenic adhesive tape. Clinical history, physical examination, and patch test results were all determining factors in establishing a diagnosis.

Statistical Analysis

All data were entered into a Microsoft Excel spreadsheet (version 2003) and statistical analysis was performed using version 11.5 of the SPSS program for Windows. Absolute and relative frequencies were calculated for qualitative variables and means (SD) for quantitative variables.

Associations between study variables were evaluated by analytical statistical methods, using the Pearson χ^2 test for categorical variables and the *t* test and the F test for quantitative variables. Statistical significance was set at $P<.05$ and 95% confidence intervals (CIs) were calculated. The strength of associations was measured using odds ratios (ORs) with their corresponding 95% CIs; logistic regression was used for multivariate analysis. The association between different sensitizations was analyzed using contingency tables and the weighted κ statistic. Strength of agreement measured with this statistic was graded as poor (0-0.2), fair (0.2-0.4), moderate (0.4-0.6), good (0.6-0.8), and excellent (0.8-1).

Results

Descriptive Analysis of the Sample

Of the 1092 patients studied, 673 were female (61.6%) and 419 were male (38.4%); the age range was 1 to 90 years, with a mean (SD) age of 41.4 (16.5) years. Given the wide age distribution of the sample, it is interesting to note that the median age was 41 years. In total, 72.9% of the patients lived in a city while just 6.8% lived in a rural environment. The time since onset of the lesions studied was between 1 month and less than a year in 49% of the sample, between 1 and 5 years in 31.7%, and less than a month in 4.4%.

The most widely represented occupations were homemakers (26.2%), professional occupations (12.5%), metalworkers (8.7%), clerical workers (6.3%), and construction workers (5.3%). The most common lesion site was the hands (39.7%; on the palms in 27.8% of cases and the dorsal surface in 11.9%), followed by the face (7.3%), the neck (5.6%), and the eyelids (4.4%). Forty-five percent of patients had lesions in 2 sites and just 26.3% had lesions in a single site. A personal and family history of atopy was detected in 15% and 7.5% of patients, respectively.

Fifty-five percent of the sample (601 patients) had at least 1 positive patch test result. The most common allergens were nickel sulfate (29.3%), palladium chloride (11.7%), cobalt chloride (10.8%), potassium dichromate (7.5%), fragrance mix (6.3%), paraphenylenediamine (PPD) (6.1%), balsam of Peru (5.3%), thiomersal (4.1%), and thiuram mix (3.3%). The allergens with the greatest clinical relevance were mercapto mix, mercaptobenzothiazole, tixocortol pivalate, and p-toluene sulfonamide formaldehyde resin (Table 2).

The extended standard patch test series was sufficient to establish a definitive diagnosis in 78.1% of the patients diagnosed with a form of contact dermatitis; in the remaining 21.9%, the use of a specific series was necessary. The diagnoses were allergic contact dermatitis (28.2%), irritant contact dermatitis (20.1%), allergic contact photodermatitis (2.2%), and phototoxic contact dermatitis (1.2%). Contact dermatitis and photodermatitis were ruled out in 48.3% of patients. A positive association with occupation was found in 41.1% of all the patients with contact dermatitis in its various forms (51.7% of series). The predominant sensitizing agents were metals, drugs, cosmetics, and rubber products.

The demographic characteristics of the patients diagnosed with contact dermatitis were described in accordance with the MOAHLFA index, which shows the proportions of the following variables: male sex (38.4% in our case), occupational dermatitis (21.2%), atopic dermatitis (15%), hand involvement (39.7%), leg involvement (4.4%), face involvement (7.3%), and age >40 years (50.2%).

Associations Between Variables

In the following section, we present our findings for the different study variables analyzed and discuss statistically significant associations detected with other variables.

- *Age*. The prevalence of patch test positivity increased with age, reaching a peak in patients aged 60 to 69 years, although the differences compared with other age groups were not statistically significant. There was a predominance of female patients in all age groups, explaining the greater proportion of female than male patients in the group as a whole. A diagnosis ruling out contact dermatitis predominated in all age groups except the 0-9 year group, in which allergic contact dermatitis was most common. Age was also found to be associated with the cause of contact dermatitis, with significant associations found for metals in the 10-59 age group, household products in the 30-59 age group, drugs in the 50-69 age group, and cosmetics in the 20-49 age group.
- *Sex*. This variable was significantly associated with occupation, with shoemakers, carpenters, drivers, electricians, construction workers, and rubber industry workers predominating in the group of men, and homemakers and domestic workers predominating in the group of women. The greatest number of positive patch test results was detected in the 20-29 age group in the case of women and in the 50-59 age group in the case of men, confirming that sensitization occurs at an earlier age in women (Figures 1 and 2). It is noteworthy that a positive association with occupation was detected in 68.7% of sensitized male patients; this association was not found for 74.1% of the women.
- *Percentage of positive patch tests*. The proportion of women with patch test positivity (63%) was significantly higher than that of men ($P<.001$). Patch test positivity was also significantly associated with occupation (indicating the existence of job-specific allergens) and diagnosis (at least 1 positive result was detected in 99.3% of patients with allergic contact dermatitis, 63.9% of those with irritant contact dermatitis, and 100% of those with allergic contact photodermatitis).
- *Clinical diagnosis*. A time since onset of between 1 month and less than a year was significantly associated with all diagnoses except the 2 forms of contact photodermatitis, where the predominant time since onset was less than a year. Hand lesions were present in 47.9% of patients with allergic contact dermatitis and in 56.1% of those with irritant contact dermatitis. Over half (57.3%) of the patients with occupational contact dermatitis had irritant contact dermatitis. On analyzing the patients by sex, the contact dermatitis lesions were of occupational origin in 68.7% of men but just 25.9% of women. Metals and drugs were predominantly associated with allergic contact dermatitis and household products with irritant contact dermatitis.

