

Clinical Study of 124 Patients Having Perianal Dermatitis

Alfredo-Daniel Agulló-Pérez, MD, Marcos Hervella-Garcés, MD, Saioa Oscoz-Jaime, MD, Maialen Azcona-Rodríguez, MD, Mónica Larrea-García, MD, and Juan-Ignacio Yanguas-Bayona, MD

Background: Perianal complaints are often consulted in dermatology clinics, and in many cases, a conclusive diagnosis is not easily made.

Objective: The aim of this study was to study and identify the epidemiological, clinical, and contact allergy features of patients with perianal dermatitis who attended at a contact dermatitis unit in a tertiary hospital in Spain.

Methods: Adult patients with long-lasting (>4 weeks) perianal dermatitis were recruited during the past 10 years for investigation and follow-up. Every patient underwent a diagnostic workup consisting of dermatological exploration and patch tests with the standard and specific series, as well as the patients' own products. General surgical exploration was also performed in some patients.

Results: One hundred twenty-four patients were included. The MOAHLFA index was as follows: 43.5, 0, 4.8, 11.3, 1.6, 8.1, and 75. The main final diagnoses were allergic contact dermatitis (32.3%), psoriasis (24.2%), irritant contact dermatitis (17.7%), and lichen simplex (neurodermatitis) (10%). Eighty-one patients (66.1%) showed 1 or more positive reactions, and in 52 patients (43%), positive reactions relevant to the present disease were found.

Conclusions: Contact allergy in patients with long-lasting perianal complaints is frequent. It is mandatory for these patients to be referred to a dermatologist for an adequate evaluation and patch testing. Methylchloroisothiazolinone/methylisothiazolinone seems as the most common allergen implicated in perianal contact dermatitis.

Perianal pruritus and rashes are a frequent reason of dermatologic consultation and can be difficult to diagnose and treat due to their paucity of clinical signs and to their varied, often multicausal nature. Perianal dermatitis is the most common cutaneous disorder of the anogenital area, but studies on causative factors and published data on the role of patch testing regarding this dermatitis are limited.^{1,2}

METHODS

Between April 2004 and August 2016, every adult patient with signs or symptoms of the perianal region lasting 4 or more weeks (ie, pruritus ani or a suspected perianal dermatitis) visiting our office was recruited for a diagnostic protocol, consisting of dermatological exploration, blood and stool analysis, swabs for microbiologic cultures, and patch tests with the standard series of the Spanish research group in allergic contact dermatitis (ACD)³

From the Department of Dermatology, Complejo Hospitalario de Navarra, Pamplona, Spain.

Address reprint requests to Alfredo-Daniel Agulló-Pérez, MD, Department of Dermatology, Complejo Hospitalario de Navarra, 3 Irúnlarrea St, Centro de Especialidades Príncipe de Viana, 31008 Pamplona, Navarra, Spain. E-mail: tegatreides@gmail.com.

The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0000000000000274

© 2017 American Contact Dermatitis Society. All Rights Reserved.

(TRUE test; Mekos Laboratories ApS, Denmark; and some additional allergens from Chemotechnique Diagnostics, Vellinge, Sweden). Depending on the clinical history, specific test series and patient-suspected own products were also tested. Occasionally, a skin biopsy of the perianal region or a proctoscopy was performed, when needed.

The patch tests were occluded for 2 days, and reading was performed on day (D) 2, D4, and in some cases, also D7. Every positive result in the patch test was classified as current clinical relevance, past relevance, unknown relevance, and cross-reaction.

Two diagnostic categories were defined: main diagnosis (meaning the most likely or suitable cause of the present complaint) and secondary diagnosis (aggravating or triggering condition associated with and relevant to the main present diagnosis). All data of each patient were manually entered into a computerized database (Excel 2'2') and later analyzed with the SPSS program. $P < 0.05$ was considered statistically significant, and several statistical analyses were performed when needed (χ^2 test and multinomial logistic regression).

