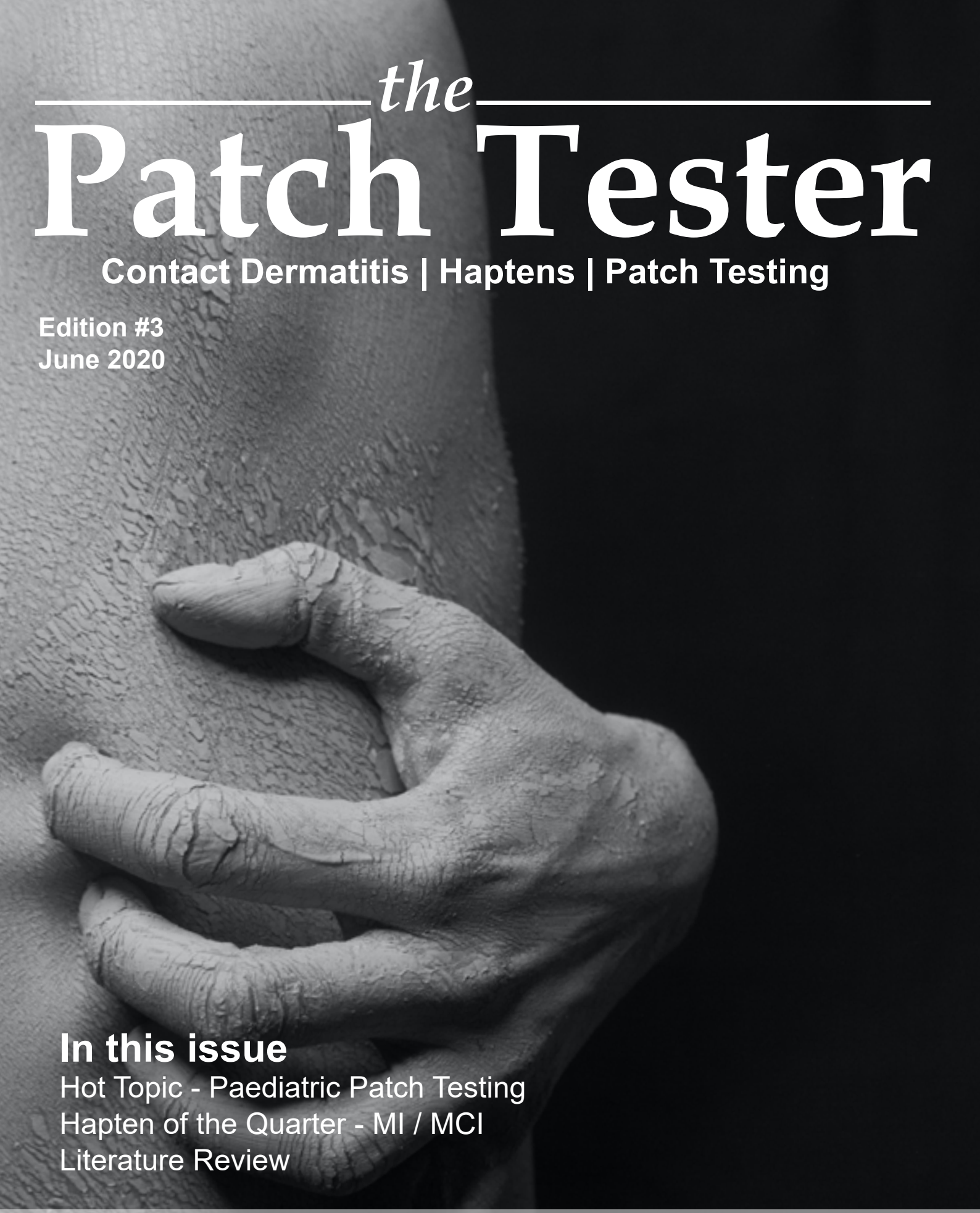
the Patch Tester

Contact Dermatitis | Haptens | Patch Testing

Edition #3
June 2020



In this issue

"The Patch Tester" is a quarterly e-magazine from Chemotechnique to the Patch Testers of the world.