Prevalence of Sensitization

Of the 673 female patients studied, 424 (63%) had at least 1 positive patch test result; the total number of sensitizations was 1088 (73.4%) (sensitization index [number of sensitizations per patient], 2.6). The most common allergens detected were nickel sulfate (42.5%), palladium chloride (17.1%), cobalt chloride (13.5%), potassium dichromate (6.7%), PPD (6.5%), and fragrance mix (6.5%). Of the 419 male patients studied, 177 (42.2%) had at least

Table 2 Distribution of Sensitization to Allergens From Standard Series by Sex, Total Number of Positive Results by Allergen, and Percentage of Sensitizations With Positive Relevance for Each Allergen

Standard Patch Test Series Allergens	Sex						Positive Relevance
	Male Patients (n=419)		Female Patients (n=673)		Positive Results		
	+	%	+	%	No.	%	%
Potassium dichromate (0.5%)	37	8.8	45	6.7	82	7.5	91.5
PPD 1%	23	5.5	44	6.5	67	6.1	55.2
Cobalt chloride (1%)	27	6.4	91[a]	13.5[a]	118	10.8	87.3
Balsam of Peru (25%)	22	5.3	36	5.4	58	5.3	37.9
Nickel sulfate	34	8.1	286[a]	42.5[a]	320	29.3	96.3
Nickel sulfate (2.5%)[c]	15	3.6	155[a]	23[a]	170	15.5	98.8
Mercapto mix (1%)	3	0.7	6	0.9	9	0.8	100
Neomycin sulfate (20%)	3	0.7	10	1.5	13	1.2	84.6
Palladium chloride (1%)	13	3.1	115[a]	17.1[a]	128	11.7	96.1
Gold sodium thiosulfate (0.25%)	3	0.7	6	0.9	9	0.8	44.4
Thiuram mix (1%)	18	4.3	18	2.7	36	3.3	97.2
Colophonium (20%)	14[b]	3.3[b]	6	0.9	20	1.8	75
IPPD (0.1%)	12[b]	2.9[b]	4	0.6	16	1.5	81.3
Quinoline mix (6%)	0	0	0	0	0	0	0
Clioquinol (5%)	3	0.7	1	0.2	4	0.4	75
Chlorquinaldol (5%)	1	0.2	0	0	1	0.09	0
Parabens (16%)	3	0.7	5	0.7	8	0.7	75
Carba mix (3%)	5	1.2	3	0.5	8	0.7	87.5
Lanolin alcohol (30%)	6[b]	1.4[b]	3	0.5	9	0.8	44.4
Epoxy resins (1%)	8[b]	1.9[b]	1	0.2	9	0.8	88.9
Fragrance mix (8%)	25	6	44	6.5	69	6.3	59.4
Ethylenediamine (1%)	2	0.5	5	0.7	7	0.6	42.9
Benzocaine (5%)	9	2.6	16	2.4	25	2.3	16
Thiomersal (0.1%)	16	3.8	29	4.3	45	4.1	8.8
Mercury (0.5%)	11	2.6	14	2.1	25	2.3	16
PTBP formaldehyde resin (1%)	8	1.9	14	2.1	22	2	86.4
Mercaptobenzothiazole (2%)	3	0.7	2	0.3	5	0.4	100
Cinnamic alcohol (1%)	1	0.2	2	0.3	3	0.3	33.3
Cinnamic aldehyde (1%)	0	0	4	0.6	4	0.4	50
Eugenol (1%)	6	1.4	4	0.6	10	0.9	70
Amyl cinnamic aldehyde (1%)	0	0	1	0.2	1	0.09	0
Hydroxycitronellal (1%)	3	0.7	8	1.2	11	1	81.8
Geraniol (1%)	4	0.9	8	1.2	12	1.1	75
Isoeugenol (1%)	7	1.7	5	0.7	12	1.1	83.3
Oak moss (1%)	7	1.7	6	0.9	13	1.2	76.9
Sorbitan sesquioeate (20%)	0	0	1	0.2	1	0.09	100
Quaternium-15 (1%)	4	0.9	4	0.6	8	0.7	87.5
Lactone mix (0.1%)	0	0	1	0.2	1	0.09	0
Imidazolidinyl urea (2%)	2	0.5	2	0.3	4	0.4	100
Cetyl/stearyl alcohol (20%)	4	0.9	0	0	4	0.4	100
Euxyl K-400 (1%)	10[b]	2.4[b]	5	0.7	15	1.4	73.3
Dibromo-dicyanobutane (0.3%)	10	2.4	7	1	17	1.6	76.5
Phenoxyethanol (1%)	1	0.2	1	0.2	2	0.2	100
Tixocortol pivalate (1%)	1	0.2	6	0.9	7	0.6	100
Budesonide (0.1%)	3	0.7	2	0.3	5	0.5	80
Hydrocortisone-17-butyrate (1%)	0	0	4	0.6	4	0.4	75
Formaldehyde (1%)	8	1.9	7	1	15	1.4	60
Kathon CG (0.01%)	3	0.7	11	1.6	14	1.3	64.3
Turpentine (10%)	3	0.7	2	0.3	5	0.4	40
Propylene glycol (5%)	1	0.2	0	0	1	0.09	100

Table 2 Distribution of Sensitization to Allergens From Standard Series by Sex, Total Number of Positive Results by Allergen, and Percentage of Sensitizations With Positive Relevance for Each Allergen *(continuation)*

Standard Patch Test Series Allergens	Sex						Positive Relevance
	Male Patients (n=419)		Female Patients (n=673)		Positive Results		
	+	%	+	%	No.	%	%
P-toluene sulfonamide formaldehyde resin (10%)	0	0	12a	1.8a	12	1.1	100
Diallyl disulfide (1%)	1	0.2	18a	2.7[a]	19	1.7	94.7
Total	395	1088	1483	80			

Abbreviations: IPPD, isopropyl-phenyl PPD; PPD, paraphenylenediamine; PTBP, para-tertiary butylphenol.
[a]Sensitizations that were statistically significant in female patients.
[b]Sensitizations that were statistically significant in male patients.
[c]Tested in 703 patients only.