RESULTS

One hundred twenty-four patients were included in this study, accounting for 7.4% of all individuals studied in our contact department during that period. The age range was 20 to 85 years (mean, 50.7 years); 56.5% of the patients were women (age range, 20–85 years; mean, 50.7 years; median, 48.5 years) (Fig. 1). The

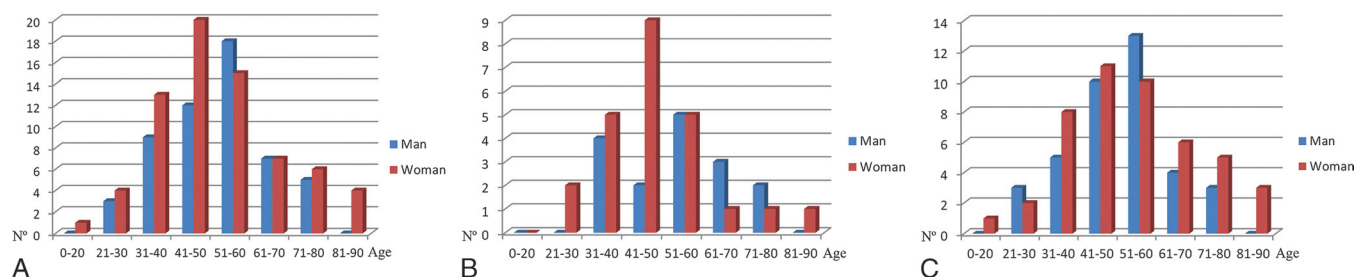


Figure 1. Age distribution by sex. A, All patients (N = 124). B, Patients with ACD (n = 40). C, Patients with other diagnosis (n = 84).

mean age of patients with atopic dermatitis (AD) was significantly lower than its counterpart for the rest of the patients (38 years), and all patients were women. Furthermore, 100% of the patients with AD as the main diagnosis had also disseminated lesions (neck, face, hands, and legs).

The duration of perianal symptoms ranged from 1 to 240 months (mean, 15 months; median, 12 months). No statistically significant differences were found between the duration of symptoms and the main diagnosis. Furthermore, 49.2% of the patients had only anal-perianal lesions, 16.1% had also genital-inguinal lesions or symptoms, and 34.7% of the patients had lesions at various locations (Fig. 2).

Thirty-two patients (25.8%) had an associated proctologic diagnosis (hemorrhoids, anal fissure, and sphincter insufficiency, among others) among these patients; ACD was less common than in the rest (19% vs 37%). Eighteen individuals (14.5%) showed clinical signs of corticoid overuse (cutaneous atrophy, telangiectasia, and pigment alterations), and 19 patients (15.3%) had psychopathologic symptoms, mainly anxiety (9 patients), compulsive habits (4 patients), and venereophobia (4 patients).

The MOAHLFA (male, occupational dermatitis, AD, hand, face, leg, and age > 40 years) index of this group was as follows: 4.8% of the patients were atopic, 11.3% had hand eczema, 1.6% had leg eczema, and 8.1% had concomitant facial dermatitis. As said before, 43.6% of the patients were men (age range, 22–75 years;

mean, 50.7 years; median, 51.5 years). No patient in our study had a dermatosis related to his/her job.

Thirty-nine patients (31.5%) had a pre-patch test diagnosis of nonspecific eczema (including chronic and subacute), 24.2% (20) had a prepatch diagnosis of psoriasis/seborrheic dermatitis, 19.2% had a prepatch diagnosis of ACD of whom 19.83% actually had ACD, 8.1% had a prepatch diagnosis of irritant contact dermatitis (ICD), and 17% had other pre-patch test diagnoses (including lichen simplex chronicus [LSC], pruritus ani, and AD).

The main final diagnoses were ACD (32.3%), psoriasis-seborrheic eczema (24.2%), and irritant contact dermatitis (17.7%). Allergic contact dermatitis was present as a secondary diagnosis in 11 patients (9%). For a comparison in prepatch diagnosis, psoriasis was the second more common pathology, and ACD was the third, whereas idiopathic dermatitis was the most frequently suggested diagnosis (Fig. 3).

Patients with ACD were commonly women (60%), with a mean age of 49.9 (median, 49.5) years and a mean duration of symptoms of 17.3 months. Patients with other diagnosis had a similar age (mean, 49.9 years), with a slightly less proportion of women (54.8%), and had a mean duration of symptoms of 31 months.