We bring you the latest relevant news and developments in Patch Testing

Chemotechnique Diagnostics
Chemotechnique cosmeceuticals

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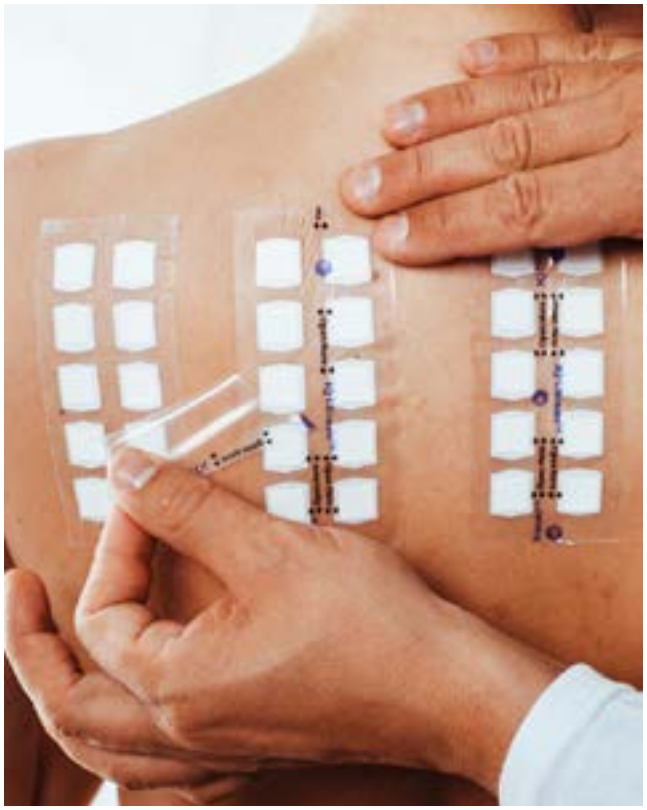
If you would like to contact Chemotechnique about any aspect of The Patch Tester, or any other topic of mutual interest, then please write to us by clicking the “Contact” box on the front cover, or here.

ACKNOWLEDGEMENTS

Production Editors: David Niklasson & Steve Lee

CHEMOTECHNIQUE DIAGNOSTICS



The trusted name in Patch Testing

Chemotechnique MB Diagnostic AB has provided Patch Test solutions since 1981 and is proudly recognized as the Trusted name in Patch Testing.

Through continuous research and development our range of products is constantly being updated, most recently with the addition of the **IQ Ultimate™** Patch Test Unit - our most advanced Patch Test Unit to date.

For more information on our whole product range, visit **www.chemotechnique.se**

Topical Haptens

Chemotechnique offers the widest range of commercially available high quality topical haptens. The 555+ different preparations are available for purchase in sets of series or as individual preparations. The composition of the various Baseline Series, as well as the additional Screening Series, has been carefully selected based on published studies and in close co-operation with leading contact dermatitis societies.

IQ Ultimate™

Elastic, transparent and water resistant. In addition to the features shared with the **IQ Ultra™**, **IQ Ultimate™** has the above named added benefits as a result of the 25 micron thin carrier film. Allowing for both showers and moderate exercise - **IQ Ultimate™** is the ideal Patch Test Unit for the diagnosis of contact allergy in active patients.

IQ Ultra™

Comfortable and chemically inert - **IQ Ultra™** is the reliable patch test choice. The **IQ Ultra™** is designed to take full advantage of the acclaimed IQ Chambers. The strong adhesive properties of the premium quality, hypoallergenic and latex free carrier tape eliminates the need for extra reinforcement for patients with normal skin. The **IQ Ultra™** Patch Test Units are most cost effective as filter papers and protective covers are not add-ons, but integrated into the design.

Accessories

Chemotechnique provides a full range of accessories and spot tests that makes patch testing efficient.

COVID-19 Pandemic and Patch Testing

The German dermatologist, Josef Jadassohn (1863-1936), first presented the results of his innovative patch-testing technique in 1895. The safety and efficacy of this diagnostic tool has stood the test of time and is still the gold standard for the diagnosis of allergic contact dermatitis (ACD). That history makes patch testing 125 years old.

Arguably, only two World Wars have ever had such a suppressive effect on the practice of patch testing, until the COVID-19 pandemic burst onto the world's stage just a few short months ago.

Now, since early February, the world has in many respects come to a suspension of time and activity, and perhaps especially a suspension of dermatological services to the world's population. Unfortunately for the practice of patch testing, this has probably one of the lowest priorities even within dermatological services. Accordingly, patch test clinics have essentially been at a standstill for the past 2 months, globally.