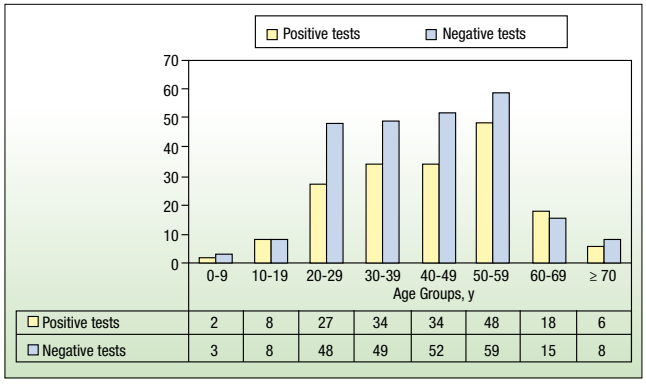

Figure 1 Distribution of male patients by skin patch test results and age group (absolute numbers).

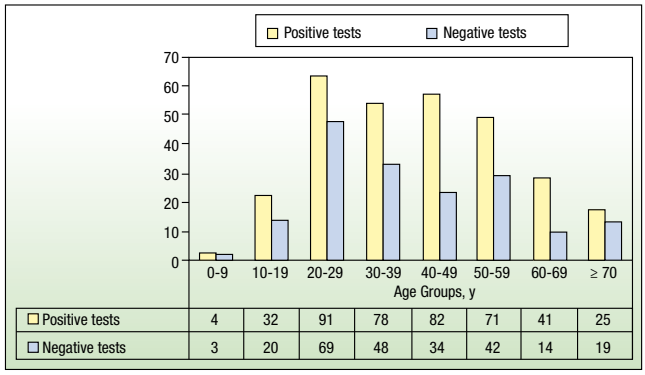

Figure 2 Distribution of female patients by skin patch test results and age group (absolute numbers).

1 positive result, with a total of 395 sensitizations (26.6%) (sensitization index, 2.2). The most common allergens in this group were potassium dichromate (8.8%), nickel sulfate (8.1%), cobalt chloride (6.4%), fragrance mix (6%), and PPD (5.5%) (Table 2).

- *Nickel sulfate (29.3%)*. Sensitization to 5% nickel sulfate was significantly associated with sex ($P<.001$) as 89.4% of sensitized patients were female (prevalence of sensitization, 42.5%) and clinical relevance (positive patch test result in 96.3% of cases). Nickel sulfate 5% was also significantly associated with occupational origin stratified by sex, as 94.4% of men that tested positive worked with this substance (high exposure among metalworkers). An occupational origin was not detected in 76.7% of the women sensitized to this agent.
- *Palladium chloride (11.7%)*. Significantly, 89.8% of the positive patch tests to 1% palladium chloride were in female patients ($P<.001$) (prevalence of sensitization, 17.1%). Clinical relevance was detected in 91.1% of all patients sensitized to this metal.
- *Cobalt chloride (10.8%)*. Sensitization to 1% cobalt chloride was significantly associated with sex ($P<.001$); 77.1% of the positive patch test results were in female patients (prevalence of sensitization,13.5%). Clinical relevance was positive in 92.6% of men and 85.7% of women. A significant association was also found between occupation and sex for 1% cobalt chloride, with an occupational origin detected in 89.5% of men and 15% of women sensitized to the substance.
- *Potassium dichromate (7.5%)*. The most common allergen in men was 0.5% potassium dichromate, although the differences with women were not significant ($P=.191$) (prevalence of sensitization in men, 8.8%). Sensitization to 0.5% potassium dichromate was significantly associated with occupational exposure, primarily attributable to exposure to cement among construction workers. An occupational origin was detected in 78.1% of men sensitized to this substance; this origin was not detected in 84.8% of women. The association between these metals is shown in Figure 4. The strongest association was found between nickel sulfate and palladium (weighted κ statistic of 0.46, indicating moderate agreement).[42]
- *Fragrance mix (6.3%)*. Sensitization to 8% fragrance mix was not significantly associated with any of the variables studied, although we did observe an increase

