

Original Research Article

An epidemiological study of allergic contact dermatitis in Greece: prevalence of sensitization to an adapted European baseline series' allergens

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ABSTRACT

Background: Contact dermatitis is a common skin disorder related to environmental exposures affecting, all age groups, and both genders. The pattern of contact sensitization to a series of allergens included in the European baseline series has already been studied for a number of EU countries by the ESSCA Network. The current study aims to explore the patterns of contact dermatitis in Greece through a patch test against a large number of allergens provoking contact dermatitis.

Methods: Retrospective analyses of routine data of 668 patients were collected during 2014 in the Laboratory of Patch Testing, National Referral Centre of Occupational Dermatoses. Sensitization in all cases was tested with a battery of 28 allergens of the European baseline series and additional ones aiming to identify new sensitizations to inform the National baseline of allergens; information for an extended MOAHLFA index was also collected.

Results: One at least positive result was found in 61.5% of the patients while 19.1% of those found to be sensitized in two or more allergens. Nickel sulphate, fragrance mix and balsam of Peru were the most prevalent allergens in the total population, as well as with respect to gender. Nickel is the most frequent allergen of baseline series, a result which is in agreement with other reports.

Conclusions: Allergic contact dermatitis surveillance is of great importance towards the clinical and systematic understanding of the disease. Further studies should be directed towards that end, in order to facilitate more effective health policies.

Keywords: Contact dermatitis, Sensitization, Allergen, Prevalence, Greece

INTRODUCTION

Contact dermatitis is a common skin disorder related to environmental exposures affecting, all age groups, and both genders. According to Gell and Coombs classification, the type IV reaction of delayed-type hypersensitivity is evaluated, in patients previously

sensitized, which present clinical signs of contact dermatitis. Patch testing is a simple in vivo well-established method to diagnose allergic contact dermatitis.¹ This method consists of a very practical test, which facilitates the evaluation and diagnosis of allergic contact dermatitis through the skin exposure to the responsible allergens.

Recommendations of the European Society of Contact Dermatitis (ESCD) are regarded through appropriate changes for specific conditions of exposure in Greece according to labor, commercial, social and national habits. We applied the baseline series and available additional series according to the medical history of the patient.^{2,3} European baseline series include several categories of metals, fragrances, preservatives, rubbers, topical therapeutics and excipients. Our choice of additional series was based on clinical relevance and the patient's medical record.

Patch test results often vary between departments and laboratories, as well as between countries. Such variations may be partly attributable to systematic effects introduced by patient characteristics, differing exposures, patient selection, or methodological differences.

Data collection from the European Surveillance System on Contact Allergies (ESSCA Network) has a task to assess structure of patients sample (between countries and departments) and the overall yield concerning to baseline series (P-measure includes patients with at least one positive reaction to allergen of the baseline series). The pattern of contact sensitization to a series of allergens included in the European baseline series has already been studied for a number of EU countries by the ESSCA network.

The current study aims to explore the patterns of contact dermatitis in Greece through patch testing against a large number of allergens provoking contact dermatitis including those that are currently included in the European baseline series. To the best of our knowledge, this is the first report concerning this topic.

METHODS

Patients

A total number of 668 Greek Caucasian patients were admitted in our laboratory during 2014. Patients were recruited based on their dermatological profile, whereas all other biometric and anthropometric criteria were kept random. The diagnosis of contact dermatitis included the detection of at least one positive reaction to the chemicals panel used in the present study. The retrospective analysis included of routine data collected in the Laboratory of Patch Testing, National Referral Centre of Occupational Dermatoses, University Hospital "Andreas Syggros", National and Kapodistrian University of Athens, Medical School.⁴ The results refer to consecutive patients in order to avoid bias due to selective testing. Sensitization in all cases was tested with a battery of 28 allergens according to the European baseline series (with addition or omission of allergens due to individual country circumstances) and additional series aiming to identify sensitizations in order to inform the national baseline of allergens.

Inclusion criteria

All patients admitted to our department, with the suspicion of dermatitis, were included in the present study. Patients were selected randomly, in order to avoid biased selective inclusion.

Exclusion criteria

Patients admitted who were under some kind of anti-inflammatory treatment, under cyclosporine treatment, chronic use of corticosteroids, under chemotherapeutics treatments as well as suffering from other chronic dermatopathies were excluded from the present study.

Patch testing and clinical evaluation

We performed the patch testing according to the guidelines of the European Society of Contact Dermatitis.² The optimal exposure time was considered to be two days (48 h). Based on the respective guidelines, it is recommended to perform a test reading two times, where the first takes place after the removal of the patches (48 h) and the second 2-4 days later.

The maximum reaction was assessed between day 3 and day 4 after the application of allergens, in the majority of patients. A third reading at day 7 was recommended, in order to reveal positive reactions to either slow-reacting allergens (neomycin, corticosteroids) which are late reactors. Reaction was assessed as positive/allergic in terms of morphology lesions on a scale of i) weak +, (ii) strong ++ and (iii) extreme +++, according to the criteria of the International Contact Dermatitis Research Group (ICDRG) and everything else as negative (including irritant reactions). This was assessed as the patch test outcome. Patch was applied at the middle upper back, which is considered the ideal anatomical position for patch testing. Patches were always applied on a hairless and free of lesions skin.

Clinical parameters and data collection

Clinical parameters

The MOAHLFAP index included characteristics of patients such as M (male), O (occupational dermatitis (OD)), A (atopic dermatitis (AD)), H (hand dermatitis (HD)), L (leg dermatitis (LD)), F (face dermatitis (FD)), A (age 40+), P (at least one positive).⁵ Further on, we have used the criterion of trunk and generalized dermatitis in our patients. We also report trunk and generalized dermatitis.⁶ This index contributes to the group description, stratifying the results as to the presence of sensitization prevalence and provides a multifunctional analysis in order to estimate the risk of sensitization (for example being male with occupational contact dermatitis).⁷

Clinical relevance is the possibility that sensitivity to a contact allergen is connected etiologically to a current or previous episode of contact dermatitis. The purpose was to combine medical history, clinical examination, accessing of exposure, and chemical analysis of the substance in order to contribute to a detailed analysis of the clinical relevance between positive allergens and the current episode of dermatitis.

