the Patch Tester

Contact Dermatitis | Haptens | Patch Testing

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THE SESQUITERPENE ISSUE

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PURPOSE

The Patch Tester is an e-mag developed by Chemotechnique to serve as an information resource for all Patch Testers and other Dermatologists around the world; not just in Sweden, or Europe, or America, but wherever the English language can be read and understood. This sixteenth issue comprises thirty eight pages with various different topics and features. Ultimately, we plan for The Patch Tester to become the forum for all of us to communicate and cooperate, in all directions.

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If you would like to contact Chemotechnique about any aspect of The Patch Tester, or any other topic of mutual interest, then please write to us by clicking the “Contact” box on the front cover, or here.

ACKNOWLEDGEMENTS

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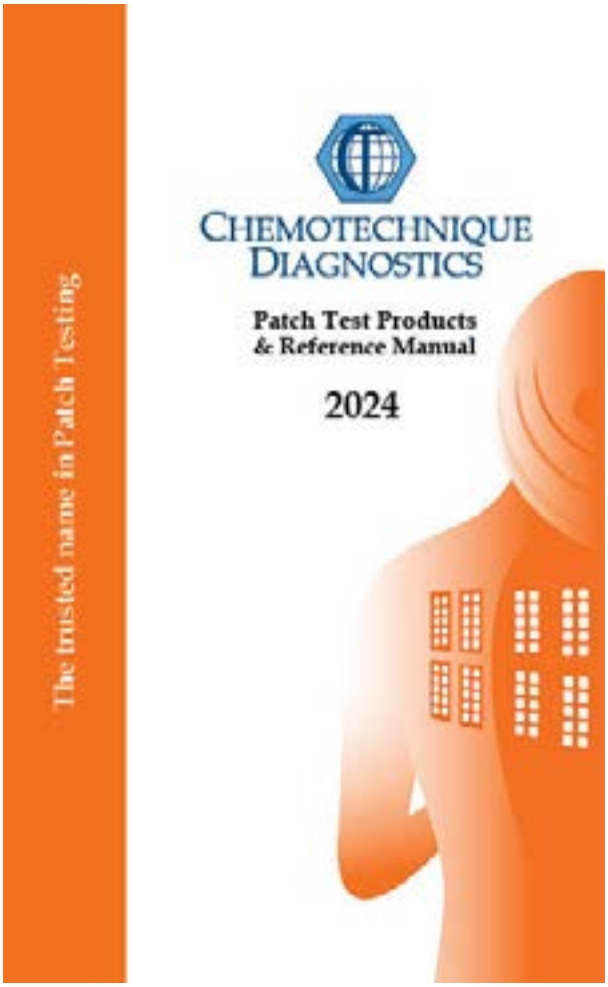
What's New in Patch Testing?



New Patch Test Product & Reference Manual

With the year coming to an end, it is time to unveil the 2024 edition of the Chemotechnique Patch Test Product & Reference Manual.

The highlight of this year's edition is the significant update to our International Comprehensive Baseline Series and North American Series. Based on the latest research findings and insights of the NACDG, these Series has been meticulously revised to ensure it remains at the forefront of patch testing for contact allergies. This update reflects our dedication to staying abreast of industry advancements and meeting the evolving needs of clinicians and dermatologists.

The 2024 Patch Test Product & Reference Manual can be downloaded on the chemotechnique webpage. Any changes in series composition presented in the catalogue will come into effect on February 1st 2024.

Changes to the North American Series

In a significant stride towards advancing dermatological research and enhancing patient care, the North American Baseline Series (NA-1000 and NAC-80) used for baseline patch testing has undergone major updates. The latest iteration of the series reflects the results of the most recent studies conducted by the North American Contact Dermatitis Group (NACDG).

The 2024 version of the series introduces a new format of placing all non-liquid haptens in alphabetical order by article number. The 10 liquid haptens are all placed on a single Patch Test Unit to facilitate application. Compared to the current (2020) Series, 21 haptens have been replaced in the ICB and NAC with haptens that are showing increased potential for diagnosing patient reaction. Please consult page 196 for specific deletions and additions.

2023 NAC-80 Composition

Red = Removal

Position	Art no	Name
1	B-004	Benzocaine
2	M-003B	2-Mercaptobenzothiazole (MBT)
3	C-020	COLOPHONIUM
4	P-006	p-PHENYLENEDIAMINE (PPD)
5	I-001A	IMIDAZOLIDINYL UREA
6	C-014	CINNAMAL
7	A-004	Amerchol L-101
8	Mx-06	Carba mix
9	N-001	Neomycin sulfate
10	Mx-01	Thiuram mix
11	C-028	Clobetasol-17-propionate
12	E-005	Ethylenediamine dihydrochloride
13	E-002	Epoxy resin, Bisphenol A
14	C-007B	QUATERNIUM-15
15	B-024	4-tert-Butylphenolformaldehyde resin (PTBP)
16	Mx-05B	Mercapto mix
17	D-022	1,3-Diphenylguanidine
18	P-014B	Potassium dichromate
19	B-001	Peru balsam
20	N-002B	Nickel(II)sulfate hexahydrate
21	D-044C	DIAZOLIDINYL UREA
22	T-036	TOCOPHEROL
23	B-032B	Bacitracin
24	Mx-24	Mixed dialkyl thiourea
25	**D-032**	**DISPERSE ORANGE 3**
26	Mx-03A	Paraben mix
27	D-049E	METHYLDIBROMO GLUTARONITRILE
28	Mx-07	Fragrance mix I
29	**G-003B**	**GLUTARAL**
30	B-015B	2-BROMO-2-NITROPROPANE-1,3-DIOL
31	Mx-18	Sesquiterpene lactone mix
32	**T-007**	**THIMEROSAL**
33	P-022	Propolis
34	H-010	2-Hydroxyethyl methacrylate
35	C-010B	CHLOROXYLENOL (PCMX)
36	**Mx-16**	**Ethyleneurea, melamine formaldehyde mix**
37	**B-022**	**2-tert-Butyl-4-methoxyphenol (BHA)**
38	**G-005A**	**Gold(I)sodium thiosulfate dihydrate**
39	E-004	Ethyl acrylate
40	**G-004**	**GLYCERYL THIOGLYCOLATE**
41	T-010	Toluenesulfonamide formaldehyde resin
42	M-013	Methyl methacrylate
43	C-017A	Cobalt(II)chloride hexahydrate
44	T-031A	Tixocortol-21-pivalate
45	B-033A	Budesonide
46	C-019	COCAMIDE DEA
47	**T-016**	**TRIETHANOLAMINE**
48	**Mx-30**	**Textile dye mix**
49	T-035B	Tea tree oil oxidized
50	Mx-25	Fragrance mix II
51	**D-036**	**Disperse Yellow 3**
52	B-010B	BENZYL SALICYLATE
53	D-065	DECYL GLUCOSIDE
54	M-035B	METHYLISOTHIAZOLINONE
55	H-010	2-Hydroxyethyl methacrylate
56	D-047B	DMDM HYDANTOIN
57	Y-001	Ylang ylang oil
58	B-008B	BENZYL ALCOHOL
59	**I-003**	**ISOPROPYL MYRISTATE**
60	**H-032A**	**Hydroperoxides of Limonene**
61	**D-057**	**Desoximetasone**
62	**P-013**	**POLYSORBATE 80**
63	I-008C	IODOPROPYNYL BUTYLCARBAMATE
64	O-004	2-n-Octyl-4-isothiazolin-3-one
65	**Mx-26**	**Disperse Blue mix 106 / 124**
66	Mx-29A	Compositae mix II
67	L-002B	Lidocaine
68	**F-003**	**Fusidic acid sodium salt**
69	**D-005B**	**Dibucaine hydrochloride**
70	**B-007**	**Benzoylperoxide**
71	**I-009**	**ISOAMYL p-METHOXYCINNAMATE**
72	L-003	HYDROXYISOHEXYL 3-CYCLOHEXENE CARBOXALDEHYDE
73	**O-007A**	**ETHYLHEXYL SALICYLATE**
74	**H-031A**	**Hydroperoxides of Linalool**
75	A-029	Amidoamine
76	C-018	COCAMIDOPROPYL BETAINE
77	F-002B	FORMALDEHYDE
78	C-009B	METHYLISOTHIAZOLINONE+ METHYLCHLOROISOTHIAZOLINONE
79	P-019B	PROPYLENE GLYCOL
80	O-005	OLEAMIDOPROPYL DIMETHYLAMINE

