American Contact Dermatitis Society Core Allergen Series: 2020 Update

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The American Contact Dermatitis Society Core Allergen series was introduced in 2013 and updated in 2017. Changes in our recommended allergens are again necessary, taking into account data from the American Contact Dermatitis Society's Contact Allergen Management Program top 100 allergens from 2018. For the updated series, we removed methyldibromoglutaronitrile and added new haptens: Lyral, Limonene, Linalool, carmine, benzyl salicylate, disperse yellow 3, jasmine, peppermint, pramoxine, shellac, and lauryl polyglucose (glucosides). These additional allergens should increase the yield of relevant positive reactions for our patients.

In 2013, the American Contact Dermatitis Society (ACDS) published a core allergen series with 80 haptens.[1] The goal of this series was to assist in logically expanding patch-testing allergen series beyond the TRUE Test (TT) (SmartPractice, Phoenix, AZ) standard allergens, currently with 35 allergens and 1 negative control. This was followed by an update in 2017, which reflected the updated TT panels, as well as adding/removing relevant allergens in the extended series panels.[2]

After 8 years of use and 2 iterations, we again feel that updating the ACDS Core Allergen Series is necessary. To evaluate the allergens on the 2017 ACDS Core Allergen series, it was compared with the top 100 allergens in the ACDS Contact Allergy Management Program (CAMP) data for the year 2018. The CAMP database allows entry of a patient's set of individual allergies and produces a list of personal care products that are free of those haptens. This database was examined for the year of 2018, and the top 100 most prevalent haptens were summarized and published.[3] Nine allergens not included in the 2017 series that the group felt to be important were identified and added to the Core Allergen Series.[3]

To treat allergic contact dermatitis (ACD), correct identification of the offending hapten is required, and the criterion standard for identification of contact allergy is the patch test.[4–6] Definitive identification of relevant allergens is a cost-effective way to improve quality of life for dermatitis patients.[4] Patch testing also reduces the cost of postdiagnosis prescriptions and office visits.[4] Limited series patch tests with 36 allergens, such as the TT, correctly identify 66% of clinically relevant reactions that would be identified using the North American Contact Dermatitis Group (NACDG) screening series.[4] Simply put, an extensive patch test reduces overall health care costs and improves the quality of life for many dermatitis patients.[7–9]

Thus, the goal of the ACDS Core Allergen series is to give patch testers who are currently using the TT as their baseline series a logical and graded tool to increase the number of allergens tested, as well as provide a helpful and scalable baseline series for those opting to use customizable patch-test screens. This should increase the yield of useful positive tests for our patients. This series was reviewed and approved by the ACDS Executive Committee.

For 2020, panels 4 to 8 have minimal changes. The first 35 allergens are primarily based on the TT panels 1.3, 2.3, and 3.3. We have chosen to substitute allergens in some cases for those not using the TT in the first 35 allergens, but the screening capability is similar. The group did not feel that the removal of allergens from the 2017 80 allergen series, other than methyldibromoglutaronitrile (MDGN), was necessary. Increasing the testing concentration of formaldehyde from 1% to 2% is recommended. This should increase reaction yields and not increase irritant reactions.[10,11] Nine important allergens identified in the CAMP top 100, as well as 2 additional common potential haptens, were added to the series (disperse yellow 3 and pramoxine).

A more extensive baseline series with relevant allergens is both a cost-effective and diagnostically effective manner to cure ACD patients. In this pursuit, we have chosen to expand the ACDS series to include a ninth allergen panel. Updated panels 1 through 9 of the ACDS Core Allergen Series are presented in Table 1. The

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TABLE 1. ACDS Core Allergen Series 2020