Clinical data

The analysis included the collection of routine data from our laboratory performing the patch test. We collected demographic, clinical data and patch testing results related to patients suspected with allergic contact dermatitis. The results were documented to an electronic data base. In case of patient’s repeated admittance, during our study period, only the initial patch test result was considered.

We calculated the overall prevalence of at least one positive reaction to a hapten of the EBS in the study population, in the different age groups and in patients with and without AD (atopic dermatitis). AD was evaluated according to the Hanifin & Rajka (1980) criteria.⁸

Data analysis

Patient’s characteristics are presented with absolute and relative frequencies (%). The proportion of positive reactors was also calculated. This proportion was further adjusted over age and sex, following the pertinent guidelines for the statistical analysis of patch test data, using the *Segi* world standard population distribution.⁹⁻¹¹ Most common allergens by patient characteristics are also presented with absolute and relative frequencies (%).

Chi-square test of independence was used to evaluate the association between having multiple positive reactions (≥ 3 from the first 28, with $\geq 1\%$) and patients’ characteristics. The characteristics that were found statistically significant were entered in a logistic regression model in order to evaluate the probability of having multiple positive reactions. The modeling of a quantitative variable based on one or more qualitative and quantitative parameters, was performed through linear regression. Multiple logistic regression was performed in order to evaluate the probability of having multiple positive reactions.

The level of statistical significance was set to $\alpha=5\%$. All analyses were conducted using the statistical software STATA SE v.13. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request. Venn diagrams were generated with the venn diagram online generator. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics statement

All experiments were conducted in compliance with the international biomedical studies stipulations, with reference to the Declaration of Helsinki of the World Medical Association. No personal data of patients were kept, while it was impossible to trace back any personal data from the data collected for the present study.

RESULTS

Patient cohort

A total number of 668 Greek Caucasian patients (211 males, 457 females) were admitted in our laboratory during 2014. Mean age of all patients was 44.91 ± 18.95 years, where males were 45.49 ± 21.17 years old and females were 44.66 ± 17.86 years old.

The MOAHLFA Index

We have estimated the MOAHLFA index for our sample of patients. In particular, 209 (31.29%) males were found to be positive for at least one allergen, 211 (31.55%) patients were found to be positive for occupational dermatitis, 234 (34.98%) for atopic dermatitis, 336 (50.20%) for hand dermatitis and 162 (24.26%) for leg dermatitis. We have also estimated the positive patients for trunk dermatitis (203, 30.28%) and head dermatitis (52, 7.29%). Further on, 389 (58.19%) patients were older than 40 years of age, while 411 (61.48%) were positive for at least one allergen. The MOAHLFA index is summarized in Table 1.

Table 1: Characteristics of patients (MOAHLFA index) (N=667).

| Characteristics | | n (%) |
|-------------------------------------|----------|-------------|
| Males | M | 209 (31.29) |
| Occupational dermatitis | O | 211 (31.55) |
| Atopic dermatitis | A | 234 (34.98) |
| Hand dermatitis | H | 336 (50.20) |
| Leg dermatitis | L | 162 (24.27) |
| Face dermatitis | F | 212 (31.65) |
| Age 40+ | A | 389 (58.19) |
| At least 1 positive reaction | | 411 (61.48) |
| Trunk dermatitis | | 203 (30.28) |
| Head dermatitis | | 52 (7.79) |

Frequencies of the most prevalent allergens

From our results it appeared that the most prevalent allergen was nickel sulphate 5% (23.90% adjusted relative frequency), followed by other allergens in the following descending order: fragrance mix (12.00%), thiomersal 0.1% (9.60%), cobalt chloride 1% (8.40%), balsam of peru (7.80%), paraphenylene diamine 1% (5.70%), potassium dichromate 0.5% (5.50%), ethylene diamene 1% (4.60%), formaldehyde 2% (3.00%), 5-

chloro-2-methyl-4-isothiazolin-3-one-2-methyl-4-isothiazoin-3-one (3:1 in water) (Kathon) 0.01% (3.00%), neomycin sulphate 20% (2.60%), thiuram mix 1% (2.50%), budenocide 0.01% (2.10%), colophony 20% (1.90%), black rubber mix 0.1% (1.60%), wool alcohols 30% (1.60%), paretertiary butyl phenol 1% (1.40%),

quaternium 15 1% (1.40%), paraben mix 15% (1.30%), benzocaine 5% (1.20%) and mercapto mix 2% (1.00%). Remaining allergens manifested an adjusted relative frequency below 1%. The relative frequencies of most prevalent allergens are summarized in Table 2.

Table 2: Patch test results and the respective frequencies of the 28 most prevalent allergens (crude relative frequencies include those observed with respect to the total sample size, while adjusted relative frequencies are with respect to the sample size that was actually measured).