2024 NAC-80 Composition

Blue = Addition

Position	Art no	Name
1	A-004	Amerchol L-101
2	**A-011**	**AMMONIUM PERSULFATE**
3	B-001	Peru balsam
4	**B-003B**	**BENZISOTHIAZOLINONE**
5	B-004	Benzocaine
6	B-008B	BENZYL ALCOHOL
7	B-010B	BENZYL SALICYLATE
8	B-015B	2-BROMO-2-NITROPROPANE-1,3-DIOL
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15	C-017A	Cobalt(II)chloride hexahydrate
16	C-019	COCAMIDE DEA
17	C-020	COLOPHONIUM
18	C-028	Clobetasol-17-propionate
19	**D-002**	**TOLUENE-2,5-DIAMINE SULFATE**
20	D-022	1,3-Diphenylguanidine
21	D-044C	DIAZOLIDINYL UREA
22	D-047B	DMDM HYDANTOIN
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44	Mx-06	Carba mix
45	Mx-07	Fragrance mix I
46	Mx-18	Sesquiterpene lactone mix
47	**Mx-19**	**Caine mix III**
48	Mx-24	Mixed dialkyl thiourea
49	Mx-25	Fragrance mix II
50	Mx-29A	Compositae mix II
51	**Mx-32**	**Textile dye mix II**
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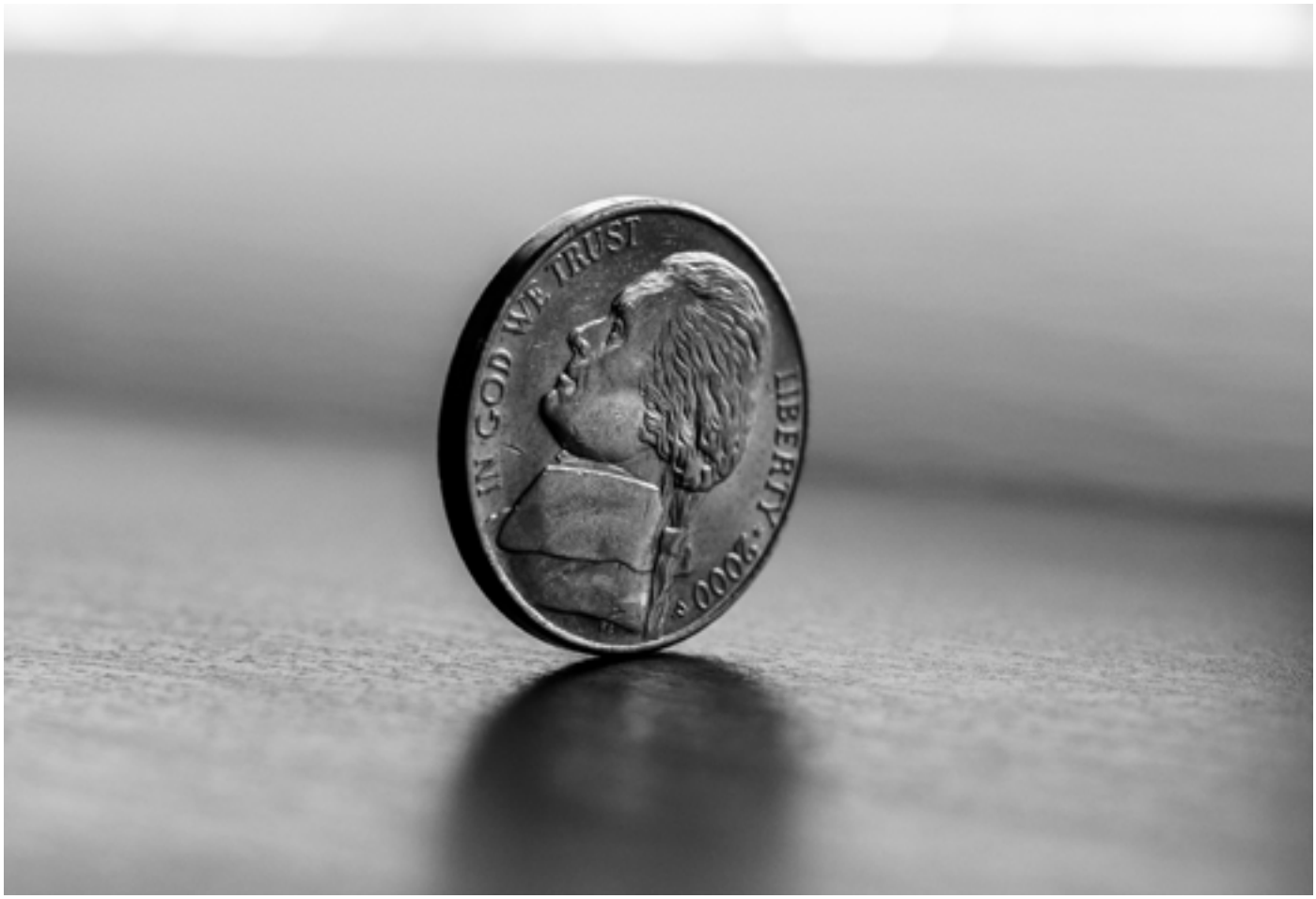
55	P-006	p-PHENYLENEDIAMINE (PPD)
56	P-014B	Potassium dichromate
57	**P-021**	**PROPYL GALLATE**
58	P-022	Propolis
59	**P-026**	**Polymyxin B sulfate**
60	**P-039**	**Pramoxine hydrochloride**
61	**S-001**	**SODIUM BENZOATE**
62	**S-004**	**SORBITAN OLEATE**
63	**S-005**	**SORBITAN SESQUIOLEATE**
64	**S-011**	**SODIUM METABISULFITE**
65	T-010	Toluenesulfonamide formaldehyde resin
66	T-031A	Tixocortol-21-pivalate
67	T-035B	Tea tree oil oxidized
68	T-036	TOCOPHEROL
69	**W-001**	**LANOLIN ALCOHOL**
70	Y-001	Ylang ylang oil
71	A-029	Amidoamine
72	**B-027**	**BENZALKONIUM CHLORIDE**
73	**C-005**	**CHLORHEXIDINE DIGLUCONATE**
74	C-009B	METHYLISOTHIAZOLINONE+ METHYLCHLOROISOTHIAZOLINONE
75	C-018	COCAMIDOPROPYL BETAINE
76	**D-053**	**3-(Dimethylamino)-1-propylamine**
77	F-002B	FORMALDEHYDE
78	M-035B	METHYLISOTHIAZOLINONE
79	O-005	OLEAMIDOPROPYL DIMETHYLAMINE
80	P-019B	PROPYLENE GLYCOL

Chemo Spot Tests



In the modern era, where metal objects are an integral part of daily life, ensuring their safety becomes paramount. Nickel and cobalt, while widely used in various industries, pose a hidden threat when present in free ion form. The Chemotechnique Chemo Nickel Test and Chemo Cobalt Test emerge as indispensable tools in the detection of these potentially harmful metals, shedding light on the importance of these tests for safeguarding public health.

Nickel and cobalt are versatile metals, finding applications in diverse fields such as electronics, jewelry, and manufacturing. However, when these metals are present as free ions, they can trigger allergic reactions in susceptible individuals. Recognizing the need for stringent quality control measures, Chemotechnique developed the Chemo Nickel and Chemo Cobalt Tests to address these concerns.

In a world where metal objects are omnipresent, the Chemotechnique Chemo Nickel and Chemo Cobalt Tests stand as indispensable guardians of public health. These tests provide manufacturers with the means to identify and mitigate the risks associated with free nickel and cobalt ions, ensuring that the products we use daily are not just functional but also safe. As we move towards a future of heightened awareness and responsibility, the adoption of these tests becomes not just a choice but a necessity in securing the well-being of consumers worldwide.

Chemo Nickel Test™

For persons sensitive to nickel, then avoidance of the metal is key to protect the skin from allergic reactions.

Chemo Nickel Test™ allows the Dermatologist or the Patient to easily detect free Nickel in metallic objects.
The test consists of an ammoniacal solution of Dimethylglyoxime (DMG) for the detection of nickel in various metallic objects. DMG produces a bright, reddish-pink insoluble salt with nickel.

The Chemo Nickel Test detects free nickel down to a limit of 10 ppm (parts/million). The sensitivity threshold of most nickel allergic patients is above 11 ppm (parts/million).
Some strongly allergic patients will however still react to objects releasing nickel ions below this threshold of the test.

Product packaging: The test solution is contained in a glass bottle with a dropper insert and screw on cap. The product is packaged in a plastic cylindrical container with a flip-top-cap alongside 2 cotton swabs and printed instructions for use.

Chemo Cobalt Test™

For persons sensitive to cobalt, then avoidance of the metal is key to protect the skin from allergic reactions.

Chemo Cobalt Test™ allows the Dermatologist or the Patient to easily detect free Cobalt in metallic objects. The test detects free cobalt down to a limit of 8.3 ppm (parts/million). The sensitivity threshold of most cobalt allergic patients is above 10 ppm. Some strongly allergic patients will however still react to objects releasing amounts below the threshold of the test.

Chemo Cobalt Test™ consists of Nitroso-R salt for the detection of cobalt in various metallic objects. Nitroso R salt produces a bright, reddish-pink insoluble salt with cobalt.

Product packaging: The test solution is contained in a glass bottle with a dropper insert and screw on cap. The product is packaged in a plastic cylindrical container with a flip-top-cap alongside 2 cotton swabs and printed instructions for use.

Available: The Chemo Cobalt Spot Test™ and the Chemo Nickel Test™ is available from Chemotechnique and their global network of national distributors.

Downloads: Nickel Test: Instructions for Use Nickel Test: Safety Data Sheet Cobalt Test: Instructions for Use

Sesquiterpene-lactone Mix

Based on article….

The Sesquiterpene-lactone mix: A review of past, present and future aspects,

by Evy Paulsen,
in CONTACT DERMATITIS, December 2023,Volume 89, Issue 6, pp 434-441.

The sesquiterpene lactones (SLs) are secondary plant metabolites, which are wide-spread in the Compositae/Asteraceae plant family.

Members of the Compositae/Asteraceae plant family comprise over 32,000 known spcies of flowering plants.
The family Asteraceae, with the original name Compositae, consists of over 32,000 known species of flowering plants in over 1,900 genera within the order Asterales. Commonly referred to as the aster, daisy, composite, or sunflower family, Compositae were first described in the year 1740. The number of species in Asteraceae is rivalled only by the Orchidaceae, and which is the larger family is unclear as the quantity of extant species in each family is unknown.

Most species of Asteraceae are annual, biennial or perennial herbaceous plants, but there are also shrubs, vines and trees within the family. There is an almost global distribution, from subpolar to tropical regions in a wide variety of habitats. Most occur in hot desert and cold or hot semi-desert climates, and they are found on every continent except Antarctica. Their primary common characteristic is flower heads, technically known as capitula, consisting of sometimes hundreds of tiny individual florets enclosed by a whorl of protective bracts.
Asteraceae is an economically important family, providing food staples, garden plants, and herbal medicines.

In Asteraceae, the energy store is generally in the form of inulin rather than starch. They produce iso/chlorogenic acid, sesquiterpene lactones, pentacyclic triterpene alcohols, various alkaloids, acetylenes (cyclic, aromatic, with vinyl end groups) and tannins. They have terpenoid essential oils that never contain iridoids. Asteraceae produce secondary metabolites, such as flavonoids and terpenoids. Some of these molecules can inhibit protozoan parasites such as Plasmodium, Trypanosoma, Leishmania and parasitic intestinal worms, and thus have potential in medicine.