It is hard to imagine a Dermatologist or Allergy Specialist being able to attend a patient, and administer patch tests, all whilst maintaining scrupulous safety precautions to prevent possible virus transmission.

Even the evaluation of patch test reactions requires close patient contact as digital photographs taken by the patient and emailed to the Specialist are far from ideal.

Today, mid-May 2020, we are still far from ready for the resumption of normal medical practice, and again, patch testing will be far down the list of activities to be resumed as soon as possible.

In the supply industry, manufacturers have been striving to maintain production schedules at the manufacturing premises, and business activities primarily at home offices, whilst protecting the health and safety of their employees. Fortunately, for Chemotechnique in Vellinge Sweden, the government-imposed restrictions on personal activities have been remarkably light, so the disruption to the actual running of the business have been minimal, certainly far less than the disruption of clinical services globally. We are ready just as soon as the Dermatologists and their patients are back in action!

MI / MCI

A freshly published study that proposes a new optimised patch test for MCI/MI should re-awaken the interest in this significant contributor to allergic contact dermatitis.

This Hapten of the Quarter topic is covered by a review of the article immediately below, supplemented by relevant input from 9 other articles on MCI/MI.

Can patch testing with methylchloroisothiazolinone / methylisothiazolinone be optimised using a new diagnostic mix? – A multicentre study from the Swedish Contact Dermatitis Research Group

by *Malin Engfeldt, et al*
in **Contact Dermatitis, May 2020, Volume 80, Issue 5, Pages 283-289**.

In the early 1980s a preservative called Kathon CG was introduced on the market. It contained a mixture of methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI). Due to the conditions present during synthesis of this preservative, MCI was formed and found at a three times higher concentration than MI. MCI/MI in the ratio 3:1 has been patch tested in Sweden in the concentration 0.02% aq. since the mid-1980s.

It has been shown to be an extreme sensitiser in both humans and animals.

In the early 2000s, MI by itself was introduced as a preservative in industrial products. The first cases of occupational allergic contact dermatitis from MI in industrial products were reported in 2004. In 2005, MI by itself was allowed as a preservative in cosmetics. Because MI is a weaker preservative and also a less-potent sensitizer than MCI, a higher concentration was allowed in cosmetics compared to MCI/MI.

However, the use of MI became widespread and it was soon evident that the allowed concentration indeed did cause sensitisation, as an unprecedented rise in the contact sensitisation frequencies to MCI/MI and MI was seen, for example, in Europe in recent years.

MCI/MI in the ratio 3:1 is well known for its steep dose response curve when patch tested in serial dilutions, and a slight change in concentration can affect the patch test reactivity and irritancy significantly.

At present there are two patch test preparations containing MI in the European Baseline Series and in the Swedish Baseline Series;

•	MCI/MI Aq.	0.02% v/v	150 ppm MCI	50 ppm MI
•	MI Aq.	0.2% v/v	0 ppm MCI	2000 ppm MI

Ideally, only one preparation combining both MCI and MI each at their own optimal concentration, should be needed in the screening of MCI and MI sensitisation, which would save space on the patient’s back or enable a replacement with another contact allergen test.

As a one-line summary, the researchers ascertained that….
a mix of 150 ppm of MCI plus 2000 ppm of MI, so at a final concentration of 0.215% v/v, is ideal.

With the proposed new aqueous mix, the prevalence figures in this study changed from 7.3% for MCI/MI at 0.02% v/v, plus 8.4% for MI at 0.2% MI to 13.2% for MCI/MI at 0.215% v/v. MCI/MI 0.215% aq. detected significantly more patch test positive individuals than both MCI/MI 0.02% aq. ($P < .001$) and MI 0.2% aq. ($P < .001$) when compared separately. The preparation of MCI/MI 0.215% aq. detected significantly more positive reactions than the two other preparations did together ($P < .001$), even if this mix did not pick up all allergic individuals; 6 were missed (0.4%).

The products that caused the dermatitis could be either occupational or household; including dishwashing liquid, putty, paints, wall-covering glue, and cleaning liquids, or personal hygiene products and cosmetics.

Based on the results from this study, MCI/MI and MI do not seem to belong to the group of allergens that show delayed reactions so a D3/4 reading is adequate. However other studies have shown that reactions would have been missed on D3/4, so reading on D7 was necessary.

Of note, major differences in the frequency of contact sensitisation among the five centres in the study were seen. There are many possible explanations. This variation implies that standardisation is warranted not only for the dose of the patch test but also when various combinations of morphological features should be ascribed as irritant, doubtful, or weak reactions.