Of the 124 patients with perianal dermatoses, 66.1% showed 1 or more positive reactions, and in 43% of them, this reaction was relevant to the present disease. There were a total of 75 positive relevant allergens among the 54 patients with a positive relevant reaction (1.39 allergens per case).

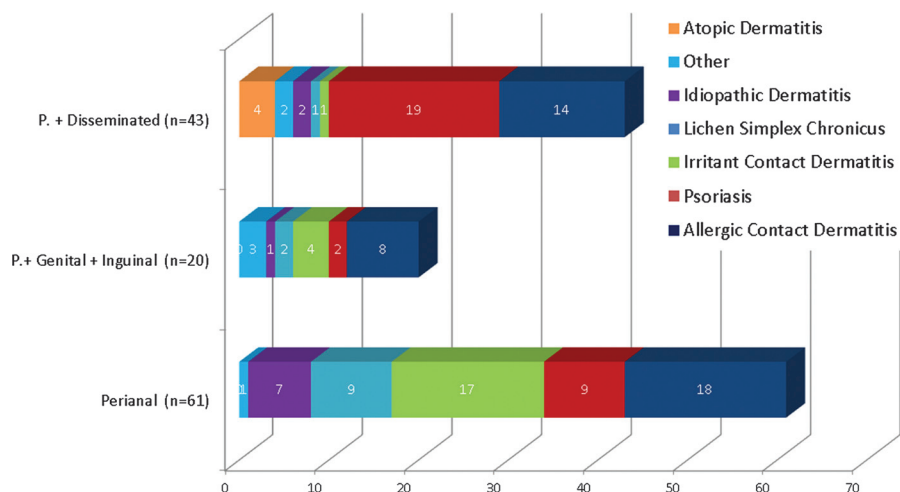


Figure 2. Main diagnosis distribution by anatomical location.

