Contact allergy and sociodemographic characteristics

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ABSTRACT

The aim of the study was to determine the frequency of positive patch test reaction to different contact allergens according to patients age, sex, occupation and clinical features. Between 1999 and 2003, patch testing was performed in 3293 patients with respective clinical diagnoses. Patch testing was done by the standard technique proposed by the International Contact Dermatitis Research Group (ICDRG). Study results showed statistically significant differences in patch test response according to sex and age for three allergens (cobalt chloride, nickel sulfate and thiomersal); according to occupation for nine allergens (cobalt chloride, nickel sulfate, balsam of Peru, fragrance mix, thiuram mix, wood tars, neomycin sulfate, thiomersal and detergents), and clinical diagnosis for two allergens (nickel sulfate, and wood tars). The most common and relevant allergens were: nickel sulfate, cobalt chloride and carba mix. They were found in all examinees regardless of age, sex, occupation and diagnoses. The increased awareness of allergens and their potential sources may help to limit the usage of these chemicals in manufacture of consumer products.

Key words*: contact sensitivity, epidemiology, patch testing*

INTRODUCTION

Patch testing is considered the gold standard for the diagnosis of contact allergy (CA). The diagnosis is not usually apparent from history or physical examination, and patch testing is necessary for identify etiology of CA [1]. Patch testing is a method to identify a causative substance and permit diagnosis of allergic contact dermatitis (ACD). As yet, there are no commonly accepted measurement scales to quantify extend and severity of ACD which could be comparable to other instruments known in atopic dermatitis. For most individuals, allergen avoidance results in resolution of the dermatitis [1]. Early diagnosis increases the response to treatment and decreases treatment costs[2-3]. Several studies have assessed the reproducibility of different patch test systems, with different results[4-11].

Many studies have been conducted to identify the most prevalent allergens[5,12]. Nickel was the most common allergen for CA in different studies[4,13-18,23-30]. CA to a certain substance often depends on several factors. The aim of the present study was to identify the most common allergens in our patients. This retrospective study was designed as to reassess the validity and reproducibility of patch testing[4].

MATERIALS AND METHODS

The study was carried out at the Allergy Clinic of the University Department of Dermatology and Venerology, Zagreb University Hospital Center in Zagreb, Croatia. We reviewed the files of 3 293 patients with various clinical diagnosis who submitted to patch testing between 1999 and 2003. There were 2 335 (70.9%) female and 958 (29.1%) male patients, age range 3 to 80 years, mean age of 38 years. The clinical diagnoses were ACD (n=2 321 , 70.5 %), contact irritant dermatitis (CD) (n=215 , 6.5%), atopic dermatitis (AD) (n=422 , 12.8%), psoriasis vulgaris (PV) (n=37 , 1.1%), seborrhoeic dermatitis (SD) (n=137 , 3.2%) and other inflammatory dermatoses (OID) (n=161 , 4.9%). According to occupational history, the patients were mostly administrative personnel (n=1527 , 46.4%), followed by students (n=482 , 14.7%), medical and related professions (n=473 , 14.4%), workers (n=453 , 13.8%) and pensioners (n=358 , 10.9%). The standard patch test series of allergens were tested on the upper back in all patients. Using a standard technique proposed by the International Contact Dermatitis Research Group (ICDRG), the test have been read at 48 and 72 hours, with positive results defined morphologically as + to +++ reaction[13-14]. We haven't doubtful (erythematous) reactions and + was red as allergic reaction. Patients receiving topical or systemic steroids or immunosuppressive, and those suffering from chronic illnesses were excluded from the study. Statistical data analysis was done by the Statistica 6.0 (StatSoft Inc., Chicago, USA) software package for Windows, and data entry and collection by Microsoft Office Excel 2003. χ^2 test was used to estimate differences between categories of variables and odds ratio with relative risks to calculate the probability of predictors. All statistical values were considered significant at the p-level of 0.05.