Concerning irritant reactions, only eight such reactions in four patients were reported, which is a low number.

In 95.7% of the occupational cases, the exposure to MCI/MI and/or MI was considered clinically relevant, which is a very high figure. The offending relevant causes were similar to what other studies have shown. This is in contrast to the non-occupational cases, (personal hygiene products), in which 72.3% were considered clinically relevant. However, even this figure is very high.

The results from this multicentre study are in line with a similar study performed within the International Contact Dermatitis Research Group (ICDRG) (to be published).

In the updated ICDRG baseline series from 2019, MCI/MI 0.02% aq. and MI 0.2% aq. will be replaced by MCI/MI 0.215% aq.

Based on the results from this Swedish study reported here, the preparations MCI/MI 0.02% aq. and MI 0.2% aq. will be replaced by MCI/MI 0.215% aq. as the screening substance in the Swedish Baseline Series from 2020, since this new preparation yields significantly more positive reactions, a high share of clinical relevance, and a low number of irritant reactions.

As always, for further information, please read the original article.

Interesting quotes from the Recommended Reading articles (as numbered further below):

- Nine patch-testing clinics representing 9 countries participated in the study from January 1, 2014, to December 31, 2014. Among the 284 MI-allergic patients, 144 (50.7%) had facial dermatitis, 132 had hand eczema, 55 had eczema on the arms, 40 had eczema on the trunk, 35 had eczema on the legs, 34 had eczema on the neck, 19 had eczema on the feet, 10 had genital or perianal eczema, and 7 had eczema on the scalp. (1).

- Contact allergy to MI 0.2% alone without any simultaneous contact allergy to MCI/MI 0.02% was diagnosed in 93 patients (2.4% of all tested patients). The hands (equally common in men and women) and face (significantly more common in women) were the most common sites of dermatitis in these MI-allergic patients. The contact allergy to MI and/or MCI/MI could explain or contribute to the dermatitis in 63% of the patients. Therefore, MI 0.2% needs to be patch tested on its own to not miss contact allergy, and a micropipette should be used to get an exact dose. (1).

- Most common sources of Exposure for MCI/MI and MI in NACDG Patients (2013-2014). (2).

- Preservative Prevalence versus Positive Reaction Rates. Preservatives in the upper right quadrant (especially MCI/MI) are of the greatest concern as contact allergy hazards because these preservatives are both common in products and have a high incidence of ACD. Preservatives with a low incidence of contact allergy and a high prevalence in topical products (e.g. parabens) are of the lowest concern. (3).

- Twenty most common preservatives found in the USA-based CAMP database. (3).

- Since 2010, an alarming increase in the prevalence of MCI/MI and/or MI contact allergy to a concerning level of 18.9% in 2015 in patients referred for patch testing. A European epidemic of ACD caused by isothiazolinones has been widely reported, starting between 2009 and 2010, after MI was permitted at higher concentrations in industrial applications and cosmetics with allowed concentrations of up to 100 ppm. As a consequence, risk management measures were adopted between 2013 and 2015 and the Scientific Committee on Consumer Safety of the European Union established that there were no safe concentrations of MI in leave-on products and considered a concentration of 15 ppm as safe in the rinse-off products, finally being regulated in 2017. The increasing number of cases of ACD from isothiazolinones published by dermatologists and subsequent regulatory action have enabled a dramatic decrease in the incidence of ACD to isothiazolinones, as reflected in our study. The incidence has markedly decreased since 2015, from a maximum of 18.9% in 2015 to 7.2% in 2018 and 3.1% in 2019. (4).

- Polysensitisation may be an important factor among MCI and MI allergic patients. Interestingly, clinically relevant co-sensitisers included fragrances and preservatives, frequent allergens in cosmetics that represent the most common source of contact allergy as reported in several studies. (4).

- Causative products were mostly cosmetics (89.3%; n = 217), including gels, shampoos, creams, moisturising lotions, deodorants, and aftershave lotion. Besides cosmetics, household (10.3%, n = 25) and industrial (0.4%, n = 1) products (especially cleaning agents and wall paints) were the most frequent. (4).

Recommended articles for further reading:

1. **Multicenter Patch Testing With Methylisothiazolinone and Methylchloroisothiazolinone/ Methylisothiazolinone Within the International Contact Dermatitis Research Group**
   by Marlene Isaksson, et al.
   in Dermatitis: May/June 2017, Volume 28, Issue 3, Pages 210-214.