| Inv. | Allergen | Number of patients tested | % positives (crude) | % positives (adjusted) | 95% CI | |
|------|--|---------------------------|---------------------|------------------------|-----------|-----------|
| | | | | | Lower (%) | Upper (%) |
| 1 | Nickel sulphate 5% | 667 | 25.90 | 23.90 | 22.10 | 25.80 |
| 2 | Fragrance mix (i) 8% | 667 | 14.20 | 12.00 | 10.60 | 13.40 |
| 3 | Thiomersal 0.1% | 667 | 7.10 | 9.60 | 8.30 | 10.90 |
| 4 | Cobalt chloride 1% | 667 | 7.50 | 8.40 | 7.20 | 9.60 |
| 5 | Balsam of peru 25% | 667 | 9.80 | 7.80 | 6.60 | 9.00 |
| 6 | Paraphenylenediamine 1% | 667 | 4.90 | 5.70 | 4.60 | 6.70 |
| 7 | Potassium dichromate 0.5% | 667 | 5.60 | 5.50 | 4.50 | 6.50 |
| 8 | Ethylenediamine 1% | 667 | 5.10 | 4.60 | 3.60 | 5.50 |
| 9 | Formaldehyde 2% | 667 | 2.90 | 3.00 | 2.20 | 3.70 |
| 10 | 5-chloro-2-methyl-4-isothiazolin-3-one-2-methyl-4-isothiazoin-3-one (3:1 in water)(kathon) 0.01% | 667 | 2.80 | 3.00 | 2.20 | 3.70 |
| 11 | Neomycin sulphate 20% | 667 | 2.90 | 2.60 | 1.90 | 3.30 |
| 12 | Thiuram mix 1% | 667 | 2.40 | 2.50 | 1.80 | 3.20 |
| 13 | Budesonide 0.01% | 667 | 2.80 | 2.10 | 1.40 | 2.70 |
| 14 | Colophony 20% | 667 | 2.10 | 1.90 | 1.30 | 2.50 |
| 15 | Black rubber mix 0.1% | 667 | 1.40 | 1.60 | 1.00 | 2.10 |
| 16 | Wool alcohols 30% | 667 | 1.50 | 1.60 | 1.10 | 2.20 |
| 17 | Paratertiary butyl phenol 1% | 667 | 1.30 | 1.40 | 0.80 | 1.90 |
| 18 | Quaternium 15 1% | 667 | 1.10 | 1.40 | 0.90 | 2.00 |
| 19 | Paraben mix 15% | 667 | 1.10 | 1.30 | 0.80 | 1.80 |
| 20 | Benzocaine 5% | 667 | 1.10 | 1.20 | 0.70 | 1.60 |
| 21 | Mercapto mix 2% | 667 | 0.80 | 1.00 | 0.50 | 1.40 |
| 22 | Primin 0.01% | 667 | 0.80 | 0.80 | 0.40 | 1.20 |
| 23 | Epoxy resin 1% | 667 | 0.70 | 0.70 | 0.30 | 1.00 |
| 24 | Mercury 0.05% | 667 | 0.60 | 0.50 | 0.20 | 0.80 |
| 25 | Quinoline mix (oxyquinoline mix) 6% | 667 | 0.50 | 0.40 | 0.10 | 0.70 |
| 26 | 2-mercaptodenzothiazole (mbt) 2% | 667 | 0.20 | 0.20 | 0.00 | 0.40 |
| 27 | Benzalkonium chloride 0.1% | 667 | 0.40 | 0.20 | 0.00 | 0.40 |
| 28 | Petrolatum control 100% | 667 | 0.00 | 0.00 | 0.00 | 0.00 |

Frequencies of the most prevalent allergens with respect to gender

We have further analyzed the prevalence of positive allergens with respect to gender. In particular, the most prevalent allergen for females was nickel sulphate (32.03%), followed by fragrance mix (14.73%) and balsam of Peru (8.91%). The remaining most prevalent allergens, for females, were the following in descending order: cobalt chloride (7.66%), thiomersal 0.1% (6.92%), paraphenylenediamine 1% (5.89%), potassium dichromate 0.5% (4.71%), ethylenediamine 1% (4.34%),

neomycin sulphate 20% (3.09%), kathon 0.01% (3.09%), formaldehyde 2% (2.87%), budenocide 0.01% (2.36%), colophony 20% (1.91%), thiuram mix 1% (1.77%), black rubber mix 0.1% (1.55%), quaternium 15 1% (1.40%), benzocaine 5% (1.33%), paratertiary butyl phenol 1% (1.33%) and wool alcohols 30% (1.25%). Respectively, the most prevalent allergens for males were fragrance mix (13.11%), nickel sulphate 5% (12.46%) and balsam of Peru (11.65%). The remaining most prevalent allergens, for males, were the following in descending order:

Potassium dichromate 0.5% (7.61%), thiomersal 0.1% (7.61%), cobalt chloride 1% (7.28%), ethylenediamine 1% (6.80%), thiuram mix 1% (3.72%), budesonide 0.01% (3.72%), formaldehyde 2% (3.07%), paraphenylenediamine 1% (2.75%), neomycin sulphate 20% (2.43%), colophony 20% (2.43%), kathon 0.01% (2.27%), wool alcohols 30% (2.10%), paraben mix 15%

(1.46%), black rubber mix 0.1% (1.13%), epoxy resin 1% (1.13%) and paratertiary butyl phenol 1% (1.13%). All frequencies are summarized in Table 3. Interestingly, most allergens were common between the two genders, with the exception of benzocaine 5% and quaternium-15 1%, which is unique to females, while paraben mix 15% and epoxy resin 1%, which is unique to males (Figure 1).

Table 3: Patch test results and the respective frequencies of positive reactions for the most prevalent allergens with respect to gender.