RESULTS

Between 1999 and 2003, a total of 3 293 patients had positive patch test reactions. Women were sensitized significantly more often than men (2335vs958). Statistically significant differences according to sex and hypersensitivity was recorded for potassium dichromate, cobalt chloride, nickel sulfate, epoxy resin, mercury praecipitate, carba mix, rubber mix (PPD mix), parabene mixture and thiomersal (Table 1). Analysis according to age groups (3-20 , 21-60 , 61-80) revealed a decreasing sensitivity with age for cobalt chloride, nickel sulfate, urshiol, and thiomersal (Table 2). In contrast, on increasing sensitivity with age was observed for potassium dichromate, carba mix, balsam of Peru, fragrance mix, thiuram mix and wood tars. Statistically significant differences according to age and sex was observed for cobalt chloride, nickel sulfate and thiomersal, and according the age for cobalt chloride, nickel sulfate, balsam of Peru, fragrance mix, neomycin sulfate, and thiomersal (Table 2). The analysis of the clinical diagnoses in according to sex and patch test reaction revealed positive reactions to prevail in all clinical diagnoses mostly in ACD. Analysis according to five different occupations and patch test results yielded statistically significant differences for cobalt chloride, nickel sulfate, balsam of Peru, fragrance mix, thiuram mix, wood tars, neomycin sulfate, and thiomersal (Table 3). In the five occupation categories, relevant relative risk (RR) factors were for two allergens, nickel sulfate (RR 0.18) and cobalt chloride (RR 0.14). According to clinical diagnosis and distribution of positive patch test reaction, RR was demonstrated for nickel sulfate, cobalt chloride, fragrance mix, potassium dichromate, and carba mix in ACD patients (Table 4), cobalt chloride, nickel sulfate, thiomersal, carba mix and potassium dichromate in CD patients, nickel sulfate, cobalt chloride, potassium dichromate, carba mix and neomycin sulfate in AD patients, cobalt chloride, nickel sulfate, carba mix, wood tars, thiomersal and fragrance mix in PV patients, and nickel sulfate, cobalt chloride and carba mix in SD and OID patients.

DISCUSSION

Results of a representative study on CA are briefly described. Patch testing remains the gold standard to identify one or more substances that may contributing to the etiology of CA. Results of present study confirmed CA in a large population with different diagnoses and wide range of occupations, which is not presented in other studies. The results of our study showed concordance between allergens and clinical diagnoses. Nickel sulfate, cobalt chloride and carba mix were found to be the most relevant allergens. Patients with a relevant CA were much more likely to improve, especially patients with ACD, than patients with negative test results. Nickel sulfate is the leading allergen, as in the majority of previous analyses, whereas thiomersal was the least common one. However, a limitation of the study was the fact that study groups are not sex matched. Women were sensitized significantly more often than men (70.90%vs29.10%). Similar study group were included in the study by Dou and Veien study[29-30]. In all five clinical diagnoses there was a female predominance of positive reaction, mostly in ACD. Nickel and cobalt allergy was more frequent in female, like in studies of Schefer et al.[29] and Vein et al.[30], however, nickel sensitivity decreased with age of women, which could be explained by a reduced exposure to nickel (jewelry) and increase public awareness[30]. In their study covering the 1996-1999 period , Veien et al. report 19.3 % of study women allergic to nickel.
Our study is not randomized, so the results could not be extrapolated to explain contact sensitivity in the general population. Systemic contact dermatitis due to nickel caused by continual local skin contact with nickel could elicit systemic reaction[23]. We found the rate of positive reactions to nickel (17.6% to 10.8%) and thiomersal (6.8% to 1.6%) to decrease with age, respectively similar to Wöhrl et al.[24]. This authors report on 3.3% of cobalt allergy, considerably lower than the rate observed in our study (8.6%)[24]. Some occupations such as