Core Allergen Panel I
(1) Nickel sulfate 2.5% pet.*
(2) Lanolin alcohol (Amerchol 101) 50% pet.* (TT = wool alcohol)
(3) Neomycin 20% pet.*
(4) Potassium dichromate 0.25% pet.*,†
(5) DMDM hydantoin 1% pet.
(6) Fragrance mix I 8% pet.*,†
(7) Colophony 20% pet.*
(8) Paraben mix 12% pet. *
(9) Methylisothiazolinone 0.2% aq.
(10) Balsam Peru (*Myroxylon pereirae*) 25% pet.*

Core Allergen Panel II
(11) Ethylenediamine dihydrochloride 1% pet.*
(12) Cobalt chloride 1% pet.*,†
(13) *p*-tert-Butylphenol formaldehyde resin 1% pet.*
(14) Epoxy resin 1% pet.*
(15) Carba mix 3% pet.*,†
(16) Black rubber mix 0.6% pet.*
(17) Methylchloroisothiazolinone/methylisothiazolinone 100 ppm. aq.*
(18) Quaternium 15 2% pet.*
(19) Hydroxyperoxides of Linalool 0.5% pet.
(20) *p*-Phenylenediamine 1% pet.*

Core Allergen Panel III
(21) Formaldehyde 2% aq.*,†
(22) Mercapto mix 1% pet.*
(23) 2-Bromo-2-nitropropane-1,3-diol 0.5% pet.
(24) Thiuram mix 1% pet.*
(25) Diazolidinyl urea 1% pet.*
(26) Benzocaine 5% pet.‡
(27) Tixocortol-21-pivalate 1% pet.*
(28) Gold sodium thiosulfate 2% pet.*
(29) Imidazolidinyl urea 2% pet.*
(30) Budesonide 0.1% pet.*

Core Allergen Panel IV
(31) Hydrocortisone-17-butyrate 1% pet. *
(32) Mercaptobenzothiazole 1% pet.*
(33) Bacitracin 20% pet. *
(34) Fragrance mix II 14% pet.
(35) Disperse blue 106/124 mix 1.0% pet.*,§
(36) Lidocaine 15% pet.
(37) Propylene glycol 30% aq.
(38) Iodopropynyl butylcarbamate 0.1% pet.†
(39) Polymyxin B sulfate 3% pet.
(40) Cocamidopropyl betaine 1% aq.†

Core Allergen Panel V
(41) Mixed dialkyl thioureas 1% pet.
(42) Dimethylaminopropylamine 1% aq.
(43) Hydroxyethyl methacrylate 2% pet.
(44) Oleamidopropyl dimethylamine 0.1% aq.
(45) Decyl glucoside 5% pet.
(46) Methyl methacrylate 2% pet.
(47) Lavender absolute 2% pet.
(48) Cinnamic aldehyde 1% pet.
(49) D/L-α-Tocopherol 100%.

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TABLE 1. *(Continued)*

(50) Ethyl acrylate 0.1% pet.
(51) Tea tree oil 5% pet.
(52) Chlorhexidine digluconate 0.5% aq.
(53) Propolis 10% pet.
(54) Chloroxylenol (PCMX) 1% pet.
(55) 2-Hydroxy-4-methoxybenzophenone (benzophenone-3) 10% pet.
(56) Tosylamide formaldehyde resin 10% pet.
(57) Sesquiterpene lactone mix 0.1% pet.
(58) Cocamide DEA (Coconut diethanolamide) 0.5% pet.
(59) Hydroxyperoxides of limonene 0.2% pet.
(60) Benzalkonium chloride 0.1% pet.†

Core Allergen Panel VII
(61) 2-Hydroxy-4-methoxybenzophenone-5-sulfonic acid (benzophenone-4) 2% pet.
(62) Sodium benzoate 5% pet.
(63) Sorbic acid 2% pet.
(64) Ylang-ylang 2% pet.
(65) Compositae mix II 5% pet.
(66) Ethyleneurea melamine-formaldehyde 5% pet.
(67) Sorbitan sesquioleate 20% pet.
(68) n,n-Diphenylguanidine 1% pet.
(69) Lyral 5% pet.
(70) Ethylhexylglycerin 5% pet.