Sesquiterpenes are a class of terpenes that consist of three isoprene units and often have the molecular formula C15H24. Like monoterpenes, sesquiterpenes may be cyclic or contain rings, including many unique combinations. Biochemical modifications such as oxidation or rearrangement produce the related sesquiterpenoids.
One example of a sesquiterpene-producing Asteraceae member is Big Sagebrush (Artemisia tridentata) which contains sesquiterpene lactones which are sesquiterpenoids (built from three isopre-

ne units) and contain a lactone ring, hence the name. These compounds are found in many other plants and can cause allergic reactions and toxicity if consumed in excess, particularly by grazing livestock.
Lactones are cyclic carboxylic esters, containing a 1-oxacycloalkan-2-one structure (−C(=O)−O−), or analogues having unsaturation or heteroatoms replacing one or more carbon atoms of the ring. Lactones are formed by intramolecular esterification of the corresponding hydroxycarboxylic acids, which takes place spontaneously when the ring that is formed is five- or six-membered. Lactones with three- or four-membered rings (α-lactones and β-lactones) are very reactive, making their isolation difficult. Special methods are normally required for the laboratory synthesis of small-ring lactones as well as those that contain rings larger than six-membered. Naturally occurring lactones are mainly saturated and unsaturated γ- and δ-lactones, and to a lesser extent macrocyclic lactones. The γ- and δ-lactones are intramolecular esters of the corresponding hydroxy fatty acids. They contribute to the aroma of fruits, butter, cheese, and other foods. Cyclopentadecanolide is responsible for the musk-like odour of Angelica root oil. Of the naturally occurring bicyclic lactones, phthalides are responsible for the odours of celery and lovage oils, and coumarin for woodruff. Lactones are present in oak wood, and they contribute to the flavour profile of barrel-aged beers.
Lactones contribute significantly to the flavour of fruit, and of unfermented and fermented dairy products. They are therefore used commercially as flavours and fragrances.

Some examples are:

- γ-decalactone (4-decanolide), which has a characteristic peach flavour;
- δ-decalactone (5-decanolide), which has a creamy coconut/peach flavour;
- γ-dodecalactone (4-dodecanolide), which also has a coconut/fruity flavour,
- γ-octalactone (4-octanolide), which also has a coconut/fruity flavour although it also has a herbaceous character;
- γ-nonalactone, which has an intense coconut flavour, despite not occurring in coconut;
- γ-undecalactone.
- Lactone rings occur widely as building blocks in nature. Examples are:
- Ascorbic acid, kavain, nepetalactone, gluconolactone,
- Hormones, such as spironolactone, mevalonolactone,
- Enzymes, such as lactonase,
- Neurotransmitters, such as butyrolactone, avermectins,
- Antibiotics, such as the macrolides erythromycin; amphotericin B,
- Anti-cancer drugs, such as vernolepin, epothilones,
- Phytoestrogens, such as resorcylic acid lactones, cardiac glycosides.

Sesquiterpene lactones (SLs) are a class of sesquiterpenoids that contain a lactone ring. They are most often found in plants of the family Asteraceae (daisies, asters). Other plant families with SLs are Umbelliferae (celery, parsley, carrots) and Magnoliaceae (magnolias). SLs are a collection of colourless, lipophilic solids, and are a rich source of drugs. They can be allergenic and toxic in grazing livestock causing severe neurological problems in horses.
Some SLs are also found in corals such as Maasella edwardsi.
The SLs are important in plant growth, development and defence because of their antimicrobial, antifeedant, and allelopathic properties, the last-mentioned representing a form of chemical plant-to-plant or plant-to-microbe communication.

Sesquiterpene lactones can be divided into several main classes:

A: Germacranolides
B: Heliangolides
C + D: Guaianolides
E: Pseudoguaianolides
F: Hypocretenolides
G: Eudesmanolides.

Some plants containing these SL compounds include:

- Artichoke = Cynara cardunculus
- Boneset = Eupatorium perfoliatum
- Burdock = Arctium spp.
- Calea ternifolia
- Chamomile
- Chrysanthemum
- Cocklebur = Xanthium spp.
- Feverfew = Tanacetum parthenium
- Gaillardia
- Ginkgo biloba
- Laurus nobilis
- Lettuce = Lactuca spp.
- Marsh elder = Iva annua
- Mugwort = Artemisia spp.
- Parthenium
- Poverty weed = Iva axillaris
- Pyrethrum = Pyrethrum spp.
- Ragweed = Ambrosia spp.
- Sagebrush = Artemisia tridentata
- Sneezeweed = Helenium autumnale
- Spinach = Spinacea oleraceae
- Star anise = Illicium verum
- Sunflower = Helianthus annuus
- Ironweed = Vernonia spp.
- Wormwood = Artemisia absinthum
- Yellow star thistle = Centaurea solstitialis

Several of the above species are well known weeds, and in particular the Ragweeds, Wormwood, and Mugwort are ubiquitous.
The first SLs were detected more than 100 years ago, and ACD from Compositae has been reported since the beginning of the 1900s, but it was not until the late 1960s and early 1970s that a collaboration between dermatologists, chemists and botanists led to the detection of SLs as the main allergens of Compositae plants.

In the 1980s, the SL mix, consisting of equimolar amounts of alantolactone, costunolide and dehydrocostus lactone, was developed as a patch test screening agent for Compositae sensitisation.

Nowadays, after inclusion of SL mix in various patch test baseline series, the mean prevalence of reactions has been measured to be in Europe around 1%, and in North America 0.8% and in the rest of the world from 0% to 10.7%.
The difference in prevalence rates, for example relatively high in northern Europe including UK and Scandinavia, compared to comparatively low rates in Mediterranean countries such as Spain and Italy, can at least partially be explained by the climatic differences leading to differences in native flora. Another factor can be the cultivation of some relevant species in specific areas, for example sunflowers.

Another relevant factor is the prevalence in any country of the practice of herbal medicine. For example, in Germany this is widely and sometimes intensively practised, and as several of the potential culprit species are to be found in the compendium of herbal medicine then higher prevalence rates of sensitisation could be expected. Good examples are Camomile and Arnica.
Besides used as herbal medicines, several of the potential plant sensitisers are used as foods, for example camomile in tea, chrysanthemum in tea.
The appears to be little cross-reactivity or co-sensitisation with other potential sensitisers, though there have been claims that isobornyl acrylate, as is used in some medical devices such as in situ diabetes monitoring devices, may cross-react with SLs.

The question of clinical relevance of an apparent sensitisation is a difficult one, as it seems to vary from region to region, with the incidence of positivity being lower in USA than in Europe, but the level of clinical significance being higher. Another example is the fat that the prevalence rates of 1.7% and 2% in New Zealand and Australia are high, but the clinical relevance is low.

It was evident from early days that the SL mix of three substances did not detect all patients sensitised to Compositae species. When the SL mix was compared with the plant extract-based Compositae mix 6% pet., the detection rate with the plant mix was generally higher.
On the other hand, the Compositae mix 6%, originally developed in Germany and applied for 24 h in the local patch testing procedure, had an irritant and sensitising potential when applied for 48 h, and the mix was thus not suitable for the baseline series when it would have been applied alongside other test substances for 48 hour periods. Obviously, the prevalence of positive SL mix reactions is much higher in selected patch test populations, such as those with chronic actinic dermatitis (20% to 36%), Indian patients with allergic contact dermatitis (14%), and European patients with airborne contact dermatitis (about 16%).
The highest detection rate of the SL mix on routine screening, when compared with plant extracts, was around 65%, and this illustrates the limitation of the SL mix. It has been suggested that the SL mix be expanded from the current three similar chemicals to include 3 more dissimilar chemicals, but this proposed new mix has never become commercially available. Therefore, in current practice, the commercially available SL mix should be supplemented with a mix of SLs from locally prevalent allergenic plants.

The quality of the commercial preparations of the SL mix seems not to be in doubt as the individual chemicals are stable; however, it may be useful if comparative evaluations were to be performed in parallel to determine if there is in fact any difference between the commercially available preparations.

It is clear that the SL mix by itself is inadequate when used alone as the only screening mix for

Compositae sensitisation. Ideally, patch testing with extracts of locally grown and native plants would provide additional information on the culprit plant species and together with chemical studies indicate which additional chemicals would be useful in a supplementary SL mix in that geographical area. Until that ideal situation has been achieved, it is necessary to supplement the SL mix with commercial Compositae plant extracts and chemical haptens/allergens.

According to ESSCA data and the European Baseline Series Taskforce, the commercially available dilution of the Compositae mix II 5% pet. to 2.5% pet. seems to be a safe, but insufficient supplement to the SL mix, as it did not yield significantly higher numbers of positive patch test reactions. Therefore, for at least European-based clinics, it was recently recommended to use the Compositae mix II 5% pet. as an addition to the European Baseline Series, despite rare cases of sensitisation to this mix that have been reported previously.
In conclusion, the current prevalence rate of positive reactions to SL mix suggests its continued use in baseline test panels for most European countries, North America, New Zealand, Australia and probably also China.

For further information, please read the original article in CONTACT DERMATITIS journal.

Patch Test Hapten from Chemotechnique

Art no	Name	Conc. Veh.
Mx-18	Sesquiterpene lactone mix	0.1% pet

Contact Allergy to Corticosteroids: Is the European Baseline Series sufficient?

by Sebastien Vigand Svendsen, Carsten Bindslev-Jensen, Charlotte G. Mortz
in CONTACT DERMATITIS, October 2023, Volume 89, Issue 4, pp 277-283.
https://doi.org/10.1111/cod.14358

Within the European Baseline Series (2023), patients are routinely screened for contact allergy to corticosteroids with tests for Budesonide and Tixocortol-21-pivalate.

Within the TRUE Test® patch test system there are three corticosteroids included, with the addition of hydrocortisone-17-butyrate.

There exists also a supplementary series “Corticosteroids” available commercially from both Chemotechnique and SmartPractice, which may be used for more definitive identification once the 2 or 3 marker haptens/allergens indicate a sensitivity to corticosteroids.

The big question is, are the 2 or 3 currently used marker haptens/allergens fit for purpose in identifying sensitivity to corticosteroids, all corticosteroids; or does there need to be more representative haptens or different representative haptens in the European Baseline Series.

The prevalence of sensitisation to Corticosteroids is estimated to be between 1.5% and 4.1%, with the higher rates in patients over 40 years of age. This phenomenon may possibly be due to cumulative exposure.

The routes of contact sensitisation to Corticosteroids are primarily cutaneous (75%), followed by inhalation of aerosols (7%), or by ophthalmic preparations (6%).
Corticosteroid sensitisation may usually be suspected when treatment with the Corticosteroid fails to resolve the original malady, or as the authors of the study phrase it so succinctly “in cases of therapeutically unresponsive inflammatory dermatoses or concomitant immunological allergic response conflicting with the pharmacological anti-inflammatory effect of the corticosteroid”.

The aims of the study were three-fold:

1. To evaluate the frequency of CS sensitisations and associated clinical relevance in patients with possible or suspected CS allergy.
2. To evaluate a possible difference between different test systems (TRUE Test vs. Corticosteroids in petrolatum or ethanol.
3. To assess co-sensitisations between Corticosteroids in petrolatum / ethanol.