2. **Epidemic of Isothiazolinone Allergy in North America: Prevalence Data from the North American Contact Dermatitis Group, 2013–2014**
   by Matthew Zirwas, et al.
   in Dermatitis: May/June 2017, Volume 28, Issue 3, Pages 204-209

3. **Prevalence of Preservatives Across All Product Types in the Contact Allergen Management Program**
   by Kevin Beene, et al.
   in Dermatitis, Jan/Feb 2017, Volume 28, issue 1, Pages 81-87.

4. **Contact allergy to isothiazolinones epidemic: Current situation**
   by Jorge Magdaleno-Tapial, et al.
   in Contact Dermatitis, February 2020, Volume 82, Issue 2, Pages 83-86.

Chemotechnique MB Diagnostics AB manufacture currently four different preparations of MCI/MI, plus four different preparations of MI.

METHYLISOTHIAZOLINONE+ METHYLCHLOROISOTHIAZOLINONE

Art. no	Conc. Veh.
C-009A	0.01% aq.
C-009B	0.02% aq.
C-009C	0.01% pet
C-009D	0.02% pet

METHYLISOTHIAZOLINONE

Art. no	Conc. Veh.
M-035A	0.02% aq
M-035B	0.2% aq
M-035C	0.05% aq
M-035D	0.2% pet

The newly proposed preparation of MCI/MI at 0.215% v/v is now under active development by Chemotechnique, and so will become commercially available in due course.

Paediatric Patch Testing

ACD is a common problem in paediatric patients, with reported frequencies as high as 20%. Indeed, one study reports a 52.1% prevalence of ACD. ACD also needs to be differentially diagnosed from the also common dermatitis due to IgE-mediated allergy to ingestant allergens such as dairy and nuts and other foods, as well as to inhalant allergens such as House Dust Mite.

There is currently no defined patch testing standard for use in children, which is a situation that should be resolved by the world's leading patch test organisations.

This Hot Topic is covered by a review of the very recent article immediately below, supplemented by relevant input from 9 other articles on paediatric patch testing.

Expanded Series and Personalised Patch Tests for Children – a Retrospective Cohort Study

by *Reid Collis et al*

in **Dermatitis, March/April 2020, Volume 31, Issue 2, pp 144-146.**

This study was designed to assess patch test positivity in paediatric patients with or without a clinical history of allergic contact dermatitis, and to compare results between the North American 80 Comprehensive Series and the SmartPractice T.R.U.E. Test.

Of the 29 patients (mean age 10.9 + 5.1 years (SD)) 25 children exhibited at least 1 positive patch test reaction, with 81 reactions overall. 40 (49.4%) of those positive reactions came from haptens not included in the T.R.U.E. Test hapten list, and those haptens are commonly found in household products. Cocamidopropyl betaine was a particularly relevant haptens in the study population, as it is not included in the T.R.U.E. Test.

The haptens with positive reactions were in Table A. Be aware that the T.R.U.E. Test as used in USA has a very slightly different composition from the TRUE Test as used in the rest of the world. The NAC 80 Comprehensive Series patch test, used for most patients in this study, includes 50 haptens not included in the T.R.U.E. Test. Of these, 42.0% (21) caused at least 1 reaction in the patients of the study.

Art. no	Hapten	Responses	RPPT
C-017A	Cobalt(II)chloride hexahydrate	9/22	40.9%
C-018	COCAMIDOPROPYL BETAINE*	8/29	27.6%
N-002A	Nickelsulfate hexahydrate	6/24	25.0%
B-007	Benzoylperoxide*	5/21	23.8%
N-001	Neomycin sulfate	4/22	18.2%
F-002A	FORMALDEHYDE	4/29	13.8%
P-019A	PROPYLENE GLYCOL*	4/29	13.8%
Mx-26	Disperse blue 106/124 mix	3/28	10.7%
B-001	Peru Balsam	3/29	10.3%
G-005A	Gold(I)sodium thiosulfate dihydrate	2/21	9.5%
P-022	PROPOLIS*	2/22	9.1%
A-029	Amidoamine*	2/27	7.4%
D-065	DECYL GLUCOSIDE*	2/27	7.4%
L-003	HYDROXYISOHEXYL 3-CYCLOHEXENE CARBOXALDEHYDE*	2/27	7.4%
C-007A	QUATERNIUM-15	2/27	7.4%
A-004	Amerchol L-101 *	2/29	6.9%
Mx-06	Carba mix	2/29	6.9%

Haptens marked in pink are not present in the T.R.U.E Test
RPPT = Relevant Positive Patch Test

Table A

Three of the Top Ten most common haptens causing skin reactions, and 49.4% (40) of the haptens triggering reactions in the study, are not found in the T.R.U.E. Test, thereby underscoring the importance of expanded series testing as a more comprehensive alternative in potential ACD cases in paediatric patients.