cashiers and hairdressers, imply risk factors for nickel allergy[25]. Female sex was strongest risk factor for nickel (prevalence ratio 3.74, 95% CI: 3.51- 3.98) in study by Uter et al. [25]. In our study RR for ACD to nickel is 0.455, increasing steadily and significantly with decreasing age for nickel as well for cobalt chloride. In adolescents (age 10 to 19) found Duarte et al. (2003) found ACD more frequently in fair faced girls, and on the face in patients sensitive to nickel (31%) and tosylamide-formaldehyde resin (12%). These two substances are related to adolescent habits and behavior[18]. In our study, the rate of nickel sulfate sensitivity was lower (17.6%) in this age group and in young female. The increasing sensitivity to fragrance allergens recorded in our study (from 4.8% to 13.9) was similar to the others[17,21,31]. In Denmark is CA to fragrance second, and in Israel the third most common cause of ACD[17]. Axillary dermatitis is a common problem, particularly in individuals with CA to fragrance. Deodorants containing hydroxycitronellal can cause axillary dermatitis in a few weeks[21]. Propolis is an important allergen itself but cannot be used as a screening substance for fragrance allergy[31]. In the present study, the most common and relevant allergens were cobalt chloride, nickel sulfate, balsam of Peru, fragrance mix, thiuram mix, wood tars, neomycin sulfate, thiomersal as in other studies[16,19,20,24,26-29]. In our study, patch test positive rates to potassium dichromate did not differ significantly among different age groups (3-20 year, 6.6% and 61-80 year, 7.7%).This study yielded no major difference or reduction in the prevalence of dichromate sensitivity, unlike the study of Olsavszky et al.[32]. Sensitization to chromium is often caused by occupational exposure to soluble chromium compound in cement or leather and is often the leading allergen in Eastern European reports. In Croatia, there is no addition of ferrous sulfate to cement either. It is important to consider the possibility of ACD due to chromates by handling a cellular phone (containing hexavalent chromium plating)[22]. Hegewald et al. (2005) found 11.05% patients positive to nickel, 2.10% to potassium dichromate and 2.32% to cobalt chloride[33]. Food workers are recommend to undergo standard patch testing to the rubber and to

Compositae series allergens, as high sensitivity rates to nickel sulfate thiuram mix, formaldehyde and compositae mix[27] have been reported in food processing industry. Our study did not include food industry workers. The rate of CA to mercury was 10.38% (p<0,001) with steadily constant values with decreasing age. CA to thiomersal has not been considered a marker for mercury allergy, since there is a low degree of cross-sensitivity to inorganic as well as to organic mercury salts. In our study thiomersal positivity was 9% in medical and related professions, due to exposure to thiomersal containing vaccines etc. in 300 patients administered a standard series Santucci et al (1998) found concomitant positive reactions to thiomersal and ethylmercury chloride in only 3.6% of subjects if methylmercury chloride was added[34]. Due to the complexity of some research questions, regarding CA allergy require typical profile of certain allergens, demographic variables of sensitized patients, spectrum of cosensitization and address certain subpopulations with their spectrum allergens[35]. In 2002 and 2003, Uter et al. (2005) found nickel sulfate to be most common allergen (17.3%) followed by balsam of Peru (Myroxylon pereirae, 5.8%) and fragrance mix (6.4%) in 10,511 study patients. Regarding CA to chromium compounds, different frequencies were noted in two centers focused on occupational dermatitis (2.3%vs7.4). Surveillance of CA in the clinical population of patch tested patients has proven useful to detect time trends, such as decrease of nickel allergy in young females[36-37]. The reproducibility of patch-testing ranges from 80% to 85%, with reference to real-life testing, mirror image testing, or r-testing within 10 years[38].

CONCLUSION

This study as retrospective analysis of demographic data and patch-test results with standard series allergens produced some interesting observations. Patch testing remains the main diagnostic tool to examine and identify clinically suspect CA. The most relevant allergens in our study, i.e. nickel sulfate, cobalt chloride and carba mix, were found in all study subjects irrespective of age, sex, occupation and diagnoses. However, according to our experience with CA in this study, standard CA measures such as sensitivity and specificity as well as its prevalence should be determined in a prospective study. Direct consultation and liaising with biostatisticians is always advisable. A limitation of the study was the fact that the study groups were not sex matched. In a prospective study, reflectance confocal microscopy (RCM) at 72 hours of patch removal will be needed as an adjunctive tool to clinical evaluation. Further research is needed to fully understand the implications to contact hypersensitivity and to analyze various occupation. It is concluded that contact allergy in influenced by sociodemographic parameters and plays an important role in the general population.