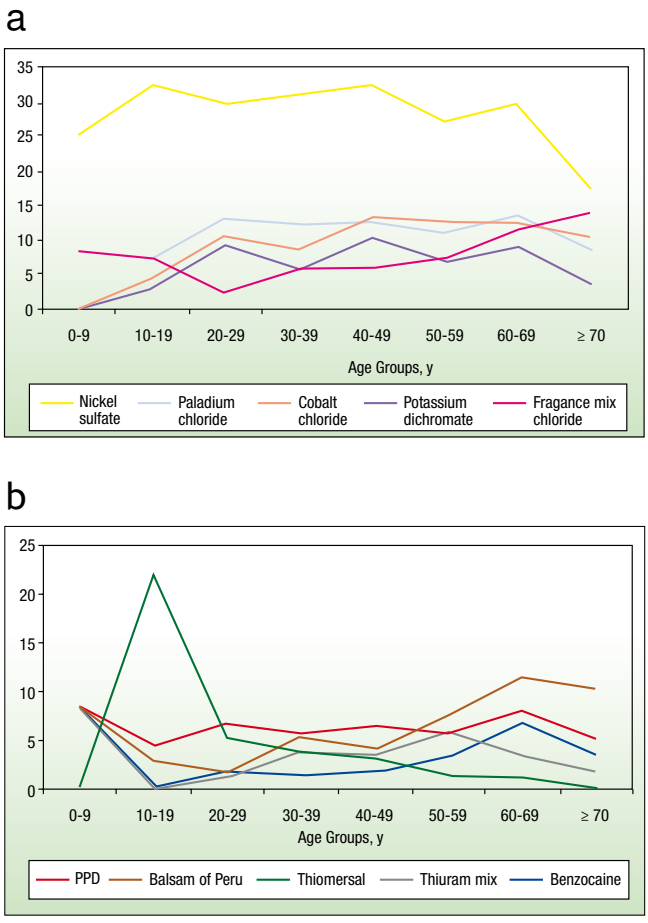

Figure 3 A, graph showing prevalence of sensitization to nickel sulfate, palladium chloride, cobalt chloride, potassium dichromate, and fragrance mix by age group. B, Graph showing prevalence of sensitization to paraphenylenediamine (PPD), balsam of Peru, thiomersal, thiuram mix, and benzocaine by age group.

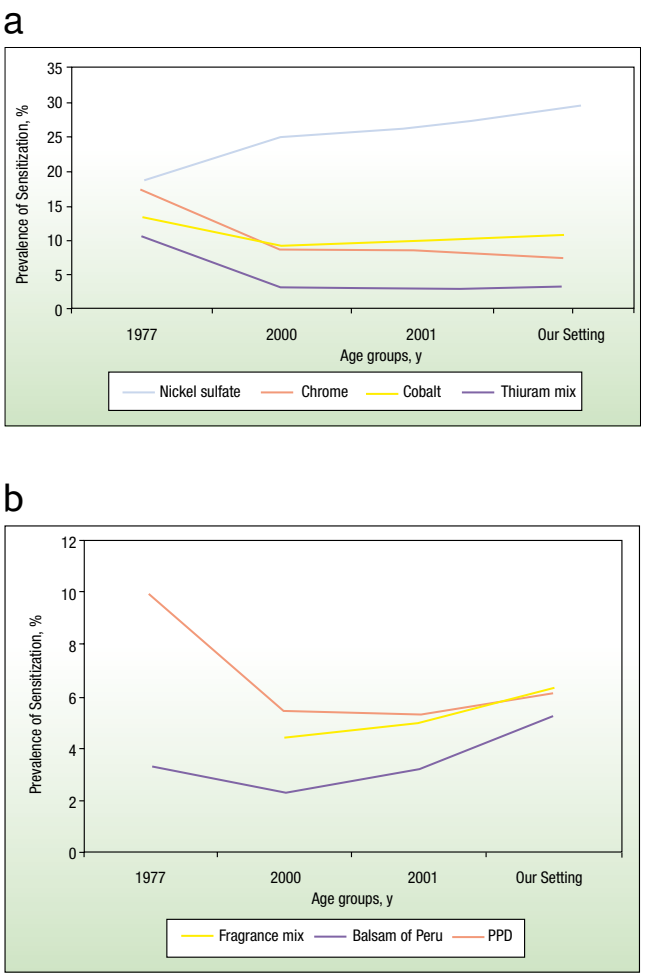

Figure 4 Changes in prevalence of sensitization to the most common allergens in Spanish studies (1977, 2000, and 2001) and comparison of results from our series. PPD indicates paraphenylenediamine.

in the prevalence of sensitization with age (highest in patients older than 70 years) (Figure 3A). We detected a significant association between positive patch test results to the fragrance mix, balsam of Peru, and rosin (all fragrance sensitization markers); 39.1% of patients sensitized to the fragrance mix were also sensitized to balsam of Peru (moderate agreement, weighted κ statistic of 0.40) and 7.3% were sensitized to rosin (poor agreement, weighted κ statistic of 0.08). Concordance analysis revealed good agreement (weighted κ statistic of 0.61) between the fragrance mix and its components, with 52.2% of patients with fragrance mix positivity also testing positive to at least 1 of the components of this mix. Conversely, 81.8% of the patients sensitized to a component of the fragrance mix had a positive test result to the mix.

- *PPD (6.1%)*. There was no statistically association between 1% PPD positivity and any of the other variables analyzed, although the highest prevalence of sensitization was detected in patients older than 70 years (Figure 3b). An occupational origin was detected in 31.3% of the patients with a positive result to 1% PPD, attributable to exposure to this substance among hairdressers, although the association was not significant.
- *Balsam of Peru (myroxylon pereirae) (5.3%)*: Of note was the fact that a positive result with 25% balsam of Peru was only significantly associated with a personal history of atopy (24.1% of patients sensitized to balsam of Peru 25% were atopic). This could be because this product is present in numerous topical treatments used by these patients.
- *Thiomersal (4.1%)*. Sensitization to 0.1% thiomersal was significantly associated with age (highest prevalence of

sensitization [22.1%] detected in the 10-19 age group) and atopy (28.9% of patients sensitized to the substance were atopic).

- *Thiuram mix (3.3%)*. Sensitization to 1% thiuram mix was significantly associated with occupation stratified by sex, with an occupational origin detected in 83.3% of the male patients sensitized to the substance; no evidence of occupational exposure was found in 66.7% of the female patients.
- *Benzocaine (2.3%)*. There was no statistically significant association between a positive reaction to 5% benzocaine and any of the study variables.
- *Mercury (2.2%)*. No significant associations were found for 0.5% mercury.
- *Para-tertiary butylphenol (PTBP)* formaldehyde *resin (2%)* There was a significant association between 1% PTBP formaldehyde resin and age, with the majority of positive patch test results detected in the 0-9 age group.
- *Colophonium (1.8%)*. There was a significant association between 20% rosin positivity and sex (70% of those that tested positive were male); 20% and 15% of patients sensitized to colophonium were also sensitized to the fragrance mix and balsam of Peru, respectively. These associations were statistically significant but with poor agreement (weighted κ statistics of 0.08 and 0.02, respectively).
- *Diallyl disulfide (1.7%)*. There was a significant association between 1% diallyl disulfide positivity and female sex, as 94.7% of all sensitized patients were female.