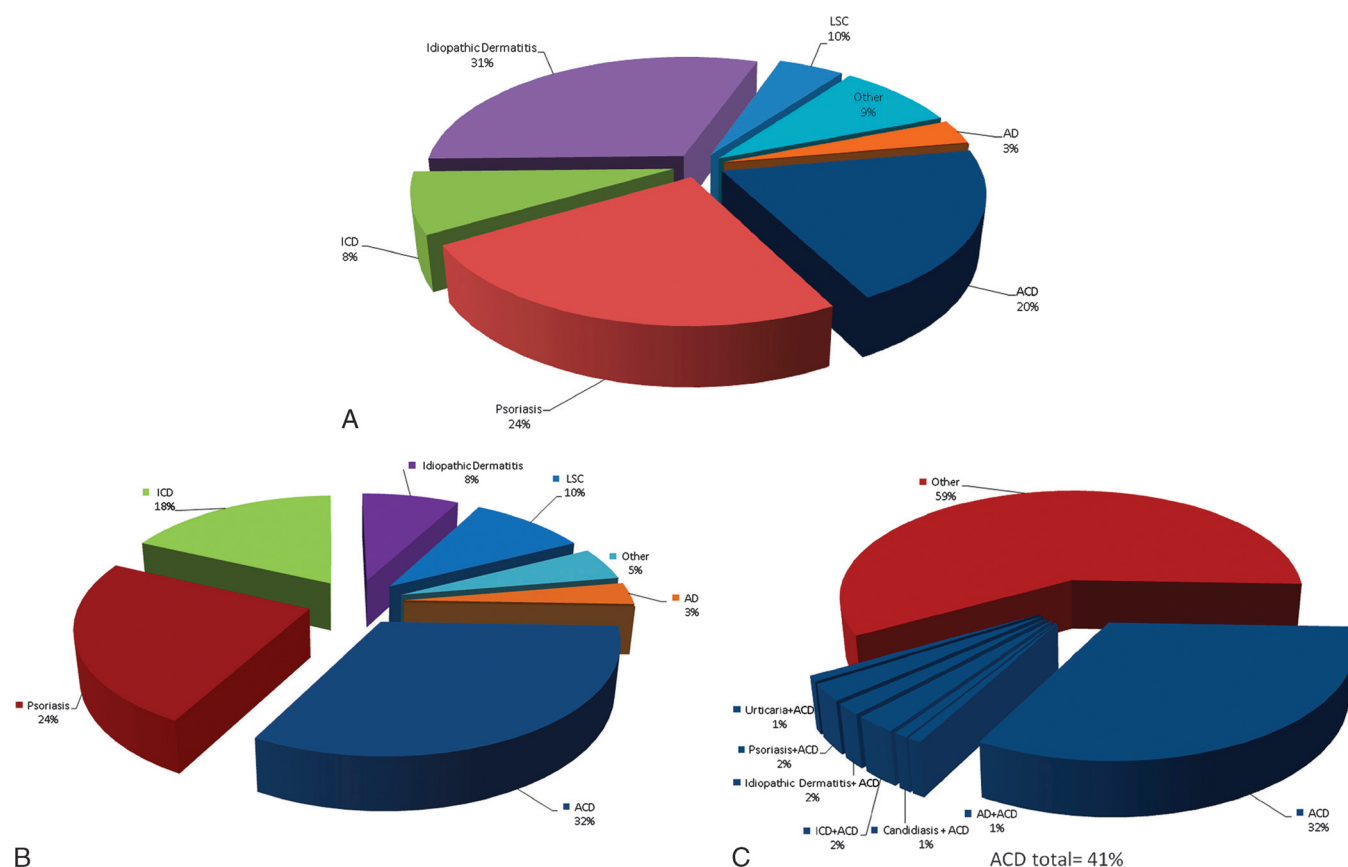


Figure 3. A, Prepatch diagnosis: 38 patients (31%) with idiopathic dermatitis, 30 patients (24%) with psoriasis, and only 25 patients (20%) with ACD, with the total number of patients of 124. B, Main diagnosis: 40 patients (32.3%) had ACD, as opposed to 84 (67.7%) who had a different diagnosis. Notice how, after patch testing, idiopathic dermatitis represents only 8% of the total diagnosis. C, Three patients with ICD and psoriasis, 2 with idiopathic dermatitis, 1 with AD, 1 with candidiasis, and 1 with urticaria had currently relevant positive reactions when patch tested and were given a diagnosis of secondary/aggravating ACD. Taking together the main and secondary diagnoses, 51 patients (41%) had contact allergies that were important for their present complaints.

The most common positive allergen with current relevance was methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) (23%), taking together also patients who react only to MCI or MI; the number of positive reactions with current relevance rose to 30.1% of the total. The second more common sensitizer was neomycin (14.7%). Of the patients with positive reactions of past relevance, the most frequent allergen was nickel sulfate (44.4%), followed by neomycin (11.1%). Among the founded allergies of uncertain relevance, the most common allergen was nickel sulfate (34.8%), followed by thimerosal (10.9%) (Table 1).

In 29 (76%) of the 40 cases of ACD as the main diagnosis, the Spanish standard series³ was able to identify the principal allergen.

Own products were tested in 47 patients. Nearly half (43%) of the tests showed a relevant reaction.

DISCUSSION

Perianal dermatoses are commonly consulted and often poorly managed because, in many cases, a conclusive diagnosis is not easily made. Several reports have confirmed that most patients

with pruritus ani or perianal complaints have a dermatosis as the underlying cause and that many of them have developed contact sensitivities to the various topical medications used.⁴⁻⁶

The etiologic diagnosis of perianal disease is a dermatologic challenge, and the use of patch tests is invaluable. The basic diagnostic algorithm to discard a systemic disease must not be overlooked, and support from colorectal surgeons is often gratifying, if not essential; proctologic disorders, dietary disturbances, and psychological factors are also to be considered in these patients.⁴

Previous works have noticed that some diagnoses could be more common in women than in men, such as LSC.⁷ In our work, LSC and AD were more frequently associated with women, whereas psoriasis was seen more frequently among male patients.