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KONTAKTNA PREOSJETLJIVOST I SOCIODEMOGRAFSKE ZNAČAJKE

SAŽETAK

Prikazani su rezultati učestalosti pozitivnih reakcija na alergene standardne serije u epikutanom (patch) testu u odnosu na spol, dob i zvanje, te kliničku dijagnozu. U razdoblju od 1999 do 2003 testirano je 3293 bolesnika. U bolesnika je postavljena klinička dijagnoza. Svi su testirani po uobičajenom standardnom postupku prema propozicijama International Contact Dermatitis Research Group (ICDRG). Naše istraživanje je dokazalo statistički značajne razlike u testiranih bolesnika u odnosu na zadane parametre. Za tri alergena (kobalt klorid, nikal sulfat i timerosal) razlike su iskazane u odnosu na spol i dob. Za 9 alergena (kobalt klorid, nikal sulfat, peruvijanski balzam, smjesa mirisa, smjesu tiurama, drveni ugalj, neomicin sulfat, timerosal i detedžente) statistički značajne su razlike u odnosu na zanimanje. U odnosu na kliničke dijagnoze, najučestaliji su dva alergena (nikal sulfat i katrani drvenog uglja). Najčešći alergeni u svih ispitanika u odnosu na spol, dob, zanimanje i dijagnozu bili su: nikal sulfat, kobalt klorid i smjesa karbamata. Sve veća svijest o senzibilizaciji na kontaktnu preosjetljivost te njihovo otkrivanje bit će korisno u izostavljanju ovih kemijskih tvari u proizvodima za široku potrošnju.

TABLE 1

POSITIVE REACTIONS OF PATCH TESTING IN 3 293 PATIENTS ACCORDING SEX

	Male		Female		χ^2	p
	n	%	n	%		
Potassium dichromate	229	9.8	369	6.9	19.40	<0.001
Cobalt chloride	257	11.0	783	14.6	18.00	<0.001
Nickel sulfate	207	8.8	1146	21.3	175.00	<0.001
Formaldehyde	18	0.8	45	0.8	0.09	0.760
Urushiol	47	2.0	89	1.7	1.16	0.280
Balsam of Peru	126	5.4	220	4.1	6.33	0.010
Epoxy resin	50	2.1	54	1.0	15.69	<0.001
Colophony	14	0.6	42	0.8	0.76	0.380
White mercury praecipitate	137	5.9	224	4.2	10.38	<0.001
Benzocaine(anesthesine)	52	2.2	84	1.6	4.08	0.043
Carba mix	200	8.6	357	6.6	8.80	<0.003
Mercapto mix	24	1.0	45	0.8	0.65	0.420
Rubber mixture (PPD mix)	70	3.0	100	1.9	9.66	<0.001
Fragrance mix	212	9.1	395	7.4	6.55	0.010
Thiuram mix	38	1.6	105	2.0	0.98	0.322
Wood tars	136	5.8	264	4.9	2.67	0.102
Parabene mixture	36	1.5	44	0.8	8.22	<0.004
Neomycin sulfate	106	4.5	284	5.3	1.94	0.163
Quaternium 15	12	0.5	38	0.7	0.96	0.328
Thiomersal	178	7.6	301	5.6	11.24	<0.001
Detergents	190	8.1	381	7.1	2.51	0.113

TABLE 2

RESULTS OF PATCH TESTING IN 3293 PATIENTS ACCORDING TO AGE

	TOTAL	YEAR 3-20		YEAR 21-60		YEAR 61-80		χ^2	p
		n	%	n	%	n	%		
Potassium dichromate	598	117	6.6	429	8.2	52	7.7	4.87	0.080
Cobalt chloride	1040	249	13.9	733	14.0	58	8.6	15.10	<0.001
Nickel sulfate	1353	315	17.6	965	18.4	73	10.8	23.55	<0.001
Formaldehyde	63	15	0.8	43	0.8	5	0.7	0.06	0.971
Urushiol	136	41	2.3	88	1.7	7	1.0	5.21	0.074
Balsam of Peru	346	67	3.8	218	4.2	61	9.1	36.25	<0.001
Epoxy resin	104	25	1.4	72	1.4	7	1.0	0.54	0.760
Colophony	56	10	0.6	37	0.7	9	1.3	4.18	0.130
White mercury praecipitate	361	82	4.6	248	4.7	31	4.6	0.06	0.970
Benzocaine (anesthesine)	136	28	1.6	97	1.8	11	1.6	0.67	0.714
Carba mix	557	115	6.4	377	7.2	65	9.6	7.53	0.023
Mercapto mix	69	24	1.3	40	0.8	5	0.7	5.29	0.070
Rubber mixture (PPD mix)	170	41	2.3	112	2.1	17	2.5	0.51	0.775
Fragrance mix	607	86	4.8	427	8.1	94	13.9	57.73	<0.001
Thiuram mix	143	22	1.2	103	2.0	18	2.7	6.59	0.037
Wood tars	400	76	4.3	273	5.2	51	7.6	10.89	0.004
Parabene mixture	80	24	1.3	47	0.9	9	1.3	3.26	0.197
Neomycin sulfate	390	125	7.0	211	4.0	54	8.0	38.09	<0.001
Quaternium 15	50	9	0.5	32	0.6	9	1.3	5.63	0.060
Thiomersal	479	121	6.8	347	6.6	11	1.6	26.67	<0.001
Detergents	571	193	10.8	351	6.7	27	4.0	45.53	<0.001