These results support the recent conclusions of the Paediatric Contact Dermatitis Research work group of the American Contact Dermatitis Society to regularly perform more comprehensive testing in children.

Based on their findings, the researchers recommend a more complete

patch test series for use in paediatric patients with suspected ACD. More limited patch test series, such as T.R.U.E. Test, do not include haptens to which a significant proportion of their paediatric cohort reacted, and which are frequently found in personal care products.
Without expanded series testing, many of these haptens' sensitivities would remain undiscovered, and the continued use of products within which they are found would prolong existing ACD.

As always, for full information please read the original article.

Highlighted sections from the Recommended Reading articles (as numbered further below):

• Participants at the 2017 meeting of the ACDS were queried on which of the listed haptens or potentially unlisted haptens they would include in a baseline series for North American paediatric ACD patients older than six years.
Haptens receiving more than 60% of the votes were automatically included in the baseline series. Interested members and experts in the field of paediatric ACD were invited to participate in two interactive breakout discussions at the meeting. Haptens receiving less than 60% of the votes were discussed for inclusion or exclusion in the series during the meeting.

Thirty-one haptens from a list of 102 haptens were chosen by more than 60% of the respondents. Subsequently, the testing panel was expended to encompass 38 haptens. See the Table B.
This panel represents a starting point, and future published data using this panel will generate evidence for haptens with true clinical relevance and prevalence in children and serve as an indicator of what should not be tested. Their goal was to decrease barriers to patch testing in children and increase the detection rate of ACD. The 38 haptens reflected in Table B are a minimum number that the group recommended be studied in this population. This number specifically lead to two vacant spots on the patch test panel, which serve us an indication to consider what other additional haptens might be relevant for that particular patient. The work group experience was that the back of a child aged six years can fit 40 to 60 haptens, therefore allowing for expanded testing with additional haptens. It is anticipated that evidence-based data gathered from children undergoing patch testing will lead to revisions of the workgroups initial surveillance panel and establish trends to guide future inclusion and exclusion of patch test haptens (1).

Art. no	Hapten	Responses	RPPT NACDG	RPPT PCDR
N-002A	Nickelsulfate hexahydrate	29/29 (100%)	25,60%	13%
C-007A	QUATERNIUM-15	29/29 (100%)	3,20%	2,60%
N-001	Neomycin sulfate	28/29 (96.55%)	6,60%	4,40%
B-001	Peru Balsam	28/29 (96.55%)	5,60%	6,50%
Mx-07	Fragrance mix I	28/29 (96.55%)	4.9%	9,40%
C-009A	MI / MCI	28/29 (96.55%)	2.7%	3,10%
B-032A	Bacitracin	27/29 (93.1%)	5.2%	4.6%
	PG	27/29 (93.1%)	2.2%	5%
M-035A	METHYLISOTHIAZOLINONE	27/29 (93.1%)	NA	3.6%
Mx-25	Fragrance mix II	27/29 (93.1%)	1.9%	3.4%
	CAPB	26/29 (89.66%)	1.1%	4.6%
C-017A	Cobalt(II)chloride hexahydrate	25/29 (86.21%)	9.1%	4%
F-002A	FORMALDEHYDE	25/29 (86.21%)	2.9%	4.4%
P-022	PROPOLIS	25/29 (86.21%)	1.7%	1.9%
T-031A	Tixocortol-21-pivalate	25/29 (86.21%)	1.2%	1.8%
H-021A	Hydrocortisone-17-butyrate	25/29 (86.21%)	0.8%	0.5%
D-044A	DIAZOLIDINYL UREA	23/29 (79.31%)	1.1%	1.3%
D-047A	DMDM HYDANTOIN	23/29 (79.31%)	0.9%	0.8%
B-033A	Budesonide	23/29 (79.31%)	1.1%	0.5%
Mx-06	Carba mix	22/29 (75.86%)	2.7%	1.9%
I-001A	IMIDAZOLIDINYL UREA	22/29 (75.86%)	0.8%	0.8%
A-004	Amerchol L-101	21/29 (72.41%)	NA	3.5%
Mx-29A	Compositae Mix II	21/29 (72.41%)	2.3%	1.8%
H-025	Hexyl cinnamic aldehyde	21/29 (72.41%)	1.4%	1.9%
Mx-03A	Paraben mix	20/29 (68.97%)	0.9%	0.9%
Mx-01	Thiuram mix	20/29 (68.97%)	1.7%	1%
B-015A	2-BROMO-2-NITROPROPANE-1,3-DIOL	19/29 (65.52%)	1.8%	3.4%
	SQL	19/29 (65.52%)	0.9%	1.2%
C-020	COLOPHONIUM	18/29 (62.07%)	1.2%	2.2%
B-024	4-tert-Butylphenolformaldehyde resin (PTBP)	18/29 (62.07%)	1.0%	1.8%
C-028	Clobetasol-17-propionate	18/29 (62.07%)	0.3%	0.8%
D-065	DECYL GLUCOSIDE	12/15 (80%)	2.3%	NA
I-008C	IODOPROPYNYL BUTYLCARBAMATE	12/15 (80%)	0.6%	1.3%
H-014C	BENZOPHENONE-3	11/15 (73.33%)	0.5%	0.1%
A-029	Amidoamine	10/15 (66.67%)	0.3%	1.8%
	TTO	9/15 (60%)	0.3%	NA
	Carmine	9/15 (60%)	2.1%	NA
D-053	3-(Dimethylamino)-1-propylamine	8/15 (53.33%)	1.1%	0.9%