| Females | | | | Males | | | |
|------------------------------|---------------------------|------------------------------|-------------------------|-----------------------------|---------------------------|------------------------------|-------------------------|
| Allergen | Number of patients tested | Number of positive reactions | % of positive reactions | Allergen | Number of patients tested | Number of positive reactions | % of positive reactions |
| Nickel sulphate 5% | 459 | 147 | 32.03 | Fragrance mix (I) 8 | 209 | 27 | 13.11 |
| Fragrance mix (I) 8% | 459 | 68 | 14.73 | Nickel sulphate 5 | 209 | 26 | 12.46 |
| Balsam of Peru 25% | 459 | 41 | 8.91 | Balsam of peru 25 | 209 | 24 | 11.65 |
| Cobalt chloride 1% | 459 | 35 | 7.66 | Potassium dichromate 0.5 | 209 | 16 | 7.61 |
| Thiomersal 0.1% | 459 | 32 | 6.92 | Thiomersal 0.1 | 209 | 16 | 7.61 |
| Paraphenylene diamine 1% | 459 | 27 | 5.89 | Cobalt chloride 1 | 209 | 15 | 7.28 |
| Potassium dichromate 0.5% | 459 | 22 | 4.71 | Ethylenediamine 1 | 209 | 14 | 6.80 |
| Ethylenediamine 1% | 459 | 20 | 4.34 | Thiuram mix 1 | 209 | 8 | 3.72 |
| Neomycin sulphate 20% | 459 | 14 | 3.09 | Budesonide 0.01 | 209 | 8 | 3.72 |
| Kathon 0.01% | 459 | 14 | 3.09 | Formaldehyde 2 | 209 | 6 | 3.07 |
| Formaldehyde 2% | 459 | 13 | 2.87 | Paraphenylenediamine 1 | 209 | 6 | 2.75 |
| Budesonide 0.01% | 459 | 11 | 2.36 | Neomycin sulphate 20 | 209 | 5 | 2.43 |
| Colophony 20% | 459 | 9 | 1.91 | Colophony 20 | 209 | 5 | 2.43 |
| Thiuram mix 1% | 459 | 8 | 1.77 | Kathon 0.01 | 209 | 5 | 2.27 |
| Black rubber mix 0.1% | 459 | 7 | 1.55 | Wool alcohols 30 | 209 | 4 | 2.10 |
| Quaternium 15 1% | 459 | 6 | 1.40 | Paraben mix 15 | 209 | 3 | 1.46 |
| Benzocaine 5% | 459 | 6 | 1.33 | Black rubber mix 0.1 | 209 | 2 | 1.13 |
| Paratertiary butyl phenol 1% | 459 | 6 | 1.33 | Epoxy resin 1 | 209 | 2 | 1.13 |
| Wool alcohols 30% | 459 | 6 | 1.25 | Paratertiary butyl phenol 1 | 209 | 2 | 1.13 |

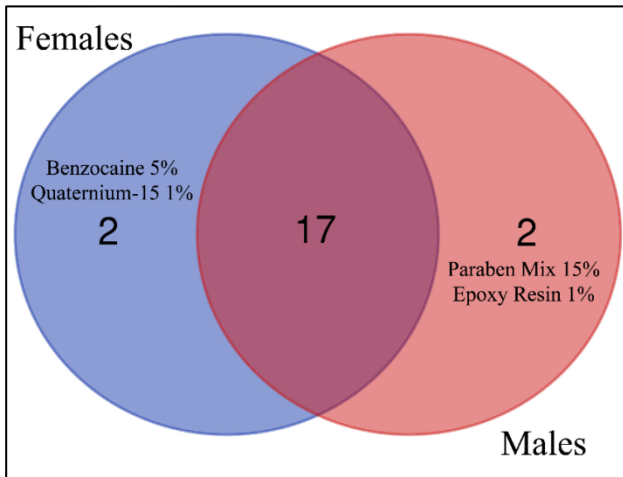


Figure 1: Venn diagram of the common allergens with respect to gender. Emphasis is given to the differences between the two genders. In particular, females manifested two different allergens with respect to males that is benzocaine 5% and quaternium-15 1% while males differed from females as to paraben mix 15% and epoxy resin 1%.

Frequencies of the most prevalent allergens with respect to age groups

We have further analyzed the prevalence of positive allergens with respect to age groups. Patients have been divided into two main age groups, namely those under 40 years of age (age<40 years) and those over 40 years of age (age>40 years). In particular, the most prevalent allergen for those of age more than 40 years of age, nickel sulphate 5% (28.21%), thiomersal 0.1% (14.29%) and fragrance mix (I) 8% (11.02%) were the most prevalent allergens for those of more than 40 years of age. The remaining most prevalent allergens, for those of more than 40 years of age, were the following in descending order: cobalt chloride 1% (9.32%), paraphenylenediamine 1% (6.78%), balsam of Peru 25% (6.05%), potassium dichromate 0,5% (5.08%), ethylenediamine 1% (4.00%), kathon 0,01% (3.63%), formaldehyde 2% (3.39%), neomycin sulphate 20% (2.54%), black rubber mix 0.1% (1.94%), thiuram mix 1% (1.82%), colophony 20% (1.82%), wool alcohols 30% (1.82%), paratertiary butyl phenol 1% (1.82%), quaternium 15 1% (1.82%), budesonide 0,01% (1.69%), benzocaine 5% (1.45%), mercapto mix 2% (0.97%) and paraben mix 15% (0.97%). Respectively, the most prevalent allergens for those below 40 years of age were nickel sulphate 5% (24.26%), fragrance mix (i) 8% (16.52%) and balsam of peru 25% (12.43%). The remaining most prevalent allergens, for those of below than 40 years of age, were the following in descending order: cobalt chloride 1% (6.26%), potassium dichromate 0.5% (6.00%), ethylenediamine 1% (5.91%), paraphenylenediamine 1% (3.57%), budesonide 0.01% (3.57%), neomycin sulphate 20% (3.13%), thiuram mix 1% (2.78%), formaldehyde 2% (2.61%), colophony 20%

(2.26%), kathon 0.01% (2.26%), thiomersal 0.1% (2.00%), wool alcohols 30%(1.30%), paraben mix 15% (1.13%), primin 0.01% (1.13%) and black rubber mix 0.1% (1.04%). All frequencies are summarized in Table 4.

Frequencies of the allergens with respect to the localization of dermatitis

Analyzing the frequencies of positive patch tests with respect to the localization of the diagnosed dermatitis. In particular, the three most prevalent allergens in hand dermatitis were nickel sulphate 5% (22.72%), fragrance mix 8% (12.36%) and balsam of Peru (8.64%). Similarly, the three most prevalent allergens in face dermatitis were nickel sulphate (28.50%), fragrance mix 8% (17.51%) and balsam of Peru 25% (9.29%). Further on, the three most prevalent allergens for head dermatitis were nickel sulphate 5% (25.33%), paraphenylenediamine 15% (19.23%) and fragrance mix 8% (12.66%). In addition, the three most prevalent allergens for leg dermatitis were nickel sulphate 5% (18.60%), fragrance mix 8% (12.10%) and balsam of Peru 25% (11.92%). Finally, the three most prevalent allergens for trunk dermatitis were nickel sulphate 5% (24.04%), fragrance mix 8% (13.74%) and balsam of peru (11.92%). Results are summarized in Table 5. Interestingly, most allergens were common between all anatomic positions, with the exception of hand, head and leg, where thiuram mix 1%, black rubber mix 0.1% and colophony 20% were unique for each anatomic location respectively (Figure 2).