Contact allergy of the perianal region may be a primary, or secondary, worsening condition that topical treatment abuse or disease perseverance adds to a nonhealing anal disease. The reported rates of relevant contact sensitization in patients with perianal complaints in 7 large series were 21%,² 24.6%,⁸ 26.2%,⁹ 34.8%,⁵ 43.2%,¹ 45%,⁴ and 63.4%.⁷ In our series, 51 patients (41.1%)

TABLE 1. Positive Allergens, Relevance, and Profitability: Number of Patients Tested With Each Allergen

Allergens	No. Patients Tested	Positive Result, n (%)	Present Relevance, n (%)	Past Relevance, n (%)	Uncertain Relevance, n (%)	Relevant Positives Among Positives (>5), %
4-Tert-butylphenol	124	1 (0.6)	—	1 (2.8)	—	
formaldehyde resin						
Alpha-hexyl-cinnamal	5	1 (0.6)	1 (1.4)	—	—	
Amerchol	58	1 (0.6)	1 (1.4)	—	—	
Amyl cinnamal	5	1 (0.6)	1 (1.4)	—	—	
Benzalkonium chloride	29	1 (0.6)	—	1 (2.8)	—	
Benzocaine	124	1 (0.6)	—	—	1 (2.2)	
Budesonide	124	1 (0.6)	1 (1.4)	—	—	
Caine mix	124	9 (5.7)	6 (8.4)	3 (8.3)	—	66.7
Carba mix	124	3 (1.9)	—	—	3 (6.5)	
Citronellol	5	1 (0.6)	1 (1.4)	—	—	
Clioquinol	124	1 (0.6)	—	1 (2.8)	—	
Cobalt chloride	124	4 (2.5)	—	3 (8.3)	1 (2.2)	
<i>Compositae</i>	41	1 (0.6)	1 (1.4)	—	—	
Ethylenediamine	124	7 (4.4)	5 (7)	1 (2.8)	1 (2.2)	71.4
dihydrochloride						
Formaldehyde	124	2 (1.3)	—	1 (2.8)	1 (2.2)	
Fragrance mix 1	124	5 (3.3)	3 (4.2)	1 (2.8)	1 (2.2)	
Fragrance mix 2	124	2 (1.3)	1 (1.4)	1 (2.8)	—	
Fusidic acid sodium salt	25	1 (0.6)	1 (1.4)	—	—	
Geraniol	5	2 (1.3)	1 (1.4)	—	1 (2.2)	
Lanolin alcohol	124	3 (1.9)	2 (2.8)	—	1 (2.2)	
Mercury	124	2 (1.3)	1 (1.4)	—	1 (2.2)	
MCI	124	5 (3.2)	4 (5.6)	1 (2.8)	—	80
MCI/MI	124	17 (10.8)	17 (23.8)	—	—	100 (92*)
Methyldibromo glutaronitrile	124	2 (1.3)	—	1 (2.8)	1 (2.2)	
MI	124	3 (1.9)	2 (2.8)	—	1 (2.2)	
Neomycin sulfate	124	15 (9.5)	11 (15.4)	4 (11.1)	—	73.3
Nickel sulfate	124	32 (20.3)	—	16 (44.4)	16 (34.8)	
p-Phenylenediamine	124	6 (3.8)	1 (1.4)	1 (2.8)	4 (8.7)	
Paraben mix	124	1 (0.6)	—	—	1 (2.2)	
Phenyl mercuric acetate	29	1 (0.6)	1 (1.4)	—	—	
Povidone-iodine	124	2 (1.3)	1 (1.4)	—	1 (2.2)	
Propolis	41	3 (1.9)	2 (2.8)	1 (2.8)	1 (2.2)	
Propylene glycol	58	6 (3.8)	4 (5.6)	—	2 (4.3)	66.7
Quaternium-15	124	1 (0.6)	1 (1.4)	—	—	
Rose absolute	5	1 (0.6)	1 (1.4)	—	—	
Thimerosal	124	6 (3.8)	1 (1.4)	—	5 (10.9)	
Thiuram mix	124	3 (1.9)	1 (1.4)	—	2 (4.3)	
Tixocortol	124	3 (1.9)	2 (2.8)	—	1 (2.2)	
Total	—	157 (100)	74 (100)	36 (100)	46 (100)	
Own product	47	20 (43)†	20 (100)‡	—	—	

*Taking individual and mixed isothiazolinones.

†Percentage of total own products tested.