Baeck grouping of the Corticosteroids was used in the analysis of results.
Baeck Group 1 includes hydrocortisone-17-butyrate + budesonide + hydrocortisone + CS Mix

Baeck Group 2 includes amcinomide
Baeck Group 3 includes betamethasone-17-valerate + clobetasol-17-propionate + dexamethasone-21-phosphate disodium salt + alclometasone-17,21-dipropionate, desoximetasone

Although first published in June 2023, the study involves test results from the period 2006 to 2020, and so utilised some patch test product brands which are no longer available. Another confounding factor is the changes during the period of the haptens in the Corticosteroid (CS)supplementary series, due to commercial availability and irrelevance, as well as changing trends in prescribing patterns.
Below are various points that can be extracted from the results, discussion and conclusion of the study:

- 1,852 patients were patch tested with TRUE Test and Corticosteroids in petrolatum or ethanol, of which 119 (6.4%) were sensitised according to TRUE Test, of which 85 (71.4%) were clinically relevant.
- Tixocortyl-21-pivalate was the most frequently encountered CS sensitisation, at 3.6% of the 1,852 tested patients.
- A total of 98 patients (5.3%) were sensitised (69/98 = 70.4% clinically relevant) to at least one CS using the extended series with allergens in pet/eth, with the most prevalent sensitisations being
  - CS mix (3.2%)
  - budesonide (2.5%)
  - hydrocortisone-17-butyrate (2.4%)
- No statistically significant difference in clinical relevance between positive reactions in TRUE Test (85/119 = 71.4%) and CSs in pet/eth (69/98 = 70.4%) was found overall ($\chi 2$, $p = 0.87$).
- By testing with the supplementary CS series, an additional 16 sensitised patients (of whom 12/16 = 75% were clinically relevant) were detected beyond those identified by TRUE Test, with six in Baeck Group 1, one in Baeck Group 2 and nine in Baeck Group 3.
- Sensitisations to CSs other than budesonide, tixocortol-21-pivalate, and hydrocortisone-17-butyrate (as tested by TRUE Test) were found in 19 of the 119 patients (12/19 clinically relevant) sensitised to the TRUE Test CSs.
- Comparing hydrocortisone-17-butyrate, tixocortol-21-pivalate, and budesonide using the two different test systems, TRUE Test gave rise to more positive patch test reactions than steroids in pet/eth from all three CS markers. This may have been due to different concentrations of the chemicals in the two different test systems.
- The association between exposure to CSs and the development of ACD was approximately 70% for the two test systems. Thus, the clinical relevance of sensitisations was equally distributed between the two test systems and may be equal in detecting ACD.
- Detection of Group 3 CSs sensitisation has previously been a diagnostic issue if using the TRUE Test and European Baseline Series. A previous study reported an overall miss of 81% of sensitisations to clobetasol propionate and betamethasone valerate if the patients are only patch tested with budesonide and tixocortol- 21-pivalate. In this current study in Denmark, the group 3 CSs clobetasol-17-propionate (in Dermovate) and betamethasone-17-valerate (in Betnovate)

are frequently used in the treatment of various inflammatory dermatoses such as eczema and cutaneous psoriasis in Denmark. In total, only nine patients sensitised to Group 3 CSs are missed out of 1,852 patch-tested patients. With clobetasol-17-propionate being a potential Group 3 CS marker, its inclusion in a screening panel might optimise the overall sensitivity n detecting sensitisation to corticosteroids.

- The study authors concluded that it is important to use supplementary tests if corticosteroid allergy is suspected or in chronic dermatitis patients.

The CS-1000 Series

1.	B-033B	Budesonide	0.01% pet
2.	B-031	Betamethasone-17-valerate	1.0% pet
3.	T-030	Triamcinolone acetonide	1.0% pet
4.	T-031B	Tixocortol-21-pivalate	0.1% pet
5.	A-023	Alclometasone-17,21-dipropionate	1.0% pet
6.	C-028	Clobetasol-17-propionate	1.0% pet
7.	D-046	Dexamethasone-21-phosphate disodium salt	1.0% pet
8.	H-021A	Hydrocortisone-17-butyrate	1.0% alc
9.	D-057	Desoximetasone	1.0% pet
10.	B-042	Betamethasone 17,21-dipropionate	1.0% pet
11.	M-036	Methylprednisolone aceponate	1.0% pet
12.	Mx-23	Corticosteroid mix	2.1% pet
13.	H-034	Hydrocortisone-21-acetate	1.0% pet

For full information on this very interesting paper please read the original article in CONTACT DERMATITIS.

Potential for Allergic Contact Dermatitis in Popular Hair Care Practices and Ingredients

by Maria Karim, et al.
In DERMATITIS, December, Vol 34, No. 6, pp 484-491.
https://doi.org/10.1089/derm.2023.0045

The incidence of allergic contact dermatitis (ACD) due to personal care products is rising in parallel with increasing product availability and consumer interest. Hair products specifically represent a significant source of potential allergens, including preservatives, surfactants, emulsifiers, fragrances, adhesives, and dyes. ACD due to hair care products can present as dermatitis in the distinctive “rinse-off” distribution, involving the neck, eyelids, and lateral face in addition to the scalp. The authors of this study review the numerous ingredients in hair care products that can cause ACD, as well as provide practical tips to aid the identification of the culprit allergens.

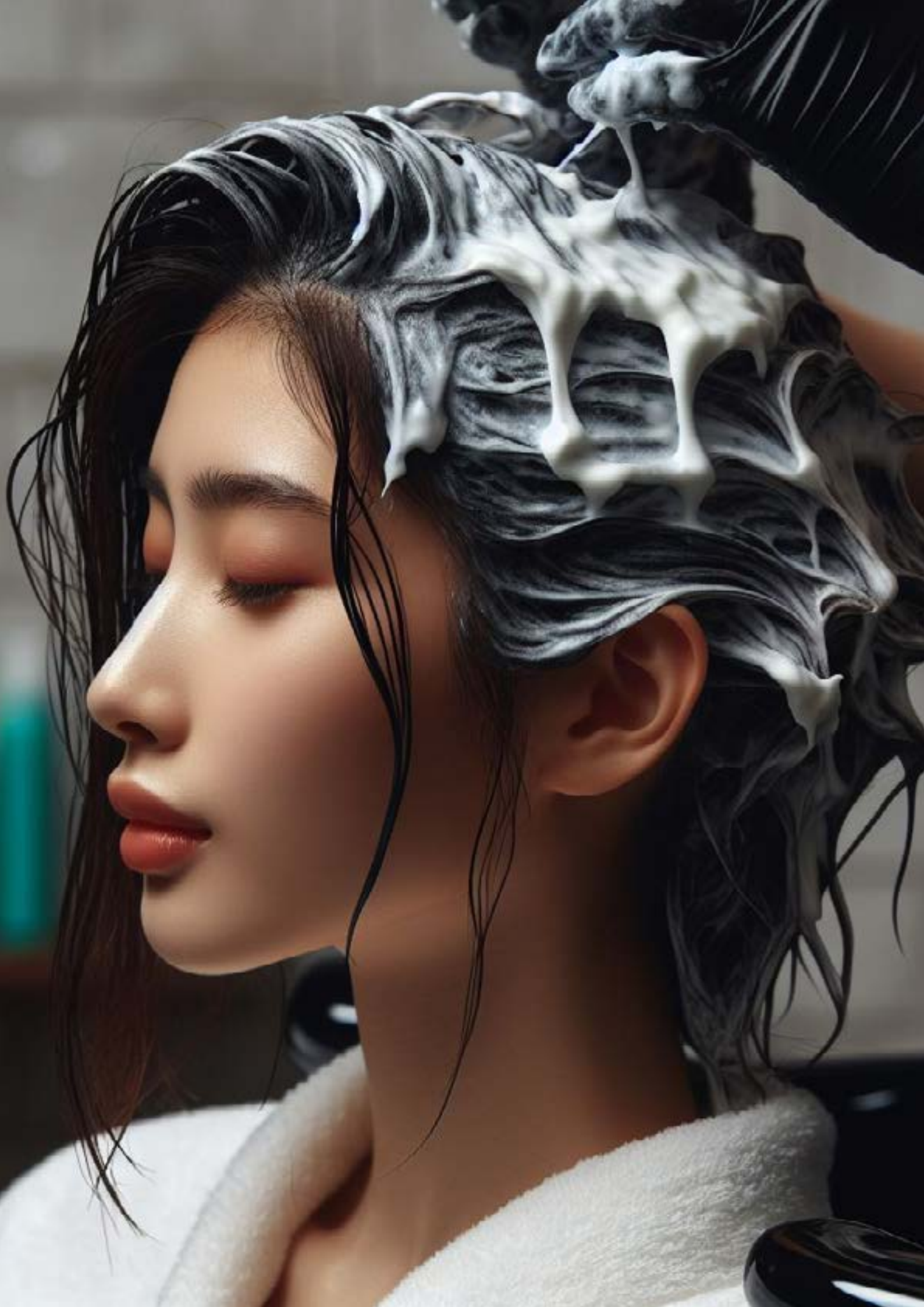
Hair products of various types represent the third most common source of contact allergens, with shampoos and conditioners being the most common sources of sensitisation.

The clinical conditions that may be caused by the various chemicals used in hair care products and procedures include the following:

- Dermatitis
- Pruritis
- Burning
- Hair-shedding
- Oedema
- Weeping
- Crusting
- Pain

Often, the scalp is not the actual site of the clinical symptoms but rather the adjacent areas of neck, eyelids or ears, which comprise the “rinse-off areas”.
It is not only the person who has undergone the hair care procedure but also and perhaps more likely the hairdresser who is experiencing adverse reactions to the hairdressing chemicals used in their professional occupational capacity. Hairdressers are very frequently exposed to multiple chemicals that act as haptens and become allergens, causing clinical symptoms.

Hairdressers occupational ACD to hair care products commonly involves their hands, thereby reflecting the pattern of exposure to the chemicals. Classic examples are the exposure to glyceryl monothioglycolate during perm application, or PPD during dye application. However, ACD in hairdressers may also spread to involve the entire hand, ipsilateral forearm, and face.