Table 3 shows the distribution of the sample by the most common occupations, the number of sensitizations per occupation, and the most common allergens per occupation. It also shows which occupations were most affected, the number of patients diagnosed, and the most common allergens detected.

On analyzing the results, we found that the proportion of positive results was 1.92% higher than it would have been had we used the standard GEIDAC series, indicating that the addition of new patch test allergens improves the sensitivity of standard test series in the detection of contact allergies.

Logistic Regression: Multivariate Analysis

Multiple logistic regression analysis was used to determine significant associations between patch test positivity and independent variables. The only significant association was found for female sex (OR=0.42; 95% CI, 0.32-0.54; $P<.001$), meaning that women had a greater risk of contact sensitization than men. Age was just above the limit of statistical significance ($P<.072$), while atopy was not statistically significant ($P<.264$) (Table 4A).

Multiple logistic regression analysis was performed separately for the most prevalent allergens. We found that female sex was significantly correlated with patch test positivity to nickel sulfate ($P<.001$), palladium chloride ($P<.001$), and cobalt chloride ($P<.001$), while sensitization to Euxyl K-400 (1,2-dibromo-2,4-dicyanobutan and 2-phenoxyethanol) was significantly higher in male patients ($P<.035$). Age was a significant risk factor for sensitization to cobalt chloride ($P<.013$), fragrance mix ($P<.001$), balsam of Peru ($P<.001$), thiuram mix ($P<.008$), benzocaine ($P<.006$), mercury ($P<.053$), isopropyl-phenyl PPD (IPPD) ($P<.008$), and neomycin sulfate ($P<.003$), with risk increasing at advanced ages. By contrast, sensitization to thiomersal was more prevalent at earlier ages ($P<.001$). A personal history of atopy was only significantly associated with sensitization to balsam of Peru, with the risk of this sensitization increasing in atopic patients ($P<.028$); an absence of a family history of atopy was significantly associated with sensitization to PTPB formaldehyde resin ($P<.019$). Occupational exposure was significantly associated with sensitization to potassium dichromate ($P<.001$), PPD ($P<.017$), thiuram mix ($P<.001$), and IPPD ($P<.001$). A lack of exposure, in contrast, was significant for nickel sulfate ($P<.007$) (Table 4B).

We performed this analysis for the most common occupations in our series and found that female sex was the only significant risk factor for sensitization in professional occupations ($P<.031$), while occupational exposure was a significant risk factor for sensitization in metalworkers ($P<.001$), construction workers ($P<.005$), and food workers ($P<.024$) (Table 4C).

Discussion

Several studies have shown that the development of allergic contact dermatitis is determined not only by exposure to a particular allergen but also by individual susceptibility.[43] The main intrinsic susceptibility factors are age,[2,44] sex,[2,45] race,[2,46] concomitant atopic dermatitis,[20,47] genetic factors,[48] and epidermal barrier integrity. Extrinsic susceptibility factors include occupation (which plays an essential role), geographic, environmental, and cultural factors (which influence skin reactivity), and physicochemical characteristics of allergens.[2]

In this study, we analyzed the influence of both intrinsic (sex, age, and atopy) and extrinsic (occupation) factors on contact sensitization.

One of the most noteworthy sociodemographic findings was the fact that there was a greater proportion of female patients than male patients (61.6% and 39.4%, respectively), a finding in agreement with the majority of reports from the literature.[11-13,16-37] While the exact role played by sex in the development of allergic contact dermatitis is still unknown, recent studies have concluded that female sex is a predisposing factor not only because women have greater susceptibility to developing this condition but also, importantly, because exposure patterns are different in men than in women.[45] A number of recent studies, for example, have confirmed that both exposure patterns and number of exposures are essential factors (even more important than sex) in allergen sensitization.[49,50] We found a significant association between sex and sensitization to several of the allergens we studied (Table 2).

Although we did not detect any significant associations between patch test positivity and age, in agreement with findings from numerous studies,[33-37] we did observe that sensitization occurred at an earlier age in women than in men (20-29 years and 50-59 years, respectively) (Figures 1 and 2). On analyzing sensitization by age group, our findings and those of other studies show that sensitization

Table 3 Distribution of Most Common Occupations by Total Number of Patients, Total Number of Sensitized Patients, and Number of Sensitizations