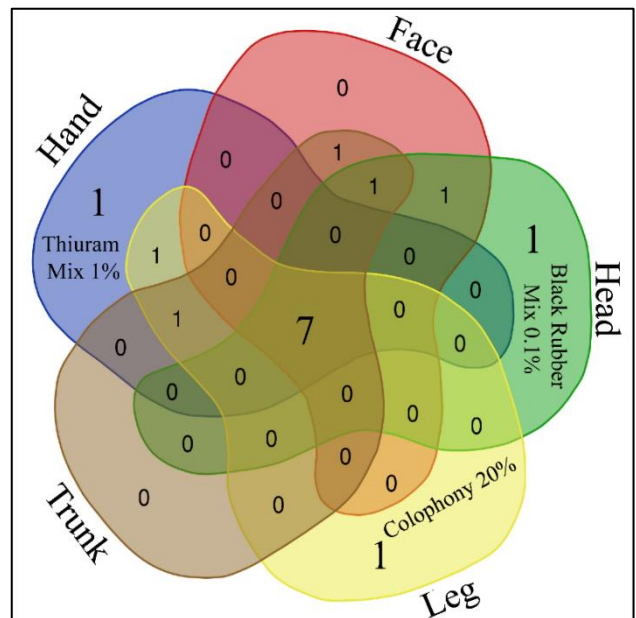


Figure 2: Venn diagram of the common and unique allergens with respect to the localization of dermatitis. The present analysis showed that among the 1- most prevalent allergens, thiuram mix 1%, black rubber mix 0.1% and colophony 20% were unique for hand, head and leg dermatitis respectively.

Table 4. Patch test results and the respective frequencies of positive reactions for the most prevalent allergens with respect to age.

| ≤40 years | | | | >40 years | | | |
|------------------------------|---------------------------|------------------------------|-------------------------|--------------------------|---------------------------|------------------------------|-------------------------|
| Allergen | Number of patients tested | Number of positive reactions | % of positive reactions | Allergen | Number of patients tested | Number of positive reactions | % of positive reactions |
| Nickel sulphate 5% | 279 | 79 | 28.21 | Nickel sulphate 5 | 388 | 94 | 24.26 |
| Thiomersal 0.1% | 279 | 40 | 14.29 | Fragrance mix (i) 8 | 388 | 64 | 16.52 |
| Fragrance mix (I) 8% | 279 | 31 | 11.02 | Balsam of peru 25 | 388 | 48 | 12.43 |
| Cobalt chloride 1% | 279 | 26 | 9.32 | Cobalt chloride 1 | 388 | 24 | 6.26 |
| Paraphenylenediamine 1% | 279 | 19 | 6.78 | Potassium dichromate 0.5 | 388 | 23 | 6.00 |
| Balsam of peru 25% | 279 | 17 | 6.05 | Ethylenediamine 1 | 388 | 23 | 5.91 |
| Potassium dichromate 0.5% | 279 | 14 | 5.08 | Paraphenylenediamine 1 | 388 | 14 | 3.57 |
| Ethylenediamine 1% | 279 | 11 | 4.00 | Budesonide 0.01 | 388 | 14 | 3.57 |
| Kathon 0.01% | 279 | 10 | 3.63 | Neomycin sulphate 20 | 388 | 12 | 3.13 |
| Formaldehyde 2% | 279 | 9 | 3.39 | Thiuram mix 1 | 388 | 11 | 2.78 |
| Neomycin sulphate 20% | 279 | 7 | 2.54 | Formaldehyde 2 | 388 | 10 | 2.61 |
| Black rubber mix 0.1% | 279 | 5 | 1.94 | Colophony 20 | 388 | 9 | 2.26 |
| Thiuram mix 1% | 279 | 5 | 1.82 | Kathon 0.01 | 388 | 9 | 2.26 |
| Colophony 20% | 279 | 5 | 1.82 | Thiomersal 0.1 | 388 | 8 | 2.00 |
| Wool alcohols 30% | 279 | 5 | 1.82 | Wool alcohols 30 | 388 | 5 | 1.30 |
| Paratertiary butyl phenol 1% | 279 | 5 | 1.82 | Paraben mix 15 | 388 | 4 | 1.13 |
| Quaternium 15 1% | 279 | 5 | 1.82 | Primin 0.01 | 388 | 4 | 1.13 |
| Budesonide 0.01% | 279 | 5 | 1.69 | Black rubber mix 0.1 | 388 | 4 | 1.04 |
| Benzocaine 5% | 279 | 4 | 1.45 | | | | |
| Mercapto mix 2% | 279 | 3 | 0.97 | | | | |
| Paraben mix 15% | 279 | 3 | 0.97 | | | | |

Descriptive statistics of the number of positive allergens with respect to gender and type of dermatitis

We have analyzed the presence of multiple positive reactions in our patient cohort with respect to gender, previous familial history of dermatitis, and the diagnosis

of atopic, hand, face, leg, trunk and head dermatitis. More specifically, it appeared that the presence of more than three positive allergenic results is significantly dependent from the presence of the diagnosis of leg dermatitis (p=0.005) (Figure 3a). Similarly, a significant relation was observed between the diagnosis of head dermatitis

and the presence of more than three positive reactions to allergens (p=0.006) (Figure 3b). The comparative results are summarized in table 6. Thus, a statistically significant association was found between the multiple positive allergens and leg dermatitis (p=0.005) as well as trunk dermatitis (p=0.006) (Table 6). More specifically, patients with leg dermatitis had more frequent (16.5%) multiple positive allergens than those without leg dermatitis (11.6%). Likewise, patients with trunk dermatitis had more frequent (15.9%) multiple positive allergens than those without trunk dermatitis (11.4%).