‡Percentage of relevance among total positive own products.

of the total) had positive relevant reactions. As stated, 40 of these subjects (32.3% of all cases) had ACD as their main final diagnosis, and in 14 more patients (11.3%), contact sensitization was an aggravating factor of other skin problems: ICD, AD, or psoriasis.

Patients with ICD and LSC had, in most cases, lesions limited to the perianal-genital area, with statistically significant differences

($P = 0.011$). Psoriasis was strongly associated with patients with non-only perianal lesions and was more common in men than women but without statistically significant differences. Atopic dermatitis was only observed in women with disseminated lesions.

In contrast with our first study of perianal dermatosis, presented in the 2006 Congress of the European Society of Contact

Dermatitis,¹⁰ we have not found a significant association between the duration of perianal complaints and a higher rate of contact dermatitis, neither between patients with only perianal symptoms and the ACD rate. In contrast, patients without previous proctologic disease associate a remarkably high proportion of ACD (36% as the principal diagnosis), whereas among the group with previous proctologic disease, ACD was observed only in 19% of the patients. The principal diagnosis among this group was nonallergic conditions: ICD (31.3%) and psoriasis (28.1%).

It must be underlined that 25 patients (20.2%) had a second diagnosis. Eighteen (15%) showed clinical signs of corticoid overuse, and 20 patients (16.7%) had psychopathologic symptoms evident enough to be registered on the diagnostic chart, mainly compulsive habits (5 patients), venereophobia (4 patients), and anxiety (3 patients). These conditions could act as a trigger factor (even causative factor) for certain perianal diseases such as LSC.

Some authors¹¹ have reported that various spices and condiments were involved in anogenital ACD and proposed that patients should also be studied with additional series containing spices and condiments. In our study, no such allergens were found, and no patient related the onset of their symptoms to such factors.

For classic authors^{12–14} (even recent works⁵), the most common allergen tends to be a topical medicament, especially anesthetic drugs and corticosteroids, used as treatment of pruritus ani and/or hemorrhoids. In our series, topical medicaments such as antibiotics antiseptics and anesthetics were responsible for 26.6% of the total relevant reactions.

Other authors such as Warshaw et al⁷ found fragrance mix 1, balsam of Peru, and preservatives as quaternium-15 as the most common allergens at a perianal site. In our work, fragrances were responsible for 12.6% of the total relevant reactions.

Since the first years of this decade, several authors have started to point to MCI/MI as an important emerging allergen primary related to the use of wet wipes.^{15–17} In 2013, MCI/MI became Allergen of the Year and one of the most frequent allergens till date.¹⁸ The irruption of MCI/MI has also affected the classical classification of perianal allergens. Last articles showed how MCI/MI became the most common perianal sensitizer, representing 19% of all positive relevant allergens² in 1 series and 54% of all allergens with present relevance¹ in another study. It is important to remember that the MCI/MI mixture can miss nearly 40% of MI allergies and, because of that, it is mandatory to test MI isolated¹⁹ and that patch testing of MCI/MI should be performed at 0.02% instead of at 0.01% to avoid underestimating its allergenic potential.¹⁷

Ten years ago, in our previous work in the same hospital, MCI/MI accounts for 19% of all ACDs, whereas in the present series, it accounts for 37.5% (19) of all ACD cases. In our study, MCI/MI remains as the most common allergen in perianal ACD, representing 30.6% of all positive relevant reactions. In most cases, this allergen was found in topical creams, wet wipes, and bath soaps.

The elevated frequency of neomycin sensitization in our series (14.9%) also needs to be underscored. This result is the highest in any recent series, and it is probably due to the generalized and

excessive use of topical antibiotic creams with neomycin in our medium due to a strong tradition in topical treatments and a slow introduction of other topical treatments. In addition, the weak and delayed reaction of neomycin in patch testing, with an optimized reading on D7, could underestimate neomycin sensitization in other series.

In conclusion, our results reinforce the idea that it is mandatory in every patient with long-lasting (>4 weeks) perianal complaints to refer to a dermatologist for adequate evaluation and patch testing because 41% of the patients could have ACD as the main or secondary diagnosis. According to our results, the location of skin lesions could bring some insights about the underlying condition because AD and psoriasis tend to appear in a disseminated shape and ICD hardly ever appears beneath the perianal area.