Occupation	Total No. of Patients	Sensitized Patients		Sensitizations, No.	Mean No. of Sensitizations/ Patient[a]	Most Common Allergens,[b] % of Total
		No.	%			
Homemaker	286	193	67.5	589	3.1	• Nickel sulfate (39.9) • Palladium chloride (15.4) • Cobalt chloride (14.3) • Fragrance mix (9.1)
Professional occupations	136	80	58.8	230	2.9	• Nickel sulfate (37.5) • Palladium chloride (15.4) • Cobalt chloride (11.8) • Thiomersal (11.8)
Metalworker	95	42	44.2	127	3	• Nickel sulfate (8.4) • Fragrance mix (8.4) • Potassium dichromate (7.4) • Cobalt chloride (7.4)
Clerical worker	69	36	52.2	119	3.3	• Nickel sulfate (33.7) • Cobalt chloride (11.6) • Palladium chloride (10.1) • Potassium dichromate (8.7)
Construction worker	58	30	51.7	84	2.8	• Potassium dichromate (29.3) • Cobalt chloride (13.8) • Nickel sulfate (13.8) • Thiuram mix (12.1)
Health worker	54	34	62.9	94	2.8	• Nickel sulfate (46.3) • Palladium chloride (22.2) • Thiomersal (11.1) • Cobalt chloride (5.6)
Cleaner	44	27	61.3	73	2.7	• Nickel sulfate (50) • Palladium chloride (22.7) • Cobalt chloride (20.5) • Potassium dichromate (11.4) • PPD (6.8)
Agricultural worker	42	19	45.2	63	3.3	• Nickel sulfate (14.3) • Palladium chloride (14.3) • Potassium dichromate (11.9) • PPD (7.1) • Fragrance mix (7.1)
Waiter	42	21	50	46	2.2	• Nickel sulfate (28.6) • Palladium chloride (19) • PPD (7.1) • Cobalt chloride (4.7) • Thiuram mix (4.7)
Retiree	37	18	48.7	82	4.5	• Nickel sulfate (10.8) • Balsam of Peru (10.8) • Fragrance mix (10.8)

Table 3 Distribution of Most Common Occupations by Total Number of Patients, Total Number of Sensitized Patients, and Number of Sensitizations *(Continuation)*

Occupation	Total No. of Patients	Sensitized Patients		Sensitizations, No.	Mean No. of Sensitizations/ Patient[a]	Most Common Allergens,[b] % of Total
		No.	%			
Construction worker	34	18	52.9	66	3.6	• Nickel sulfate (20.6) • Cobalt chloride (14.7) • Palladium chloride (11.8) • Fragrance mix (11.8)
Hairdresser	32	21	65.6	42	2	• Nickel sulfate (40.6) • PPD (34.4) • Thiomersal (5.9) • Kathon CG (5.9)

Abbreviation: PPD, paraphenylenediamine.
[a]Calculated per sensitized patient.
[b]Details given for most common allergens.

to thiomersal predominates in the early decades of life; in the following decades, the most common allergens are nickel sulfate in women and potassium dichromate in men, and in the last decades of life, the predominant sensitizing agents are balsam of Peru and fragrance mix.

The association between allergic contact dermatitis and atopic dermatitis has been the subject of much debate, with contradictory findings across studies.[51-56] One conclusion that can be drawn from an analysis of these studies is that there is no convincing evidence that allergic contact dermatitis is more common in atopic patients; this was also the case in our series, and indeed it appears that contact dermatitis and atopic dermatitis are independent conditions.[57] We detected a slightly higher rate of patch test positivity in atopic patients than in nonatopic patients (58.5% versus 54.1%), although the difference was not significant. It should also be noted that the nonatopic patients in our study were not healthy individuals. We analyzed the influence of atopy on sensitization to different allergens from the standard patch test series used in our study. In agreement with findings from other studies,[28,32,33,57] the only significant associations we found between atopic and nonatopic patients were for sensitization to thiomersal and balsam of Peru.

The prevalence of certain occupations in our series is a reflection of the geographic area studied, and, to a strong degree, the socioeconomic context of our province, with the greatest prevalence of sensitization detected in homemakers, hairdressers, and chefs.

Exposure patterns to allergens vary with changing trends, technological advances, and cultural traditions. Several studies have highlighted the fact that cultural variations influence the development of allergic contact dermatitis and modulate changes in the prevalence of sensitization between one town or city to the next.[58] On comparing the prevalence of sensitization to the allergens analyzed in our study with figures reported for Spain as a whole,[31,32] we found, first and foremost, that nickel sulfate was the most common contact allergen in both cases, coinciding with reports for other industrialized countries.[12,13,16-37,59] There are, however, variations in the rates of sensitization reported, with percentages ranging from 18.8%[60] to 26.6%.[33] In our series, 29.3% of those studied were sensitized to nickel sulfate. The growing prevalence of sensitization to this metal—linked to the deeply rooted tradition of ear piercing and use of earrings in very young children in Spain[61]—may become a serious national public health problem. To address this problem, preventive measures are required at the individual and collective level. In the latter case, compliance with European Union legislation requiring member states to reduce the nickel content in jewelry[61-63] should be ensured and the use of nickel-free jewelry encouraged.

We also detected a high prevalence of sensitization to cobalt chloride (10.8% vs 9.9% for Spain). The origin of this sensitization in women is its use in jewelry and in men, its use in the metal industry (common in our setting). It is also noteworthy that a significant proportion of patients with cobalt chloride sensitization were also sensitized to nickel sulfate.[42]

In agreement with findings from recent international studies,[64,65] we also detected an increase in the prevalence of sensitization to fragrance mix, balsam of Peru, and colophonium, reflecting a progressive increase in the prevalence of allergic contact dermatitis due to perfumes and cosmetics.

By contrast, we observed a decrease in potassium dichromate sensitization, attributable to the implementation of legislative measures and improved workplace safety. Sensitization to potassium dichromate, in agreement with reports in the medical literature,[32-36,59] was more common in men than in women in our series, and was attributable to exposure to cement in construction workers. We also detected a decrease in sensitization to thiomersal—which is presumed to cause iatrogenic sensitization due to its inclusion in obligatory vaccines around the world—and Kathon CG (methylisothiazolinone and methylchloroisothiazolinone). We believe that Kathon CG sensitization has decreased because of the legal requirement to specify the presence of this preservative on product labels and because it is being replaced by other, less allergenic, preservatives.