Further on, multiple logistic regression was performed in order to evaluate the probability of having multiple positive reactions (Table 7). In particular, patients with leg dermatitis had 44% higher probability to have multiple positive reactions than those without leg dermatitis (OR=1.44, 95% CI: 1.07-1.93, p=0.014). Likewise, patients with trunk dermatitis had 40% higher probability to have multiple positive reactions than those without trunk dermatitis (OR=1.40, 95% CI: 1.06-1.85, p=0.017).

Table 5: Patch test results and the respective frequencies of the 28 most prevalent allergens (crude relative frequencies include those observed with respect to the total sample size. while adjusted relative frequencies are with respect to the sample size that was actually measured).

| Allergen | Hand dermatitis (n=336) | | Face dermatitis (n=218) | | Head dermatitis (n=72) | | Leg dermatitis (n=187) | | Trunk dermatitis (n=236) | |
|------------------------------|-------------------------|-------|-------------------------|-------|------------------------|-------|------------------------|-------|--------------------------|-------|
| | f | % | f | % | f | % | f | % | f | % |
| Balsam of Peru 25% | 29 | 8.64 | 20 | 9.29 | 5 | 7.04 | 22 | 11.92 | 22 | 9.30 |
| Benzocaine 5% | 3 | 0.90 | 1 | 0.62 | 1 | 1.88 | 3 | 1.44 | 3 | 1.43 |
| Black rubber mix 0.1% | 2 | 0.70 | 3 | 1.55 | 4 | 5.16 | 1 | 0.72 | 2 | 0.86 |
| Budesonide 0.01% | 13 | 3.92 | 4 | 1.70 | 1 | 0.94 | 7 | 3.79 | 7 | 3.01 |
| Cobalt chloride 1% | 24 | 7.04 | 14 | 6.51 | 5 | 7.50 | 14 | 7.59 | 21 | 8.87 |
| Colophony 20% | 6 | 1.91 | 4 | 1.70 | 1 | 0.94 | 6 | 3.25 | 4 | 1.72 |
| Ethylenediamine 1% | 20 | 5.93 | 10 | 4.80 | 2 | 2.35 | 13 | 6.86 | 15 | 6.15 |
| Formaldehyde 2% | 10 | 3.12 | 5 | 2.48 | 2 | 2.35 | 5 | 2.89 | 7 | 2.86 |
| Fragrance mix (i) 8% | 42 | 12.36 | 38 | 17.51 | 9 | 12.66 | 23 | 12.10 | 32 | 13.74 |
| Kathon 0.01% | 13 | 3.92 | 5 | 2.17 | 1 | 1.41 | 6 | 3.43 | 6 | 2.58 |
| Neomycin sulphate 20% | 7 | 2.11 | 9 | 4.34 | 2 | 2.81 | 3 | 1.81 | 4 | 1.72 |
| Nickel sulphate 5% | 76 | 22.72 | 62 | 28.50 | 18 | 25.33 | 35 | 18.60 | 57 | 24.04 |
| Paraben mix 15% | 3 | 0.90 | 2 | 1.08 | 0 | 0.00 | 2 | 0.90 | 2 | 1.00 |
| Paraphenylenediamine 1% | 12 | 3.72 | 7 | 3.25 | 14 | 19.23 | 6 | 3.07 | 8 | 3.29 |
| Paratertiary butyl phenol 1% | 4 | 1.21 | 2 | 0.93 | 0 | 0.47 | 3 | 1.63 | 4 | 1.72 |
| Potassium dichromate 0.5% | 21 | 6.23 | 8 | 3.72 | 2 | 3.28 | 15 | 7.95 | 15 | 6.44 |
| Quaternium 15 1% | 5 | 1.51 | 3 | 1.39 | 0 | 0.00 | 2 | 1.26 | 2 | 0.86 |
| Thiomersal 0.1% | 27 | 8.04 | 13 | 5.89 | 3 | 4.69 | 12 | 6.32 | 14 | 5.72 |
| Thiuram mix 1% | 13 | 3.82 | 3 | 1.39 | 0 | 0.47 | 5 | 2.71 | 5 | 2.29 |
| Wool alcohols 30% | 4 | 1.21 | 2 | 1.08 | 1 | 0.94 | 4 | 1.99 | 5 | 2.29 |

Table 6: Descriptive statistics of the presence of more than three allergens simultaneously, with respect to gender, family history of dermatitis, atopic, hand, face, leg, trunk and head dermatitis. Results presented include the total number of each subpopulation (n) with the percentage (%) of patients with more than three positive allergens.

| | Multiple positive allergens (≥3) | | P value |
|-------------------------------------|----------------------------------|--------------|---------|
| | No n (%) | Yes n (%) | |
| Gender | | | |
| Female | 398 (86.70) | 61 (13.30) | 0.322 |
| Male | 185 (88.30) | 24 (11.70) | |
| Age | | | |
| ≤40 years | 239 (85.70) | 40 (14.30) | 0.083 |
| >40 years | 344 (88.30) | 45 (11.70) | |
| Family history of dermatitis | | | 0.100 |
| No | 472 (86.70) | 73 (13.30) | |
| Yes | 111 (89.80) | 13 (10.20) | |

Continued.

| | No n (%) | Yes n (%) | P value |
|--------------------------|-------------|--------------|---------|
| Atopic dermatitis | | | |
| No | 378 (87.10) | 56 (12.90) | 0.855 |
| Yes | 205 (87.40) | 29 (12.60) | |
| Hand dermatitis | | | |
| No | 291 (87.30) | 42 (12.70) | 0.947 |
| Yes | 293 (87.20) | 43 (12.80) | |
| Face dermatitis | | | |
| No | 395 (86.50) | 62 (13.50) | 0.159 |
| Yes | 188 (88.80) | 24 (11.20) | |
| Leg dermatitis | | | |
| No | 447 (88.40) | 59 (11.60) | 0.005 |
| Yes | 136 (83.50) | 27 (16.50) | |
| Trunk dermatitis | | | |
| No | 41 (88.60) | 53 (11.40) | 0.006 |
| Yes | 170 (84.10) | 32 (15.90) | |
| Head dermatitis | | | |
| No | 540 (87.60) | 76 (12.40) | 0.110 |
| Yes | 43 (83.10) | 9 (16.90) | |