Testing personal products has been revealed as a useful technique, with nearly 40% of tested products showing a positive relevant reaction.

As in other recent series, MCI/MI seems to be the most common allergen implicated in perianal dermatitis.

REFERENCES

- Gonzalez-Perez R, Sanchez-Martinez L, Piqueres Zubiaurre T, et al. Patch testing in patients with perianal eczema. *Actas Dermosifiliogr* 2014;105(7):694–698.
- Abu-Asi MJ, White IR, McFadden JP, et al. Patch testing is clinically important for patients with peri-anal dermatoses and pruritus ani. *Contact Dermatitis* 2016;74(5):298–300.
- Hervella-Garcés M, García-Gavín J, Silvestre-Salvador JF, et al. The Spanish standard patch test series: 2016 update by the Spanish Contact Dermatitis and Skin Allergy Research Group (GEIDAC). *Actas Dermosifiliogr* 2016;107(7):559–566.
- Dasan S, Neill SM, Donaldson DR, et al. Treatment of persistent pruritus ani in a combined colorectal and dermatological clinic. *Br J Surg* 1999;86(10):1337–1340.
- Bauer A, Geier J, Elsner P. Allergic contact dermatitis in patients with anogenital complaints. *J Reprod Med* 2000;45(8):649–654.
- Proske S, Lenhard BH, Hartschuh W. Perianal dermatitis and its benign simulants. *Hautarzt* 2004;55(3):259–264.
- Warshaw EM, Furda LM, Maibach HI, et al. Anogenital dermatitis in patients referred for patch testing: retrospective analysis of cross-sectional data from the North American Contact Dermatitis Group, 1994–2004. *Arch Dermatol* 2008;144(6):749–755.
- Kugler K, Brinkmeier T, Frosch PJ, et al. Anogenital dermatoses—allergic and irritative causative factors. Analysis of IVDK data and review of the literature. *J Dtsch Dermatol Ges* 2005;3(12):979–986.
- Kränke B, Trummer M, Bräbek E, et al. Etiologic and causative factors in perianal dermatitis: results of a prospective study in 126 patients. *Wien Klin Wochenschr* 2006;118(3–4):90–94.
- Hervella M, Montón S, Calvo A, et al. Allergic contact dermatitis in patients with perianal complaints. *Contact Dermatitis* 2006;55(S-1).
- Vermaat H, Smienk F, Rustemeyer T, et al. Anogenital allergic contact dermatitis, the role of spices and flavour allergy. *Contact Dermatitis* 2008;59(4):233–237.
- Goldsmith PC, Rycroft RJ, White IR, et al. Contact sensitivity in women with anogenital dermatoses. *Contact Dermatitis* 1997;36(3):174–175.

13. Lodi A, Ambonati M, Coassini A, et al. Contact allergy to “caines” caused by anti-hemorrhoidal ointments. *Contact Dermatitis* 1999;41(4):221–222.
14. van Ketel WG. Contact allergy to different antihaemorrhoidal anaesthetics. *Contact Dermatitis* 1983;9(6):512–513.
15. García-Gavín J, Vansina S, Kerre S, et al. Methylisothiazolinone, an emerging allergen in cosmetics? *Contact Dermatitis* 2010;63(2):96–101.
16. Gardner KH, Davis MD, Richardson DM, et al. The hazards of moist toilet paper: allergy to the preservative methylchloroisothiazolinone/methylisothiazolinone. *Arch Dermatol* 2010;146(8):886–890.
17. Higgins E, Kirby B, Rogers S, et al. Methylchloroisothiazolinone and methylisothiazolinone allergic contact dermatitis and the effect of patch test concentration. *Dermatitis* 2013;24(2):73–76.
18. Svedman C, Andersen KE, Brandao FM, et al. Follow-up of the monitored levels of preservative sensitivity in Europe: overview of the years 2001–2008. *Contact Dermatitis* 2012;67(5):312–314.
19. Urwin R, Wilkinson M. Methylchloroisothiazolinone and methylisothiazolinone contact allergy: a new “epidemic”. *Contact Dermatitis* 2013; 68(4):253–255.