The use of protective gloves made of rubber latex, vinyl, and polyethylene may not sufficiently reduce the exposure and the resultant ACD. The gloves themselves may indeed be the culprit, due to their constituents such as rubber accelerators, so need to be considered as a potential source of culprits causing ACD in the hairdresser or their client.
This investigation of hair care products categorises the different types of chemicals that may be involved with ACD and other clinical conditions caused by haircare products.

1. Adhesives
2. Formaldehyde
3. Cationic Surfactants
4. Surfactants
5. Persulfates
6. Propylene Glycol
7. Tea Tree Oil
8. Hair Dyes
9. Fragrances
10. Other Notable Substances

Below is a short introduction to each of these 10 categories; but for further information please read the original article in The December 2023 issue of the ACDS journal DERMATITIS.

1. Adhesives

Acrylates are utilised to attach prosthetic or synthetic hair pieces. Wigs are typically attached to the scalp with a glue mixture containing 90.6% ethyl cyanoacrylate, 0.4% hydroquinone, 9.0% of polymethyl methacrylate, and organic sulphonic acid. ACD to cyanoacrylates was previously considered to be unlikely due to their immediate polymerisation, limiting their ability to form complexes with proteins or polypeptides and their cutaneous absorption. However, cases of ACD to cyanoacrylates have been reported.

2. Preservatives

Preservatives are commonly incorporated into formulations of cosmetics and hair care products such as hair dyes, shampoos, and conditioners, to suppress the growth of microorganisms and extend the shelf life of products. Preservatives, including isothiazolinones, parabens, and formaldehyde, are common culprits of ACD. Other preservatives used in hair care products include PPD, MI and MI/MCI, all common additives to haircare products and all infamous as sensitisers.

3. Formaldehyde

This is a major preservative which deserves its own identification due to its property of being well-known irritant, carcinogen and hapten/allergen. Although pure formaldehyde is not permitted to be incorporated into cosmetic formulations, concentrations of up to 2000 ppm are allowed in final products. Application and heating of formaldehyde-containing treatments result in airborne formaldehyde vapor, which can have contact, inhalational, and systemic consequences. Formaldehyde-releasing preservatives, such as imidazolidinyl urea, diazolidinyl urea, dimethyloldimethyl (DMDM) hydantoin, and 2-bromo-2-nitropropane-1,3-diol can also cause contact dermatitis, though they are weaker sensitisers than pure formaldehyde.

4. Cationic Surfactants

Cationic surfactants and polymers soften and detangle the hair by normalising hair surface charges, decreasing friction between hairs and improving hair texture. Polyquaternium is a cationic polymer found in several hair care products, including conditioners and volumising products.

5. Surfactants

Sulphates are anionic detergents that aid in cleansing the scalp of sebum and oil and are thus common ingredients in shampoos and soaps. Excess use can cause rough breakage-prone hair. Sulphates exist in several forms with varying cleansing abilities. Sodium lauryl sulfate (SLS) is frequently found in cleansing products, soaps, and cosmetics, and is highly irritating; however, it is not an allergen capable of causing ACD. Sodium laureth sulphate is a less irritating surfactant formed by the addition of ethylene oxide to SLS. In hair products, lauryl sulphates are more commonly used for oily hair due to their strong cleansing capabilities. Other relevant surfactants include the following:

- Behentromonium methosulphate
- Cocamidopropyl betaine (CAPB)
- Decyl glucoside.

6. Persulphates

Persulphates, specifically ammonium persulhate, potassium persulphate, and sodium persulphate) are oxidising agents utilised in textiles, pharmaceuticals, and cosmetics. Ammonium persulphate is incorporated into hair bleaching and colouring formulations and in cold wave applications in concentrations up to 60%. Bleaching powders and creams are among the most utilised hair lighteners by hairstylists. A market survey of a random selection of bleaching products showed that 16 of 17 bleaching powders contained persulphates. Despite their extremely common use, persulphates are known to cause both ACD and occupational asthma.

7. Propylene Glycol

Propylene glycol is an ingredient in topical and oral products (such as mouthwash and toothpaste) and medicaments, including the very widely used minoxidil solution, topical steroids, and cosmetics, where it functions as solvent, emulsifier, and vehicle. It has been found to be an ingredient in up to 38% of shampoos. Propylene glycol can be both an irritant and a cause of ACD.

8. Tea Tree Oil

Essential oils are used in hair products or applied in pure concentrations. They coat the hair shaft and decrease breakage by preserving moisture, while offering fragrance. Commonly used oils for hair include tea tree, peppermint, rosemary, and thyme oil, of which tea tree oil has been most often reported cause of ACD. It is increasingly incorporated into personal care products due to its bactericidal, antifungal, antiviral, anti-inflammatory, and analgesic activities, and has shown to be efficacious in managing seborrheic dermatitis and acne vulgaris. Tea tree oil has been identified as an ingredient in 2.8% of hair products targeted toward ethnic hair, and in 5.3% of hair products targeted toward non-ethnic hair. Cases of ACD due to tea tree oil often du to the application of pure Tea tree oil, though lower concentrations in shampoos, shaving cream, and soap can also cause ACD.

9. Hair Dyes

Hair dye is a common cause of ACD, manifesting as severe weeping eczematous dermatitis or profound oedema of the scalp, face, and upper trunk of patients or the hands of hair stylists. The most implicated allergen in hair dyes is PPD. PPD is a very potent sensitiser, as it can cause various other

conditions, including lichen planus-like dermatosis, erythema multiforme-like dermatoses, urticaria, and lymphomatoid contact dermatitis, and even in extreme cases anaphylaxis. PPD is a dye in itself, but also functions as an antioxidant for other hair dyes, henna-based products, leather, fur, rubber, and ink products. Its small molecular size facilitates cutaneous penetration, protein binding, and rapid polymerisation that enable its effectiveness as a dye and allergen. When used in hair dyes, PPD increases the lasting power of the dye and increases pigmentation. PPD has been found to be listed as an ingredient in 78% of hair care products. Other dye constituents less frequently implicated as allergens include toluene-2,5- diamine, p-aminophenol, m-aminophenol, and ammonium persulphate.

10. Fragrances

Fragrances are very widely used in hair dyes, shampoos, conditioners, gels, oils, hair sprays, and perfumes, and represent the most common cause of ACD in personal care products. They are therefore very important causes of contact dermatitis due to hair care products. Limonene and linalool are common ingredients in fragrances with low sensitizing potential that oxidise and form hydroperoxides upon exposure to air. The hydroperoxides of limonene and linalool are conversely extremely potent sensitisers. The NACDG's most recent patch test results indicate that the hydroperoxides of linalool and limonene are among the most common allergens, eliciting positive reactions in 11.1% and 3.5% of patients, respectively.

11. Other Notable Substances

Glyceryl thioglycolate is a reducing agent used in many acid permanent wave products, being the 6th most common positive patch test allergen, accounting for 4.4% of total positive reactions. Importantly, glyceryl thioglycolate can result in prolonged ACD, as it can persist in the hair for up to 3 months after a permanent wave treatment.

Sodium and potassium metabisulphite in hair dye preparations represent additional potential allergens.

Nickel ions released from hair accessories is another source of allergen to consider, specifically when dermatitis is locally distributed on the scalp. Cases of ACD to nickel in hair clasps have been reported. Nickel ions are also released from various hair care tools such as scissors, shavers, etc.

Synthetic hair extensions have demonstrated potential to cause irritant contact dermatitis especially in atopic patients, presenting with pruritic eruptions on the neck and negative patch tests.

Diagnostic testing is necessary to confirm the identification of suspected culprit haptens/allergens amongst the hair care products used by the patient or on the patient.

Patch testing is the gold standard diagnostic test for detecting such haptens/allergens in hair care products

Testing may be started using a core allergen series for broad screening purposes, such as:

1. European Baseline Series of 32 haptens/allergens
2. European Comprehensive Baseline Series of 42 haptens/allergens
3. International Standard Series, of 30 haptens/allergens
4. International Comprehensive Baseline Series of 80 haptens/allergens
5. ACDS Core Series of 90 haptens/allergens.

These are other similar series contain many allergens relevant to hair products and practices, including nickel sulphate, PG, fragrance mix I, MI, tea tree oil, hydroxyethyl methacrylate, methyl methacrylate, decyl glucoside, and hydroxyperoxides of limonene, and many more.

Suitable supplemental series may be added to the Baseline Series, including:

1. Hairdressing Series of 37 haptens/allergens
2. Cosmetic Series of 63 haptens/allergens
3. Fragrance Series of 47 haptens/allergens

Even, in certain cases of suspicion, perhaps also other series such as

1. Rubber Additive Series of 27 haptens/allergens
2. Methacrylate Series of 12 haptens/allergens.

In addition, testing with the patient's own products is advisable. Those hair care products may be the patient's own if the hair care procedure was done in the patient's home, or the hair care products may be those used by the hair salon if that is suspected of being the source of the culprit haptens/allergens.

The investigating authors concluded that patients presenting with eczematous lesions or oedema of the scalp, face, eyelids, or in the ''rinse-off'' distribution area should be suspected of having ACD from hair care products. In reviewing a patient's risk for ACD, Dermatologists should inquire about hair care practices, styling methods, and review the ingredients in the relevant hair care products. For further information on the roles of the various chemicals found in hair care products, as well as information on the relative prevalence of sensitisation to these chemicals can be found in the original article in DERMATITIS.

Long-term Prognosis of Vaccine-induced Contact Allergy to Aluminium: Third Patch Test with additional test preparations

by Anette Gente Lidholm, et al.
in CONTACT DERMATITIS, November 2023,Volume 89, Issue 5, pp 359-367.

A high incidence of local itching with subcutaneous nodules caused by suspected aluminium allergy was observed in clinical trials of a new aluminium-adsorbed pertussis vaccine in Gothenburg, Sweden, in the 1990s. At that time, a total of 495 children with itching nodules from a total of 76,000 vaccinated children (0.65%) were patch tested with aluminium chloride hexahydrate 2% and an empty Finn Chamber®. A total of 377 (76%) gave positive patch test reactions to aluminium. When 241 of these subjects were re-tested five years later, 186 (77%) had unexpectedly lost their patch test reactivity to aluminium, accompanied by a cessation or at least reduction in clinical symptoms. Now in this current study, some of these same patients are patch tested again, a third time, to determine their current ongoing sensitisation to aluminium.