Core Allergen Panel VIII
(71) Triamcinolone 1% pet.
(72) Clobetasol-17-propionate 1% pet.
(73) Amidoamine 0.1% aq.
(74) Ethyl cyanoacrylate 10% pet.
(75) Phenoxyethanol 1% pet.
(76) Disperse orange 3 1% pet.
(77) Benzoic acid 5% pet.
(78) 2, 6-ditert-butyl-4-cresol (BHT) 2% pet.
(79) 2-Ethylhexyl-4-methoxycinnamate 10.0 pet.
(80) Benzyl alcohol 10% soft

Core Allergen Panel IX
(81) Cetyl steryl alcohol 20% pet.
(82) Carmine 2.5% pet.
(83) Benzyl salicylate 10% pet.
(84) Disperse yellow 3 1% pet.
(85) Jasmine 2% pet.
(86) Peppermint 2.0% pet.
(87) Pramoxine hydrochloride 2% pet.
(88) Shellac 20% alcohol†
(89) Lauryl polyglucose (glucosides) 3.0% pet.†
(90) p-chloro-m-cresol (PCMC) 1% pet.

**TT allergen.*

†Interpret reactions with caution, mild irritant, and/or low clinical relevance.

‡Caine mix (containing benzocaine) is the TT allergen.

§Disperse blue 106 is the TT allergen.

DMAPA, 3-(dimethylamino)-propylamine; PCMC, 4-chloro-3-cresol; pet., petrolatum; TT, TRUE Test.

TABLE 2. 2020 ACDS Core Allergen Series Changes

TRUE Test (TT) allergens
- Unchanged by manufacturer

ACDS changes to TT panels from 2017 series
- Delete methyldibromoglutaronitrile 0.5% pet.
- Changed concentration of formaldehyde from 1% to 2%

ACDS additional allergens for 2020

Added
- 19. Hydroxyperoxides of Linalool 0.5% pet.
- 59. Hydroxyperoxides of Limonene 0.2% pet.
- 69. Lyral 5% pet.
- 82. Carmine 2.5% pet.
- 83. Benzyl salicylate 10% pet.
- 84. Disperse yellow no. 3 1% pet
- 85. Jasmine 2% pet.
- 86. Peppermint 2.0% pet.
- 87. Pramoxine hydrochloride 2% pet.
- 88. Shellac 20% alcohol
- 89. Lauryl polyglucose (glucosides) 3.0% pet.

Moved
- Cetyl steryl alcohol 20% pet. to 81
- p-chloro-m-cresol (PCMC) 1% pet. to 90

changes from the 2017 Core Allergen Series are summarized in detail in Table 2.

A new change to the 2020 ACDS series is the removal of MDGN. This allergen was removed from products in the European Union in 2005 for leave-on products and in 2008 for wash-off products and was restricted for noncosmetic use in 2010.[12] The NACDG, in their last iteration of their standard series findings (2015–2016 data), had Euxyl K400 in the top 20 relevant allergens.[13] This allergen is a mix of MDGN/phenoxyethanol, which confounds the analysis regarding which is the actual hapten. The majority of positives in this data set were reported as possible, past or unknown relevance, not probable, or definite. The CAMP database lists only 237 products (4%) potentially with MDGN of 5551 total products. Although these data show that MDGN is still present in a few products and some patients still have patch-test reactions, the ACDS Core Allergen Committee's clinical experience supports that, although MDGN continues to show positive reactions in some, it is not usually a clinically relevant allergen at this time. Phenoxyethanol remains a screening allergen on the Core Allergen Series.