Table 7: Multiple logistic regression evaluating the probability of having multiple positive reactions. Multiple logistic regression was performed in order to evaluate the probability of having multiple positive reactions. Patients with leg dermatitis had 44% higher probability to have multiple positive reactions than those without leg dermatitis (OR=1.44, 95% CI: 1.07-1.93, p=0.014). Likewise, patients with trunk dermatitis had 40% higher probability to have multiple positive reactions than those without trunk dermatitis (OR=1.40, 95% CI: 1.06-1.85, p=0.017).

| | Multiple positive allergens (≥3) | | |
|-------------------------|----------------------------------|-------------|---------|
| | OR | 95% CI | P value |
| Leg dermatitis | | | |
| No | 1.44 | (1.07-1.93) | 0.014 |
| Yes | | | |
| Trunk dermatitis | | | |
| No | 1.40 | (1.06-1.85) | 0.017 |
| Yes | | | |

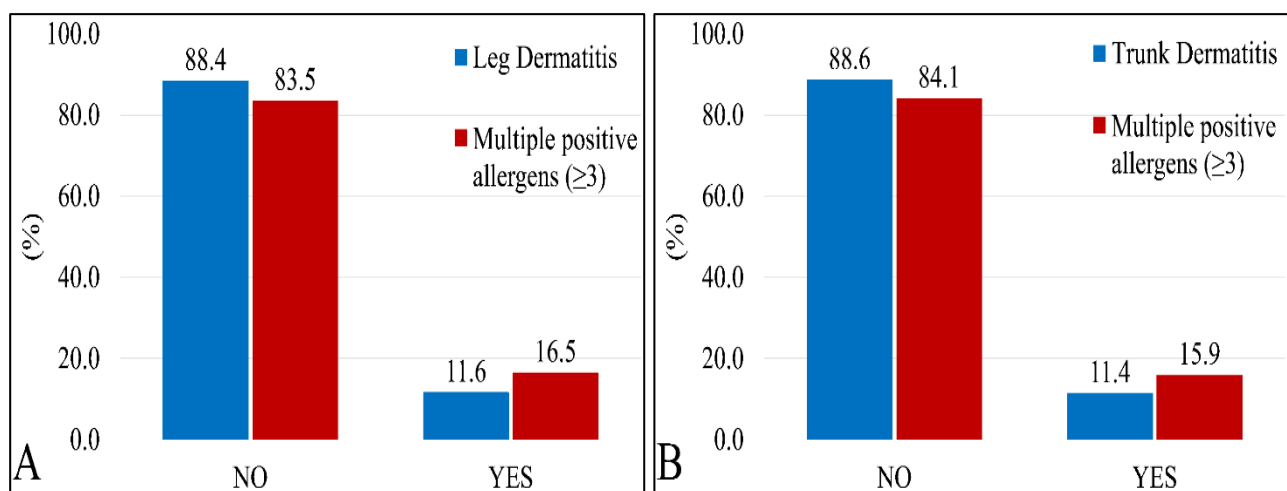


Figure 3. Relation between leg dermatitis and the presence of reaction to more than three allergens (A), as well as between trunk dermatitis and the presence of reaction to more than three allergens (B). More specifically, a significant relation was observed between the diagnosis of leg dermatitis and the presence of more than three positive allergens (p=0.005) (A), while a significant relation was observed between the diagnosis of trunk dermatitis and the presence of more than three positive allergens (p=0.006) (B).

DISCUSSION

The present study has attempted to report and analyze the prevalence of allergic contact dermatitis in a Greek patient cohort. Our results manifested that allergic contact dermatitis was prevalent in both sexes as well as in both age groups. Surveillance of contact dermatitis, has proven a useful tool since it is essential to unravel time trends in allergic pathologies or in order to discover patterns of life-style and environmental stimuli.¹² Further on, such surveillance programs are essential for public health policy making and thus the establishments of preventive policies with respect to dermatopathies.

This aspect, i.e. of public health prevention and policy making, is also linked to quality of life, which is not thoroughly investigated in allergic dermatitis patients.^{13, 14} In that sense, epidemiological studies are important towards that end, meaning that it is crucial to have data available for the quality of life of allergic contact dermatitis patients.

Recent reports have highlighted both the significance as well as the importance of contact dermatitis studies, which is reinforced by the fact that a European surveillance report is published by collecting data from several European countries and comparing contact dermatitis in a country- and ethnic-dependent manner.

Our results are in agreement with the most recent report for contact dermatitis and in particular, we have found that the MOAHLFA index had similar results with other European countries. In particular, the percentage of males with contact dermatitis, was found to be between 11.8% and 40.8% with a median of 28.75%, while our results showed a male population of 31.29%.¹⁵ Further on, OD manifested a minimum of 5.3% and a maximum of 47.6% in the European cohort study, while in our study we have found that 31.55% were diagnosed with OD.¹⁵ At the same time, AD, HD, LD and FD manifested a minimum of 10.6%, 8.7%, 1.8% and 0.9% respectively, a maximum of 38.5%, 64.2%, 22.4% and 32.9% respectively and finally a median of 24.9%, 25.75%, 4.55% and 11.75% respectively.¹⁵ In our report we have found that our patient cohort was diagnosed by 34.98%, 50.20%, 24.27% and 31.65% respectively, which shows that our results were within the European range of contact dermatitis. Finally, the diagnosed cohort with contact dermatitis aged more than 40 years was 58.19% in our study, while the minimum of the ESSCA study was 51.9% and the maximum 79.3% with a median value of 65.75%.