TABLE 3

RESULTS OF PATCH TESTING IN 3293 PATIENTS ACCORDING TO OCCUPATION

	Total	Pensioners			Students			Administrative personnel			Medical and alliend professions			Workers		
		n	%	RR	n	%	RR	n	%	RR	n	%	RR	n	%	RR
Potassium dichromate	598	76	7.3	0.02	112	6.5	0.04	231	8.6	0.08	63	7.5	0.02	116	8.19	0.04
Cobalt chloride	1040	94	9.0	0.03	251	14.6	0.08	398	14.8	0.14	95	11.4	0.03	202	14.27	0.07
Nickel sulfate	1353	126	12.0	0.04	295	17.1	0.10	503	18.7	0.18	161	19.2	0.05	268	18.93	0.09
Formaldehyde	63	8	0.8	0.00	12	0.7	0.00	17	0.6	0.01	12	1.4	0.00	14	0.99	0.00
Urushiol	136	15	1.4	0.00	35	2.0	0.01	48	1.8	0.01	15	1.8	0.00	23	1.62	0.01
Balsam of Peru	346	95	9.1	0.03	69	4.0	0.02	99	3.7	0.03	35	4.2	0.01	48	3.39	0.01
Epoxy resin	104	12	1.1	0.00	19	1.1	0.01	40	1.5	0.01	5	0.6	0.00	28	1.98	0.01
Colophony	56	12	1.1	0.00	9	0.5	0.00	21	0.8	0.01	3	0.4	0.00	11	0.78	0.00
White mercury praecipitate	361	46	4.4	0.01	70	4.1	0.02	123	4.6	0.04	34	4.1	0.01	88	6.21	0.03
Benzocaine(anesthesine)	136	23	2.2	0.01	29	1.7	0.01	45	1.7	0.01	15	1.8	0.00	24	1.69	0.01
Carba mix	557	92	8.8	0.03	117	6.8	0.04	193	7.2	0.06	60	7.2	0.02	95	6.71	0.03
Mercapto mix	69	9	0.9	0.00	19	1.1	0.01	20	0.7	0.01	4	0.5	0.00	17	1.20	0.01
Rubber mixture (PPD mix)	170	30	2.9	0.01	39	2.3	0.01	49	1.8	0.02	23	2.7	0.01	29	2.05	0.01
Fragrance mix	607	135	12.9	0.04	107	6.2	0.03	203	7.6	0.07	68	8.1	0.02	94	6.64	0.03
Thiuram mix	143	23	2.2	0.01	21	1.2	0.01	69	2.6	0.02	18	2.2	0.01	12	0.85	0.00
Wood tars	400	85	8.1	0.03	84	4.9	0.03	143	5.3	0.05	29	3.5	0.01	59	4.17	0.02
Parabene mixture	80	16	1.5	0.00	18	1.0	0.01	21	0.8	0.01	8	1.0	0.00	17	1.20	0.01
Neomycin sulfate	390	67	6.4	0.02	99	5.7	0.03	100	3.7	0.03	42	5.0	0.01	82	5.79	0.03
Quaternium 15	50	13	1.2	0.00	9	0.5	0.00	15	0.6	0.00	6	0.7	0.00	7	0.49	0.00
Thiomersal	479	25	2.4	0.01	117	6.8	0.04	188	7.0	0.06	75	9.0	0.02	74	5.23	0.02
Detergents	571	44	4.2	0.01	191	11.1	0.06	162	6.0	0.05	66	7.9	0.02	108	7.63	0.03

TABLE 4

DISTRIBUTION OF POSITIVE PATCH TEST REACTION IN 3293 PATIENTS ACCORDING CLINICAL DIAGNOSES 1999-2003.