Table B

• Patch testing can identify relevant haptens in 44% of children with eczema. In childhood eczema, the role of allergic contact dermatitis is often overlooked. Eczema affects up to 20% of children and can be triggered by dermatitis resulting from contact with hap-

tens. Children were referred for patch testing usually when the eczema was either non-responsive to treatment, was sudden in onset, was difficult to control (raising suspicion of a possible contact allergy was involved), or took a regional form (such as facial, perioral, hand and foot), that might be attributable to a local hapten. A small number of children had urticaria or angio-oedema that could have been caused by a contact hapten. (2).

• A total of 543 children were patched tested at least once. The prevalence of a reproducible positive reaction to nickel was 8.6%. A transient reactivity was observed in 111 children. A clinical relevance to nickel was found in only one child. Reproducible reactivity to fragrance mix was not found. (3).

• Contact dermatitis and identifying the suspected hapten in children are important as sensitisation occurring during childhood may cause a susceptibility to the contact dermatitis later in their life. In the present study, the frequency of positive reactions in a paediatric population were found to be 32%. It has varied from 14.5% to 70.7% in different studies so far. Nickel is the most common contact hapten in children younger than 16 years in a Turkish population. PPD was the second most common hapten in our second age group. Neomycin sulphate was the third most common hapten. (4).

• Several toys were found to be associated with contact dermatitis. These included electronics, toy cars, costume jewellery, bicycles, sqwish balls, slime, Play-Doh, and plasticine. Electronics such as video card game controllers, cell phones, iPads, and computers were implicated. In conclusion there is still an unmet need for observation of this segment of industry, with labelling of contents and ongoing surveillance. (5).

• Allergic contact dermatitis is now known to be a common problem in paediatric populations accounting for up to 20% of all dermatitis seen in children. (6).

• We found a positive patch test rate of 66%, with a peak instance among children less than three years of age (88% versus 58.9%). The most common haptens were metals, especially nickel, fragrances and, less frequently, rubber chemicals. Based on the results and their relevance, we propose a shortened standard series of patch tests for paediatric patients. (7).