Thorough screening for fragrance allergy is high yield and necessary.[14] New additions to the 2020 series include 5 fragrances—Limonene, Linalool, Lyral, peppermint, and jasmine. It is estimated that 3.5% to 4.5% of the adult population and 20% of the patch-tested population may be allergic to 1 or more fragrances.[15] Limonene, Linalool, and Lyral are fragrance ingredients that are commonly seen in personal care products, processed foods and beverages, and perfumes.[16,17] These 3 allergens seem to be of significant relevance for many patch-tested patients. Testing should be performed with the hydroxyperoxide (oxidized variant) of Linalool and Limonene. These compounds increase relevant patch-testing yield compared with the unoxidized fragrance.[16,17] Hydroxyperoxides of Linalool is available at 0.5% and 1% concentrations and hydroxyperoxides of Limonene at 0.3% and 0.2%. At the higher concentration, there is risk of questionable/irritant reactions for both Linalool and Limonene.[16,17] We recommend testing at 0.5% and 0.2%, respectively, in this series. Jasmine and peppermint are also within the realm of fragrances, as well as flavorings in some consumable items. Although reactions to jasmine and peppermint are less common than some other fragrances, it is important to include them in routine screening.[18–20]

Carmine is a natural red dye used in cosmetics and foods, derived from the *Dactylopius coccus* insect. The female insects are harvested and processed, yielding bright red pigment. The use of carmine is increasing because of use restrictions on the synthetic red dyes, which may be carcinogenic.[21] Until recently, ACD to carmine was believed to be rare. The NACDG added carmine to its screening tray in 2011, finding a 3.1% reaction rate.[22] The positives tended to be mild, and caution was recommended when reading because of the red dye leading to potential false-positive results with macular erythema.[22]

Pramoxine is a topical desensitizing agent used in many over-the-counter "anti-itch" and topical desensitization creams/lotions. Contact dermatitis to the ester and amide group anesthetics (ie, benzocaine or lidocaine) is well known, but pramoxine reactions are less common because of its novel chemical structure.[23] As of 2014, there were 6 reported cases of pramoxine contact allergy.[21] The NACDG is currently testing pramoxine routinely, and these data will be published after the next 2-year study period is completed. In addition to type IV reactions, a single report of type I anaphylactic reaction on abraded skin was reported.[24] Pramoxine use in topical over-the-counter medicaments is common, and this group feels that it is increasing, thus warranting addition of this hapten to the series.

Shellac is a resin derived from the *Laccifer lacca* insect, which is indigenous to Thailand and India. Once processed, it forms a hard lacquer, which has diverse uses in cosmetics, such as eyeliner, mascara, lipstick, lip sealants, and hair dyes and sprays.[25] It is also used as an edible food glaze and in furniture finishing applications. Reaction rates have varied from 1.6/1.7% (NACDG data 2009–2012) to 10.5% in a recent Mayo Clinic series.[26] Some have considered this allergen, which is tested in 20% alcohol to be in irritant, although the rates seen in the study of Veverka et al[26] were only 0.8%.

The alkyl glucosides are commonly found natural, plant-derived surfactants that won the honor of being the ACDS contact allergen of the year for 2017.[27] One important component, lauryl glucosides, was added to the 2020 series. Overall, use of glucosides is common, being found in 10% of the products listed in the Contact Allergen Management Program database.[28] The previous series included decyl glucosides, the fifth most prevalent surfactant in CAMP. Lauryl glucoside was the eighth most commonly used surfactant. Bai et al[29] examined 65 laundering products in the United States, finding glucosides in the top 10 most common allergenic chemicals identified in everyday laundry products. Testing for individual

components of the glucoside group may increase detection of this important group of haptens.[28]

The addition of disperse yellow 3 expands the screening for disperse textile dyes in this series. Disperse yellow 3 was recently found to have a 1.1% rate of reaction in textile dye allergic patients.[30] This allergen was not present on the CAMP 100 list but is a common exposure in synthetic clothing and is felt to be potentially relevant for our patients.

It is our goal to recommend useful and appropriate patch-testing series to allow complete evaluation of our suspected ACD patients. Using the ACDS Core Allergen Series will allow the clinician to logically extend the patch-test screening to incorporate common, rare, and emerging allergens beyond those identified by the TT.

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