	TOTAL	ACD			CD			AD			PV			SD			OID		
		n	%	RR	n	%	RR	n	%	RR	n	%	RR	n	%	RR	n	%	RR
Potassium dichromate	598	445	7.9	0.156	13	7.5	0.004	94	8.0	0.029	16	6.3	0.005	16	6.6	0.005	14	6.3	0.004
Cobalt chloride	1040	744	13.2	0.292	25	14.4	0.008	161	13.7	0.051	47	18.7	0.014	39	16.0	0.012	24	10.7	0.007
Nickel sulfate	1353	1029	18.2	0.455	18	10.3	0.005	173	14.8	0.055	39	15.5	0.012	49	20.2	0.015	45	20.1	0.014
Formaldehyde	63	43	0.8	0.013	1	0.6	0.000	14	1.2	0.004	1	0.4	0.000	1	0.4	0.000	3	1.3	0.001
Urushiol	136	107	1.9	0.034	3	1.7	0.001	12	1.0	0.004	6	2.4	0.002	4	1.6	0.001	4	1.8	0.001
Balsam of Peru	346	268	4.7	0.089	5	2.9	0.002	40	3.4	0.012	16	6.3	0.005	8	3.3	0.002	9	4.0	0.003
Epoxy resin	104	70	1.2	0.022	4	2.3	0.001	18	1.5	0.005	4	1.6	0.001	5	2.1	0.002	3	1.3	0.001
Colophony	56	43	0.8	0.013	1	0.6	0.000	8	0.7	0.002	1	0.4	0.000	1	0.4	0.000	2	0.9	0.001
White mercury praecipitate	361	275	4.9	0.091	7	4.0	0.002	52	4.4	0.016	8	3.2	0.002	9	3.7	0.003	10	4.5	0.003
Benzocaine (anesthesine)	136	91	1.6	0.028	3	1.7	0.001	26	2.2	0.008	4	1.6	0.001	6	2.5	0.002	6	2.7	0.002
Carba mix	557	392	6.9	0.135	14	8.0	0.004	79	6.7	0.025	22	8.7	0.007	29	11.9	0.009	21	9.4	0.006
Mercapto mix	69	45	0.8	0.014	1	0.6	0.000	19	1.6	0.006	1	0.4	0.000	3	1.2	0.001	0	0.0	0.000
Rubber mixture (PPD mix)	170	130	2.3	0.041	3	1.7	0.001	25	2.1	0.008	5	2.0	0.002	2	0.8	0.001	5	2.2	0.002
Fragrance mix	607	473	8.4	0.168	12	6.9	0.004	69	5.9	0.021	18	7.1	0.005	15	6.2	0.005	20	8.9	0.006
Thiuram mix	143	118	2.1	0.037	2	1.1	0.001	20	1.7	0.006	3	1.2	0.001	0	0.0	0.000	0	0.0	0.000
Wood tars	400	307	5.4	0.103	12	6.9	0.004	33	2.8	0.010	22	8.7	0.007	15	6.2	0.005	11	4.9	0.003
Parabene mixture	80	54	1.0	0.017	3	1.7	0.001	21	1.8	0.006	1	0.4	0.000	0	0.0	0.000	1	0.4	0.000
Neomycin sulfate	390	274	4.9	0.091	9	5.2	0.003	75	6.4	0.023	4	1.6	0.001	14	5.8	0.004	14	6.3	0.004
Quaternium 15	50	30	0.5	0.009	1	0.6	0.000	13	1.1	0.004	4	1.6	0.001	2	0.8	0.001	0	0.0	0.000
Thiomersal	479	341	6.0	0.116	16	9.2	0.005	73	6.2	0.023	20	7.9	0.006	14	5.8	0.004	15	6.7	0.004
Detergents	571	365	6.5	0.125	21	12.1	0.006	147	12.5	0.047	10	4.0	0.003	11	4.5	0.003	17	7.6	0.005

Legend: ACD - allergic contact dermatitis, CD - contact irritant dermatitis, AD - atopic dermatitis, PV - psoriasis vulgaris, SD - seborrhoeic dermatitis, OID - other inflammatory dermatoses