Aluminium salts, mostly aluminium hydroxide and aluminium phosphate, are used as adjuvants in vaccines to enhance the immunogenicity of the vaccine, though the exact mechanism is uncertain. All vaccines against diphtheria, tetanus, pertussis, hepatitis A and B, human papillomavirus and tick-borne encephalitis are adsorbed to aluminium adjuvants, as well as some vaccines against meningococcal and pneumococcal infections. Many antigen extracts used in allergen-specific immunotherapy treatment (ASIT) are also aluminium adsorbed though there is a strong trend away from this with other adjuvants such as mannan being used, as well as newer and more popular immunotherapy treatment modalities of sublingual drops or tablets.

With allergen immunotherapy vaccines using an adjuvant such as aluminium salts there is a depôt effect whereby the allergenic proteins are not released all in one bolus but are released slowly over time, thereby allowing a more potent or a more concentrated solution to be administered, and reduce the potential of an immunological over-reaction that would be experienced as side effects. Allergen immunotherapy vaccines that are not based on an adjuvant such as aluminium salts, for example aqueous or glycerinated solutions, have several distinct clinical disadvantages compared to the corresponding vaccines with an adjuvant.

The test materials used were an empty Finn Chamber as well as aluminium chloride hexahydrate, 2% in petrolatum. In addition, three new aluminium salt preparations were used: aluminium chloride hexahydrate 10%, aluminium lactate 2.4% and aluminium lactate 12.2%. All preparations were placed in a plastic aluminium-free chamber (IQ-UltraTM, Chemotechnique Diagnostics).
All of the patients in the original study, with the first patch test, would have subsequently been given booster doses of the pertussis vaccine, or some other vaccine such as HPV, Hep A, Hep B or tick-born encephalitis, and therefore also a reload of aluminium ions. Yet despite this reload, the incidence of positive patch tests to aluminium decreased so drastically.

Below are various points that can be extracted from the results, discussion and conclusion of the study:

- None of the participants in the third round of patch testing reacted to the empty Finn Chamber exclusively. Therefore, the role of metallic aluminium in patch testing for aluminium allergy is, in the study authors opinion, of minimal benefit, as is also reported by others.

- In this third round of patch testing, not only aluminium chloride hexahydrate 2% and aluminium metal were tested, but also aluminium chloride hexahydrate 10%, aluminium lactate 2.4% and aluminium lactate 12.2%. However, no significant difference was found in the number of positive reactions to any of the aluminium formulas in the small material.

- Interestingly, In the present study, two persons of eleven who tested positive in the first round (Patch test I) of patch tests but were negative in the second round (Patch test II; after 5 years), became positive again in this third round (Patch test III; after 20 years) of patch testing. Individual variation in test reactivity has been seen after repeated patch tests for several antigens, including aluminium, which may be due to immunological factors and differences in patch test materials and techniques. The chambers used in the 1st and 2nd rounds of patch testing were the Chemotechnique original IQ chambers, of 81 mm2 test area. Whereas, for the 3rd round of testing, the chambers used were Chemotechnique IQ Ultra of 64 mm2 test area. This means that the dose per area of sensitiser is very significantly different, which may have influenced the comparative results.

- The main finding in the present study is that the loss of reactivity that was seen in about 77% of the children during the 5–10 years between Patch test I and II has continued. Now, another 75% of the now young adults had lost their reactivity during the next 10–12 year period until Patch test III. Even if the number of tested in Patch test III is small, the tendency is nevertheless clear, and not unexpected.

- Perhaps more remarkable is the fact that seven of twenty (35%) individuals still had remaining positive reactions to aluminium chloride hexahydrate 2% and Finn Chamber as long as 18–20 years after the first test. The cause, or causes, of this phenomenon is poorly known but widely discussed.

- The great benefit of these long-term studies on the persistence of aluminium allergy after childhood vaccination is that parents can now be informed that children who may develop itching subcutaneous nodules and aluminium allergy post vaccination that the symptoms, will come to an end sooner or later and that the contact allergy, in contrast to earlier belief, also has a very good prognosis. This information is of great importance for parents and of course for the growing children themselves and, in the long term, to the Child Health vaccination programmes in general.

- By following the cohort from the Gothenburg Pertussis Vaccine Trials for so many years, and in addition to earlier findings, the study authors can confidently recommend that further vaccination with aluminium adsorbed vaccines can go on despite earlier proven aluminium contact allergy. The risk for new itching vaccination granulomas is low once the original one has vanished over time, and the itching has resolved or nearly resolved. Therefore, the recommended paediatric vaccination programmes can be subsequently fulfilled when the children grow older.

Fragrance allergens in Cosmetic Products marketed for Children in Denmark

by Sofia Botvid, et al.
in CONTACT DERMATITIS, November 2023, Volume 89, Issue 5, pp 374-381.
https://doi.org/10.1111/cod.14397

Children can be exposed to a vast number of fragrance allergens from scented cosmetic products. The study investigated the exposure to fragrance allergens among Danish children, based on a sample of 1179 cosmetic products marketed for children, out of a total of 26,537 products that contain fragrances available in Denmark.

There are currently 3,224 fragrance substances used in the fragrance industry, of which 54 fragrance chemicals and 28 natural extracts are known to be contact allergens in humans.
Approximately half (14/26) of the fragrance allergens that must be declared are presently included in Fragrance Mix I (FMI) or in Fragrance Mix II (FMII).

FMI and FMII are both included in the standard European Baseline Series (EBS).
FMI only is included in TRUE Test®, not the 14 allergens of FMII.

In EU, cosmetic safety is regulated based on the EU Regulation 1223/2009 of cosmetic products. Since 2005, the law has required labelling of 26 fragrances, with their International Nomenclature of Cosmetic Ingredients (INCI) name, if present in a concentration of 10 ppm or above in leave-on cosmetics, or 100 ppm or above in rinse-off cosmetics. Composition below these thresholds may be labelled as ‘parfum’ or ‘aroma’. The law applies to all cosmetic products, regardless of age or gender of the consumer.

Recent studies indicate that fragrance allergens are among the most common causes of contact allergy in patch-tested children in Europe, with the prevalence of fragrance contact allergy apparently increasing. Cosmetic products are believed to be the primary source of skin exposure and contact allergy to fragrance allergens in children; however, this has not been definitively confirmed by high quality studies. In this Danish study, the investigators found that more than half of all products intended for children contained one or more fragrances according to the obligatory labelling of the 26 defined fragrances. 53.8% (634/1179), and 46.6% (550/1.179) of all products were labelled with at least one of the mandatory-labelled 26 fragrance allergens, thereby indicating a significant risk of early contact with fragrance allergens for babies, infants and children.

This study was made practically possible by the utilisation of a unique, very interesting and obviously incredibly useful smartphone app that has been produced in Denmark, called ‘Kemiluppen’ (‘The chemistry loupe’). Kemiluppen was developed by the Danish Consumer Counsel (DCC) ‘THINK Chemicals’ in December 2015 with the purpose of spreading and sharing knowledge of po-

tentially harmful chemicals in cosmetic products to Danish consumers. DCC THINK Chemicals is a Danish, non-governmental independent consumer organisation that works to promote sustainable and socially responsible consumption with the aim of securing consumer rights and safety.

Kemiluppen is free of charge and available to both iPhone and Android smartphones. The application consists of a registry of cosmetic products from the Danish market, including information about labelled hazardous and potentially hazardous chemicals. The registry consists of cosmetics and personal care products and the chemical content information is based on product labels from products, scanned by Danish consumers. All products, product labels, and ingredients must be validated by DCC THINK Chemicals. Then, the producers are given 5 days to comment on the findings before the information on the products become publicly available in the registry.

Consumers use the application to scan the barcode of a product with their smartphone. If the product already exists in the registry, the app will show information about its chemical content and potential harmful constituents. If the product does not already exist in the registry, the consumers can send the product via the application to the DCC THINK Chemicals for evaluation and validation. All products are registered according to the International Nomenclature of Cosmetic Products (INCI) nomenclature.

During the study period from December 2015–November 2022, Kemiluppen was downloaded 577,866 times by Danish consumers. Considering that the entire Danish population is just 5,857,000 (in 2021) so 10% of the entire population downloaded this app. This shows the tremendous interest and benefit of this excellent public-service smartphone app.
The number of validated products in the application was 26,537, of which 1,349 were marketed for children. After elimination of duplicates, 1,179 (4.4%) individual cosmetic products for children were identified, and used for further analysis in this investigation.

Below are various points that can be extracted from the results, discussion and conclusion of the study:

Of the 1,179 cosmetic products for children, 46.6% (550/1179) of the products were labelled with at least 1 of the 26 fragrance allergen, and 53.8% (634/1179) were labelled with at least 1 of the 26 fragrance allergens and/or with ‘aroma’, ‘fragrance’, or ‘parfum’.

Only aroma, parfum, and/or fragrance were labelled in 7.1% (84/1179) of the products.

The product categories with the declared fragrance allergens were:

- Facial care 93.0% (80/86), of which 97.7% were lip balms
- Body care’ 73.5% (97/132)
- Tooth care’ 65.6% (40/61)
- Sunscreen and spray’ 64.9% (87/134)
- Hair care’ 61.6% (53/86)
- Makeup and perfume’ 47.4% (99/209)
- Baby care’ 38.0% (178/468).

The number of declared fragrance allergens per product ranged from 0 to 16 allergens per product. The highest mean number of fragrance allergens per product was 1.83, found in the facial care-product category. The highest number of the 26 mandatory-notice fragrance allergens in a single cosmetic product was 16 found in a baby perfume ‘eau de cologne’.

The most frequently labelled fragrance allergens across all product categories were limonene and linalool. Limonene was the most frequently labelled fragrance allergen:

- Tooth-care-products: 47.5% (19/40)
- Facial care-products: 43.8% (35/80)
- Hair care-products. 18.9% (10/53)
- Body care-products: 17.5% (17/97)
- Make-up and perfume-products: 17.2% (17/99)

Linalool was the most frequently declared fragrance allergen in baby care-products at 21.3% (38/178). Limonene and linalool were both labelled in 10.3% (9/87) of the sunscreen and spray-products.

A total of 25.3% (298/1179) of the cosmetic products intended for children contained one or more allergens from the FM I or FMII.

FM I allergens: the most frequent allergens from FM I were geraniol and cinnamal, found in 8% and 6.5% of the fragranced products, respectively. Geraniol was most often labelled in baby care-products, while cinnamal was most frequently labelled in facial care-products.

FM II allergens: the most frequently labelled FM II allergens, citronellol and citral were identified in 6.9% and 5.8% of the fragranced products, respectively. Citronellol was most often found in hair care-products and citral in facial care-products.