Table 4 Results of Multivariate Analysis

Table 4A

Variables	*P*	Odds Ratio (OR)	95% Confidence Interval (CI)	
			Lower Limit	Upper Limit
Female sex	<.001	0.422	0.328	0.542
Age	.072	0.993	0.985	1.001
Place of residence	.756	0.926	0.569	1.507
Atopy (personal)	.264	0.813	0.565	1.169
Atopy (family)	.600	0.877	0.536	1.434

Table 4B

Common Allergens	Variables	*P*	OR	95% CI	
				Lower Limit	Upper Limit
Nickel	Female sex	<.001	9.391	6.293	14.014
	Professional experience	.007	0.595	0.406	0.870
Palladium	Female sex	<.001	6.745	3.703	12.285
Cobalt	Female sex	<.001	2.564	1.607	4.090
	Age	.013	1.015	1.003	1.028
Chrome	Professional experience	<.001	0.377	0.227	0.626
Fragrance mix	Age	.001	1.026	1.010	1.042
PPD	Professional experience	.017	0.499	0.281	0.884
Balsam of Peru	Age	<.001	1.034	1.017	1.051
	Atopy (personal)	0.028	2.182	1.088	4.376
Thiomersal	Age	<.001	0.950	0.929	0.972
Thiuram mix	Age	.008	1.032	1.008	1.057
	Professional experience	<.001	0.135	0.062	0.291
Benzocaine	Age	.006	1.035	1.010	1.061
Mercury	Age	.053	1.025	1.000	1.051
PTPB formaldehyde resin	Atopy (family)	.019	3.895	1.249	12.151
IPPD	Age	.008	1.053	1.014	1.094
	Professional experience	.001	0.133	0.041	0.430
Euxyl K-400	Male sex	.035	0.303	0.100	0.921
Neomycin	Age	.003	1.054	1.018	1.093

Table 4C

Common Occupations	Variables	*P*	OR	95% CI	
				Lower Limit	Upper Limit
Professional occupations	Female sex	.031	0.380	0.158	0.913
Metalworker	Professional experience	.001	5.005	1.923	13.026
Builder	Professional experience	.005	5.541	1.683	18.241
Retiree	Age	.037	1.094	1.005	1.191
Food worker	Professional experience	.024	19.251	1.463	253.260

Abbreviations: IPPD, isopropyl-phenyl PPD; PPD, paraphenylendiamine.
Logistic regression model for contact sensitization in general (4A), for the allergens from the standard patch test series (4B) and for the most common occupations in our study (4C). Only statistically significant findings are shown.

We recommend that further studies be performed with palladium chloride, diallyl disulfide, and p-toluene sulfonamide formaldehyde resin within the framework of the GEIDAC, as the prevalence of sensitization in our series was greater than 1% for all these substances. It is noteworthy that the use of and number of sensitizations to palladium chloride have increased in recent years.[66] As is known, however, isolated allergy to palladium chloride is rare[42,66-69] (1.6% in our study). Most patients with palladium chloride sensitization also test positive

Table 5 Occupational Contact Dermatitis

Occupation	Total, No.	Patients With OCD		OCD, %	Common Allergens, %	Occupational ACD		Occupational ICD	
		No.	%			No.	%	No.	%
Metalworker	95	47	49.5	20.3	• Potassium dichromate (14.9) • Nickel sulfate (14.9) • Cobalt chloride (14.9) • Thiuram mix (10.6) • IPPD (10.6) • Epoxy resin (10.6)	24	51.1	23	48.9
Construction worker	58	27	46.6	11.6	• Potassium dichromate (55.6) • Nickel sulfate (25.9) • Cobalt chloride (25.9) • Thiuram mix (22.2)	20	74.1	7	25.9
Hairdresser	32	25	78.1	10.8	• PPD (44) • Nickel sulfate (44)	14	56	11	44
Waiter	42	24	57.1	10.3	• Nickel sulfate (29.2) • Palladium chloride (20.8)	7	29.2	17	70.8
Cleaner	44	19	43.2	8.2	• Nickel sulfate (47.4) • Palladium chloride (21.5) • Potassium dichromate (15.8)	7	36.8	12	63.2
Health worker	54	18	33.3	7.8	• Nickel sulfate (50) • Palladium chloride (22.2) • Thiuram mix (11.1)	4	22.2	14	77.8
Agricultural worker	42	15	35.7	6.5	• Potassium dichromate (26.7) • Ethylenediamine (13.3) • Formaldehyde (13.3)	5	35.7	9	64.3
Chef	17	10	58.8	4.3	• Nickel sulfate (40) • Thiuram mix (30) - Diallyl sulfide (20)	5	50	5	50
Food worker	34	9	26.5	3.9	• Nickel sulfate (33.3) • Cobalt chloride (33.3) • Balsam of Peru (22.2)	4	44.4	5	55.6

Abbreviations: ACD, allergic contact dermatitis; ICD, irritant contact dermatitis; IPPD, isopropyl-phenyl PPD; OCD, occupational contact dermatitis; PPD, paraphenylendiamine.

to nickel[17,52,67-70] (96.9%) and cobalt (35.9%), with these concomitant sensitizations occurring in patients with jewelry intolerance due to immunologic cross-reactivity between transition metals.[42,59,68,70] We analyzed this cross-reactivity in detail in our series and obtained very similar results to those reported elsewhere.[71] We also confirmed that the palladium-nickel association is much more common than the nickel-palladium association (96.9% and 38.8%, respectively).[42]

In agreement with reports from other studies conducted in Spain,[72,73] we found sensitization rates of over 1% for diallyl disulfide. This marker of contact sensitization to garlic was significantly associated with occupation (94.7% of those sensitized to diallyl disulfide were homemakers) and caused finger itch. Sensitization to p-toluene sulfonamide formaldehyde resin, the main sensitizing agent found in nail products,[24] was only detected in women aged 20 to 59 years, in whom it caused face and neck dermatitis.