In the present study, we have found that Nickel Sulphate 5% is the most prevalent allergen in the general population, which is in agreement with previous studies.^{5,16} In particular, it appeared that contact dermatitis from nickel sulphate, ranged from 11.9% in Denmark to 26.4% in Spain.^{5,6,16} Further on, in agreement to previous reports the second more prevalent allergen

was found to be the fragrance mix 5%, where our results showed that positive testing was found in the 14.20% of the general population while the lowest levels were manifested in Italy (4.5%) and the highest levels in 14.7% in Austria. is the most frequent allergen of baseline series among children and adults, remarkably high in young women. Contact allergy to fragrances is quite frequent, affecting between 1.1% and 2.3% of the general population in Europe.¹⁷⁻²⁰

Study limitations

One of the study limitations is the possible first stage selection bias, which cannot be ruled out. One further difficulty is the comparison of prevalence's between countries as well as the inherent differences between the similar departments among different countries. Although the present work is an ongoing study, response and data collection rates are slow, which does not always allow for timely reporting.

CONCLUSION

The present study showed that the prevalence of contact allergy in the general population was high, mostly because of nickel. The ongoing high prevalence of nickel allergy shows the importance of complying with regulations, which include consumer products. Fragrance mix appeared to be the second most prevalent allergen, also suggesting a possible need for change in health policies. The etiology and mechanisms of contact dermatitis are still largely unknown. It is estimated that it is influenced by environmental as well as genetic factors and it is still a subject of intensive research. Epidemiological studies are considered of crucial importance towards the understanding of allergic contact dermatitis and the establishment of effective clinical and laboratory tests.

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REFERENCES

1. Mowad CM, Anderson B, Scheinman P, Pootongkam S, Nedorost S, Brod B. Allergic contact dermatitis: Patient management and education. *J Am Acad Dermatol.* 2016;74:1043-54.
2. Johansen JD, Aalto-Korte K, Agner T, Andersen KE, Bircher A, Bruze M, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. *Contact Dermatitis.* 2015;73:195-221.
3. Peiser M, Tralau T, Heidler J, Api AM, Arts JH, Basketter DA, et al. Allergic contact dermatitis: epidemiology, molecular mechanisms, in vitro methods and regulatory aspects. *Current knowledge*

- assembled at an international workshop at BfR, Germany. *Cell Mol Life Sci*. 2012;69:763-81.
4. Uter W, Schnuch A, Wilkinson M, Dugonik A, Dugonik B, Ganslandt T. Registries in Clinical Epidemiology: the European Surveillance System on Contact Allergies (ESSCA). *Methods Inf Med*. 2016;55:193-9.
 5. Uter W, Gefeller O, Gimenez-Arnau A, Frosch P, Duus Johansen J, Schuttelaar ML, et al. Characteristics of patients patch tested in the European Surveillance System on Contact Allergies (ESSCA) network, 2009-2012. *Contact Dermatitis*. 2015;73:82-90.
 6. Uter W, Amario-Hita JC, Balato A, Ballmer-Weber B, Bauer A, Belloni Fortina A, et al. European Surveillance System on Contact Allergies (ESSCA): results with the European baseline series, 2013/14. *J Eur Acad Dermatol Venereol*. 2017;31:1516-25.
 7. Uter W, Rustemeyer T, Wilkinson M, Duus Johansen J. Quality in epidemiological surveillance of contact allergy. *Contact Dermatitis*. 2016;74:175-80.
 8. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm. Venereol*. 1980;60:44-7.
 9. Schnuch A. PAFS: population-adjusted frequency of sensitization. (I) Influence of sex and age. *Contact Dermatitis*. 1996;34:377-82.
 10. Uter W, Schnuch A, Gefeller O. Allergies EwgESSoC. Guidelines for the descriptive presentation and statistical analysis of contact allergy data. *Contact Dermatitis*. 2004;51:47-56.
 11. Ahmad OB, Boschi Pinto C, Lopez AD, Age Standardization of Rates: A New WHO Standard. 2001: 10-12.
 12. Uter W, Hegewald J, Aberer W, Ayala F, Bircher AJ, Brasch J, et al. The European standard series in 9 European countries, 2002/2003 -- first results of the European Surveillance System on Contact Allergies. *Contact Dermatitis*. 2005;53:136-45.
 13. Heisterberg MV, Menne T, Johansen JD. Fragrance allergy and quality of life - a case-control study. *Contact Dermatitis*. 2014;70:81-9.
 14. Kadyk DL, McCarter K, Achen F, Belsito DV. Quality of life in patients with allergic contact dermatitis. *J Am Acad Dermatol*. 2003;49:1037-48.
 15. Dittmar D, Uter W, Bauer A, Fortina AB, Bircher AJ, Czarnecka-Operacz M, et al. European Surveillance System on Contact Allergies (ESSCA): polysensitization, 2009-2014. *Contact Dermatitis*. 2018;78:373-85.
 16. Uter W, Gefeller O, Geier J, Schnuch A. Contact sensitization to cobalt--multifactorial analysis of risk factors based on long-term data of the Information Network of Departments of Dermatology. *Contact Dermatitis*. 2014;71:326-37.
 17. Thyssen JP, Johansen JD, Menne T, Nielsen NH, Linneberg A. Nickel allergy in Danish women before and after nickel regulation. *N Engl J Med*. 2009;360:2259-60.
 18. Thyssen JP, Menne T, Johansen JD. Nickel release from inexpensive jewelry and hair clasps purchased in an EU country - Are consumers sufficiently protected from nickel exposure? *Sci Total Environ*. 2009;407:5315-8.
 19. Thyssen JP, Menne T, Linneberg A, Johansen JD. Contact sensitization to fragrances in the general population: a Koch's approach may reveal the burden of disease. *Br J Dermatol*. 2009;160:729-35.
 20. Thyssen JP, Menne T, Schnuch A, Uter W, White I, White JM, et al. Acceptable risk of contact allergy in the general population assessed by CE-DUR--a method to detect and categorize contact allergy epidemics based on patient data. *Regul Toxicol Pharmacol*. 2009;54:183-7.

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