The overall five most common fragrance allergens were found to be:

- Limonene 22.2% (141/634)
- Linalool 17.8% (113/634)
- Benzyl alcohol 14.5% (92/634)
- Benzyl benzoate 10.3% (65/634)
- Geraniol 8.0% (51/634).

The frequency of the 26 mandatory-labelled fragrances in the 634 fragranced cosmetic products marketed to children was found to be as follows:

- Limonene 22.2%
- Linalool 17.8%
- Benzyl alcohol 14.5%
- Benzyl benzoate 10.3%
- Geraniol 8.0%
- Citronellol 6.9%
- Cinnamal 6.5%
- Citral 5.8%
- Hexyl cinnamal 4.7%
- Benzyl salicylate 3.3%
- Cinnamyl alcohol 2.7%
- Coumarin 2.7%
- Eugenol 2.7%
- Alpha Isomethyl ionone 2.4%
- Hydroxycitronellal 2.4%
- Butylphenylmethylpropional 1.6%
- Farnesol 1.6%
- Amyl cinnamal 1.3%
- Isoeugenol 0.9%
- HICC 0.8%
- Anise alcohol 0.6%

A quarter (298/1,179) of the cosmetic products intended for children were labelled with one or more allergens that are included in FM I or FM II, thereby illustrating the importance of using these two diagnostic markers in children suspected of contact allergy to fragrances. However, FM I and FM II together only cover 14 out of the 54 fragrance chemicals and the 28 natural extracts known to be contact allergens. Therefore, if there is a strong clinical suspicion of contact allergy to fragrances, it is advisable to supplement the EBS with additional fragrance allergens.

There is unfortunately an enormous gaping hole in the use of FM I and FM II and even the European Baseline Series when considering fragrance allergens; the fact that the two overall most common fragrance allergens were limonene (22.2%, 141/634) and linalool (17.8%, 113/634), which are not currently included in FM I, FM II, or in the EBS.

Allergic Contact Dermatitis from Essential oil in Consumer Products

by Annick Barbaud, et al.
in CONTACT DERMATITIS, September 2023, Volume 89, Issue 3, pp 190-197.
https://doi.org/10.1111/cod.14377

In recent decades, there has been an increasing interest in natural products and away from chemicals, that are considered to be artificial and damaging to health and the environment. The global aromatherapy market is considered to be in a strong growth phase, with a projected doubling during this decennium.

Of course, Essential Oils (EO) are closely intertwined with perfumes and fragrances, and are by no means all “natural”.

Allergic contact dermatitis (ACD) to essential oils (EOs) is not uncommon, which is to be expected due to the great overlap of EO with perfumes and fragrances. The problem from the dermatologist’s point of view is that so few of the EO are represented in national screening panels or even in dedicated panels because only a few of the EO are commercially available as patch test haptens.
The fragrance markers in the European Baseline Series (BSE) are not sufficient to detect sensitisation to EO; they are barely adequate to detect sensitisation to perfumes and fragrances. Therefore, the incidence, the culprits, the clinical relevance of EO and the importance of EO sensitisation are all very difficult to ascertain reliably.
EOs are complex mixtures, containing known fragrance sensitisers, as well as compounds which are not associated with a known sensitisation hazard, and compounds with unknown allergenic potential.

Unfortunately, only a very limited number of fragrances which are contained in EOs are commercially available as standardised patch test preparations.
Essential oils (EOs) are widely used in cosmetics, massage oils/fluids, perfumes, aroma therapy and natural medicine. Some EOs contain well-known contact sensitisers. Contact sensitisation to EOs has been reported in various professions, but primarily amongst massage therapists and aromatherapists, where the EO are acting as occupational allergens. Of course, the clients of masseuses and aromatherapists are also potentially susceptible to becoming contact sensitised. Private usage of EO can also of course lead to contact sensitisation.

Very few large-scale studies have been performed on contact sensitisation to EO. Perhaps the most important recent paper is from the Information Network of Departments of Dermatology (IVDK) in Germany for the years 2000 to 2008 which revealed that sensitisation to EOs occurred in a substantial number of patients. When patients were patch tested with a dedicated fragrance test series, the following rates of sensitisation to EO were revealed:

- Ylang ylang (I + II) oil 4.2%
- Lemongrass oil 2.5%
- Sandalwood oil 1.8%
- Clove oil 1.5%
- Patchouli oil 1.3%
- Jasmine absolute 1.2%.

Amongst the test results was seen a substantial concomitant reactivity between lemongrass oil with citral, and clove oil with eugenol.

Sensitisation to most of the tested EOs (or their ingredients) is significant. In the IVDK study of 10,930 patients who underwent patch testing with a series of specific EOs, 908 (8.3%) had at least one positive patch test with one of the components.

The composition of EOs may vary in a certain range. It is unknown whether the patch tested EOs indeed represent those used by consumers, so a study correlating patch test results of EOs and perfumes and fragrances with the products actually used by the patients would be useful.
The fact that only a few of the Eos are available as commercially standardised preparations for patch testing is a severe limiting factor that means in most clinical cases the researchers were not able to identify the culprit haptens. The researchers report that it would be highly desirable to develop such test preparations at least for those EO haptens of greater clinical significance.
In this current France-based study by Annick Barbaud and colleagues, they considered EO to be consumer products, and they state that these should be identified and listed and announced as ingredients on the packaging of relevant consumer products.
They recommend that fragrance labelling of cosmetics should be extended to cover also EOs, at least to those mentioned in Annex I of the SSCS Opinion on Fragrance allergens in cosmetic products of 26–27 June 2012 (SCCS/1459/11).

In this study, the investigators compiled a dedicated panel of EO haptens, from the commercially available standardised haptens from Chemotechnique.
In the list below of the haptens in the EO panel is also stated the incidence of positivity of tests on the selected cohort of patients.

Hapten	Concn/Veh	Results	%	Art no
Fragrance Mix I	(8% pet)	20/42	48%	Mx-07
Fragrance Mix II	(14% pet)	24/42	57%	Mx-25
Myroxylon pereirae	(25% pet)	11/41	27%	B-001
Colophonium	(20% pet)	5/41	12%	C-020
Hydroperoxides of limonene	(0.3% pet)	26/40	65%	H-032A
Hydroperoxides of linalool	(1% pet)	21/40	52.5%	H-031A
Tea tree oil oxidised	(5% pet)	10/41	24.4%	T-035B
Lavender absolute	(2% pet)	9/42	21.4%	L-001
Geranium oil	(2% pet)	8/42	19%	G-001
Ylang ylang oil	(2% pet)	7/40	17.5%	Y-001
Turpentine oil oxidised	(0.4% pet)	5/41	12%	T-024B
Rose absolute		5/42	12%	R-003
Cananga oil	(2% pet)	4/40	10%	C-002

Pine tar	(3% pet)	3/39	7.7%	P-012
Peppermint oil	(2% pet)	3/41	7.3%	P-036
Treemoss absolute	(1% pet)	3/42	7.1%	E-026
Sandalwood oil	(2% pet)	3/40	7.5%	S-009
Trans-anethole	(5% pet)	1/38	2.6%	A-015
Narcissus poeticus absolute	(2% pet)	1/40	2.5%	N-006
Farnesol	(5% pet)	1/40	2.5%	F-004
Carvone	(5% pet)	1/41	2.4%	C-035
Propolis	(10% pet)	1/40	2.5%	P-022
Eugenol	(2% pet)	1/42	2.4%	E-016
Jasmine absolute	(2% pet)	1/42	2.4%	J-002
Vanillin	(10% pet)	1/41	2.4%	V-001
Menthol	(2% pet)	0/40	0%	M-002
Benzyl alcohol	(10% sof)	0/40	0%	B-008B
Benzyl benzoate	(10% pet)	0/40	0%	B-038
Benzyl salicylate	(10% pet)	0/40	0%	B-010B
Chamomilla recutita extract	(1% pet)	0/40	0%	C-051
Arnica montana extract	(0.5% pet)	0/40	0%	A-024

Linalool HP was the most frequently positive patch test result among the EOs. Linalool is a major allergen present in different EOs such as lavender, ylang-ylang, rose, cypress, spearmint, citrus fruits, and cinnamon.

Limonene HP was the second most positive test patch in EOs. This allergen is a significant constituent of citrus peel oils (bergamot, grapefruit, lemon, orange, mandarin, tangerine) and tea tree oil. However, due to the widespread exposure to linalool and limonene in EOs, cosmetics, perfumed products, and household items, they cannot be considered to be specific markers for EO sensitisation.

The authors of the study concluded that their results emphasised the limited effectiveness of the EO series in detecting EO sensitisation. Instead, even though they are not specific to EO sensitisation, it would be more valuable to conduct patch tests with FM I and II, limonene, and linalool HP, as these markers frequently yield positive patch test results in EO sensitised patients. They added that if there is suspicion of sensitisation to tea tree EO, ready-to-use 5% oxidised tea tree oil appears to be a good marker. Other ready-to-use haptens may not be very useful. However, the most crucial aspect is to conduct patch testing with the patient's own EOs, as this provides the most relevant and accurate information for diagnosis and management of EO ACD.

For a non-exhaustive list of the haptens available from Chemotechnique which can be used to create a dedicated Essential Oils Series, see the list at the end of the article on "Fragrance allergens in Cosmetic Products marketed for Children in Denmark" on page XX, or the list of haptens stated in the table above.

For full information on this very interesting paper please read the original article in CONTACT DERMATITIS.

Nickel Release from Hairdressing Tools

by Cynthia X. Chan, et al.
in CONTACT DERMATITIS, December 2023, Volume 89, Issue 6, pp 480-483.
https://doi.org/10.1111/cod.14411

Occupational contact dermatitis is a global problem with significant impact on quality of life, employment, and healthcare expenditure. Nickel is the most common allergen by patch testing, including on the scalp, and is one of the most common occupational allergens among hairdressers.

In Europe there is legislation that limits on nickel release levels (no more than 0.5 µg/cm2/week) from objects intended to contact the skin. The European Chemical Agency limits nickel content to no more than 0.5 µg/cm2/week in products that may have prolonged contact with the skin, defined as potentially more than, within 2 weeks, 10 min on at least three occasions or 30 min on at least one occasion. There is no comparable policy in the United States, yet of course nickel sensitisation is no less of a clinical problem.