It is known that occupation is a key factor in contact dermatitis; indeed 90% to 95% of all occupational skin diseases are a form of contact dermatitis,[74] the most common of which (80% of cases) is irritant contact dermatitis.[75] Based on statistics from different studies, occupational contact dermatitis is more prevalent in

certain professions than others (construction workers, health workers, hairdressers, and metalworkers[24,34,75,76]), in agreement with the findings for our series (Table 5). In our case, occupational contact dermatitis was most common in metalworkers (23%), consistent with reports in the literature,[12,27,32,34] and a reflection of the importance of this industry in our setting and the high associated risk.[77] The other professions most affected were construction workers (11.6%) and hairdressers, who, consistent with previous reports,[78] had the greatest prevalence of occupational contact dermatitis (present in 78.1%).

The findings of the present study represent an important starting point for evaluating the current epidemiological situation of contact dermatitis in our health care area. We believe that the results provide clinically relevant data that will contribute to a better understanding of this disease, which not only has a major impact on health-related quality of life, but also constitutes a considerable burden in terms of health care expenditure.

Conclusions

- Just over half (51.7%) of the patients in our series were diagnosed with a clinical form of contact dermatitis.
- Fifty-five percent had at least 1 positive patch test result. The prevalence of positive results increased progressively with age.
- Metals were the most common cause of contact sensitization.
- The occupations characterized by the greatest prevalence of sensitization were homemakers, hairdressers, chefs, and health workers. Occupational contact dermatitis was detected in 21.3% of all the patients studied, with metalworkers, construction workers, and hairdressers being the most strongly represented groups.
- Contact sensitization occurred at an earlier age in women (20-29 years) than in men (50-59 years); the prevalence of patch test positivity was also significantly higher in female than in male patients.

APPENDIX

INFORMED CONSENT FORM* FOR SKIN PATCH TESTING –
DERMATOLOGY DEPARTMENT,
HOSPITAL CLÍNICO UNIVERSITARIO DE VALLADOLID

_____.

Mr/Ms _____ aged ___ years, residing at

(street address): _____ Province of _____ and National ID no. _____.

Mr/Ms _____ aged ___ years, residing at

(street address): _____ Province of _____ with National ID no. _____ in my capacity

as _____.

(Tutor, legal representative) (Name and surnames of patient)

I DECLARE

That DOCTOR _____, a member of the Dermatology Department, has told me that, in my situation, it is recommendable to do SKIN PATCH TESTS.

1. The aim is to establish and confirm a clinical diagnosis by performing a test to reproduce a skin reaction to an allergen or allergens, possibly showing the existence of delayed sensitivity. This procedure may be recorded for scientific or educational purposes.
2. The doctor told me that I will have to avoid exercise, sport, and exertion, and that I must not get the test area wet during the procedure.
3. The procedure consists of placing patches containing potentially allergenic substances on my back and evaluating them after a week.
4. I understand that, even though the tests will be correctly chosen and performed, undesirable effects may occur, such as itching, reddening, irritation depigmentation or hyperpigmentation, scarring, or active sensitization (appearance of new allergies).
   Other risks or complications that may appear in view of my personal circumstances (previous state of health, age, profession, beliefs, etc) are:
   _____
5. It is considered that this is the most appropriate diagnostic test for my particular case, even though there may be alternatives that would be indicated in another case and that I have had the opportunity to discuss with the doctor. I have also been informed of the possible consequences of not doing the test that I have been recommended.

I have understood the explanations I have received, which were expressed in clear, simple language, and the doctor that dealt with me allowed me to make any observations I had and also clarified any doubts I expressed.
I also understand that I can withdraw this consent at any time without the need to given explanations.

Figure A1

I hereby declare that I am satisfied with the information I have received and that I understand the scope and risks of this diagnostic test. Accordingly:

I CONSENT

to undergoing SKIN PATCH TESTS.

In _____ on _____Place and date).

Signed: The doctor Signed: The patient Signed: The tutor or representative

PATIENT REFUSAL TO RECEIVE INFORMATION

When the doctor responsible for my test proposed telling me about the characteristics of the diagnostic test, life risks, and complications, I refused to receive this information.

In _____ on _____(Place and date).

Signed: The doctor Signed: The patient Signed: The tutor or representative

WITHDRAWAL

Mr/Ms_____aged __ years, residing at
(Nombre y apellidos del paciente)
(street address:_____ Province of _____ with National ID no. _____.

Mr/Ms _____ aged __years, residing at
(Nombre y apellidos
(street address):_____Province of _____ with National ID no._____ in my capacity as

of _____.

(Tutor, legal representative) (Name and surnames of patient)

I withdraw the consent I provided on (date) _____ and do not wish to continue with the diagnostic skin patch tests, which I consider terminated as of today.

In _____ on_____ (place and date).

Signed: The doctor Signed: The patient Signed: The tutor or representative

*This English version of the informed consent is an unvalidated translation, provided only for comprehension purposes.

Figure A1 *(Continuation)*

- The most common allergen was nickel sulfate. The probability of sensitization to this allergen was 9.39 times higher in female than in male patients and was significantly associated with user contact.
- Female sex was the only independent variable that was significantly associated with contact sensitization. It was also significantly associated with isolated sensitization to nickel sulfate, palladium chloride, and cobalt chloride.
- Age was significantly associated with the following allergens: cobalt chloride, fragrance mix, balsam of Peru, thiomersal, fragrance mix, benzocaine, mercury, IPPD, and neomycin sulfate.
- Occupational exposure to potassium dichromate, PPD, thiuram mix, and IPPD was significantly associated with sensitization to these allergens
- The patch test series used permitted a definitive diagnosis in 78.1% of patients diagnosed with contact dermatitis.

Conflicts of Interest

The authors declare no conflicts of interest.

Appendix 1

See Figure A1.

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