The purpose of the study was to determine if the metal objects used routinely by hairdressers in the practice of their profession also contained nickel. This was ascertained by the use of a dimethylglyoxime (DMG) test whereby a swab containing the compound is touched against a metal object and a purple colour indicates qualitatively the presence of nickel ions released from the nickel in the metal object.

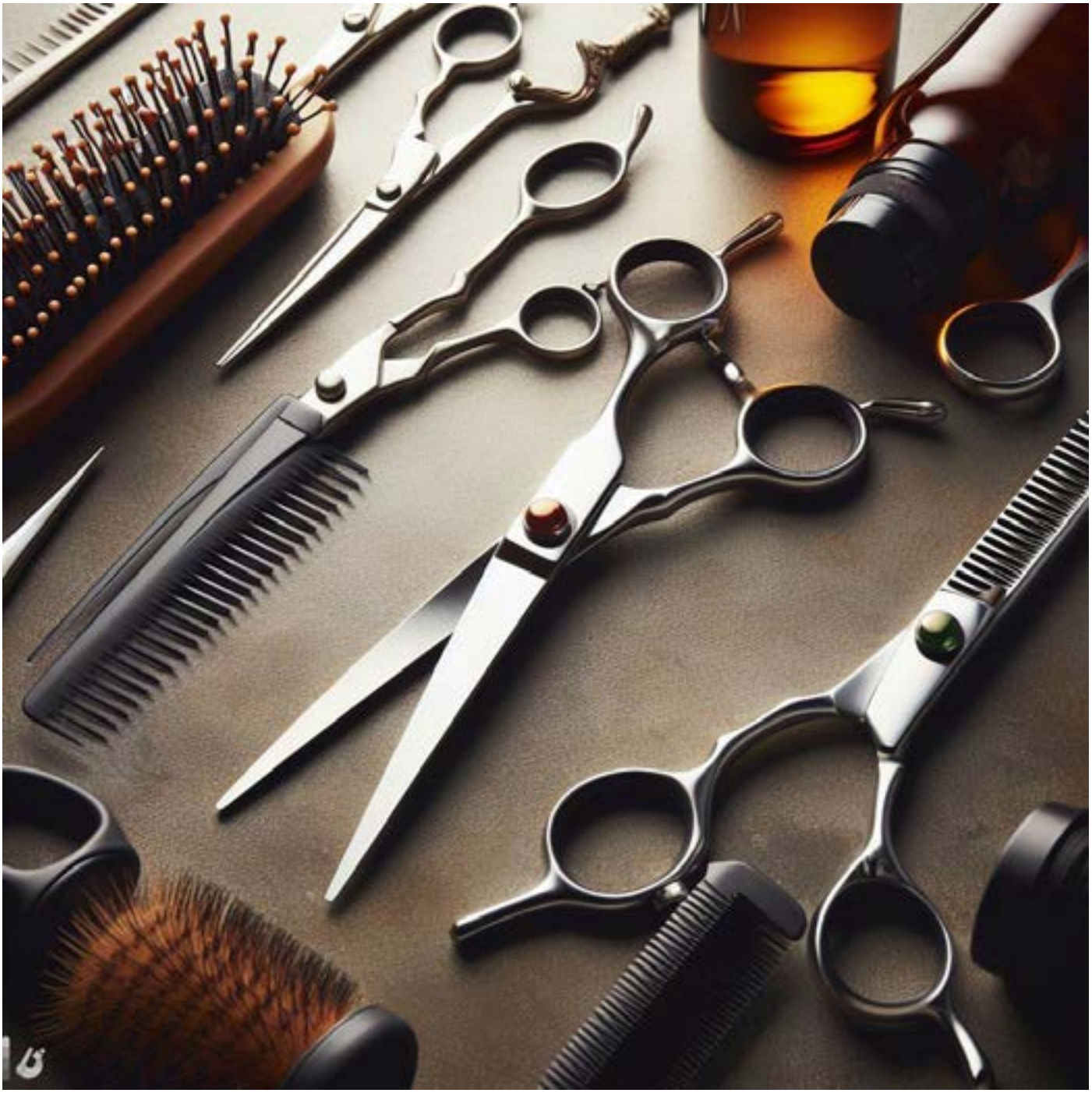
The study reported that a total of 89 tools from 9 salons and 2 over-the-counter sets were tested. Twenty-four (27%) tested positive: trimmers (100%), curling irons (100%), clippers (50%), hair clips (36%), texturizing shears (26%), and trimming shears (4%).

Nickel was detected in both professional salon tools and in consumer over-the-counter tools.
Generally, the cheaper the version of a tool, the more likely to show a positive test result.
Some parts of tools that released nickel were areas that users' hands are likely to touch, including the blade of clippers, the body of trimmers, and the handle of trimming shears/scissors.

The hair-dressing profession often involves wet work, and the use of detergents and chemicals that can compromise and inflame the epidermis, facilitating dermal exposure to various chemicals which may be haptens, that can lead to sensitisation and subsequently to clinical symptoms of Atopic Contact Dermatitis.

Hairdressers, hair stylists, barbers, cosmetologists, and beauticians are the occupational group patch tested using the North American Standard Series by the NACDG with the highest prevalence of occupational nickel contact dermatitis (14.3% between 1998 and 2016). Between 1994 and 2010, no less than 30.1% of members of these groups tested positive to nickel.

Various other studies have been undertaken in Europe in recent years which highlight the occupational sensitisation due to nickel amongst hairdressers. A UK-based study showed 19% of hairdressers who had a positive nickel patch test were suspected to have occupational exposure. A Scottish



study showed 11% of hairdressers had occupational nickel contact dermatitis. Other studies from the European Union showed 21.9% to 37% of hairdressers have been reported to have positive patch tests to nickel, indicating sensitisation to nickel.

The authors concluded that barrier protection such as gloves is important even for seemingly innocuous items such as metal tools, and also expressing the need for equivalent legislation in USA to cover occupational exposure to nickel-containing tools of the trade.

Website Review

You are invited to notify us If there is a website you would like to have reviewed in a future issue of The Patch Tester or if there is a society or other website that you would like to have included in these lists.

Dermatology Society Websites

ILDS:	*International League of Dermatology Societies*	www.ilds.org
ICDRG:	*International Contact Dermatitis Research Group*	www.icdrg.org
EADV:	*European Academy of Dermatology & Venerology*	www.eadv.org
ESCD:	*European Society of Contact Dermatitis*	www.escd.org
ACDS:	*American Contact Dermatitis Society*	www.contactderm.org
APEODS:	*Asia-Pacific Envmntl & Occupational Dermatology Society*	www.apeods.org
EAACI SAM:	*European Academy of Allergy & Clinical Immunology*	www.eaaci.org
BAD:	*British Association of Dermatology*	www.badannualmeeting.co.uk
AAD:	*American Academy of Dermatology*	www.aad.org
PDA:	*Pacific Dermatololologic Association*	www.pacificderm.org
APD:	*Association of Dermatology Professors*	www.dermatologyprofessors.org
NDA:	*Nordic Dermatology Association*	www.nordicdermatology.com
GDA:	*German Dermatology Society*	www.derma.de
FSA:	*French Society of Dermatology*	www.sfdermato.org
CDA:	*Caribbean Dermatology Association*	www.caribbeanderm.org
ACD:	*Australian College of Dermatologists*	www.dermcoll.edu.au
NZDS:	*New Zealand Dermatology Society*	www.nzdsi.org
DNA:	*Dermatology Nurses Association*	www.dnanurse.org
DermNET NZ:	*Dermatology Infomation Resource for Patients*	www.dermnetnz.org

Dermatology Meeting Websites

www.eadv.org
www.aad.org
www.dermatologymeeting.com
www.asiaderma.sg
www.dubaiderma.com
www.cairoderma.com

In this seventeenth issue of “The Patch Tester” we are taking a look at the website of the

European Society for Contact Dermatitis (ESCD)…….. at www.escd.org

The ESCD website has recently been updated, and requires a membership of the ESCD for 2024 to have full access. In fact, without membership and full access the functionality of the website is severely limited. The annual membership fee for ordinary members is a very modest €100 p.a., though application for new membership requires the support of two existing members to sponsor the applicant or failing that a CV to be sent to the society secretary. Junior membership or Retiree membership is just €50 p.a.

Note that Wiley no longer print the journal CONTACT DERMATITIS, the journal of the ESCD, and that online monthly publication is only available to ESCD members. The January 2024 edition is shown here and is available now.

The menu shows that there are now 7 sections to the website, with most of the sections having further divisions; as shown here.

Titles shown below are live links through to the relevant section in the ECDS website.

ABOUT

- Executive
- Council
- Constitution
- Standard Operating Procedures
- Working Parties & Taskforces

NEWS

CONTACT

MEMBERS

- Join or renew
- Members Forum
- Members Directory
- My Account
- Committee Minutes

NEXT CONGRESS

- General Assembly
- Other Meetings

NEWSLETTER

RESOURCES

- Patient Information Leaflets
- Guidelines, Papers & Books
- How to Patch Test
- Society Journal: Contact Dermatitis
- Patch Test Dilutions: De Groot

Don’t forget that ESCD also has a very useful Facebook profile at https://www.facebook.com/europeansocietyofcontactdermatitis

Contact Dermatitis / Patch Testing

7th March 2024
ACDS
San Diego, CA, USA
https://www.contactderm.org/events/acds-annual-mtg

4th – 7th September 2024
ESCD 2024
Dresden, Germany
https://escd.org/meetings-courses/

Dermatology - International

14th – 15th March 2024
World Dermatology Congress
London, UK
https://worlddermatology.conferenceseries.com/

15th February 2024
International Conference on Pediatric Dermatology and Atopic Dermatitis (ICPDAD
New York, USA
https://allconferencealert.net/eventdetails.php?id=2142961

8th – 12th March 2024
AAD 2024 American Academy of Dermatology
San Diego, CA, USA
https://www.aad.org/member/meetings-education/am24

The webpage at www.waset.org/dermatology-conferences-in-2023 is one potentially very useful source of information of Dermatology congresses in 2023.

WASWT is the World Academy of Science, Engineering and Technology. Their webpage states numerous dermatology-related congresses and conferences for 2023.

A word of warning, as has been stated elsewhere in the dermatology world, we need to be aware of the possibility of wishful thinking, opportunism, obsolescent statements, and even misrepresentations or false advertising for congresses. See https://www.bad.org.uk/events/eventcalendar