• 1142 cases from 34 US states, entered by 84 providers, were analysed. 65% of cases had one or more positive patch test results, with 48% of cases having one or more relevant positive patch test results. The most common haptens were nickel (22%), fragrance mix 1 (11%), cobalt (9.1%), Peru balsam (8.4%), neomycin 7.2% propylene glycol (6.8%), cocamidopropyl betaine (6.4%), bacitracin (6.2%), formaldehyde (5.7%), and gold (5.7%). The majority of providers customised their patch tests based on exposure history of the children. Although the pre-made patch testing kits, such as T.R.U.E. Test, are a convenient option for providers because they contain 35 of the more common haptens, this technique may not be as useful in children because it does not allow the option to interchange haptens based on relevant exposure history. Patch testing in children, especially younger than six years, is mostly based on specific exposures gathered in the history that allows more specificity in testing and increases the probability of finding the causative hapten. This becomes even more pertinent when considering the physical surface area of the childs back that greatly limits how many haptens may be applied during testing. In our review, in comparison to the customised tests, the T.R.U.E test could have theoretically missed 312 RPPT (24%) of all reported RPPT (Relevant Positive Patch Test), which is consistent with previously reported data by NACDG. (8).

• The paediatric contact dermatitis registry aims to identify the providers contributing, diagnosing, and treating paediatric ACD within the United States. Although patch testing is the criterion standard for a CD diagnosis, currently the commercially available patch test devices do not have a US Food and Drug Administration indication for use in children aged 18 years and younger. None-

theless, patch testing is being performed in children across 48 states and DC. Thus, as is frequently done in evaluating adults for contact dermatitis, providers often prepare custom patch tests tailored to children's exposure history. Furthermore, some providers modified hapten concentrations whereas others decrease the patch test to skin contact time. (9).

• This study provides data on one of the largest cohort of children patch tested in the recent literature. The most common haptens that did post a positive result such as nickel and cobalt, but also commonly studies from other regions as well e.g, Italy, Greece, India and different states within the United States. Potassium dichromate was more common in studies from Europe. Testing with selected supplemental haptens beyond a standardised screening series is an important component of patch testing in children. This study has shown approximately 23.6% of children had a relevant positive reaction to a supplemental hapten; these, 28.4% would not have had the relevant hapten identified if only the NACDG screening series was used. This emphasises the importance of history-taking to elucidate potential supplemental haptens for patch testing because patients are unlikely to disclose these without prompting. Approximately 67% of the children with one or more PPT would have had all their PPTs detected by the T.R.U.E. Test. Similarly, 70.1% of the children with more than one PPT would have had all their PPT's detected by the T.R.U.E. Test, an improvement over the 61.5% observed in the children tested from 2001 to 2004, when the T.R.U.E. Test consisted of only two panels of 24 haptens. A clinician who frequently uses the T.R.U.E. Test will benefit from being aware of the common haptens that yield relevant positive reactions with the NACDG series but are not a component of the T.R.U.E. Test, such as decyl glucoside, propylene glycol, fragrance mix II, propolis, alpha-tocopherol, ylang-ylang oil, iodopropynyl butyl carbamate, mixed dialkyl thioureas, and cocamidopropyl betaine. (10).

Recommended articles for further reading:

1. **Pediatric Baseline Patch Test Series: Pediatric Contact Dermatitis Workgroup**
   by JiaDe Yu, et al.
   in Dermatitis: July/Aug 2018, Volume 29, Issue 4, Pages 206-212.
2. **Patch Testing is a useful investigation in children with eczema**
   by Mana Moustafa et al
   in Contact Dermatitis, October 2011, Volume 65, Issue 4, Pages 208-212.
3. **Patch Test reactivity to nickel sulphate and fragrance mix in unselected children**
   by Hanne Johnke et al
   in Contact Dermatitis, March 2004, Volume 50, Issue 3, Page 131.
4. **Patch Test results in a Turkish paediatric population**
   by Meltem Onder et al
   in Contact Dermatitis, January 2008, Volume 58, Issue 1, Pages 63-65.
5. **Hidden Risks in Toys: A systematic review of paediatric toy contact dermatitis**
   by Justine Fenner, et al
   in Contact Dermatitis, February 2020, Volume 82, Issue 5, Pages 265-271.
6. **Dispelling the Myths behind Pediatric Patch Testing – Experience from our Tertiary Care Patch Testing Centers**
   by Sharon Jacob, et al
   in Pediatric Dermatology, May/June 2008, Volume 25, Issue 3, Pages 296-300.
7. **Usefulness of the European standard series for patch testing in children – A 3-year single-centre study of 337 patients**
   by S. Roul, et al
   in Contact Dermatitis, February 2007, Volume 40, Issue 5, Pages 232-235.
8. **Pediatric Contact Dermatitis registry Inaugural Case Data**
   by Alina Goldenberg, et al
   in Dermatitis, Sept/October 2016, Volume 27, Issue 5, Pages 293-302.
9. **Demographics of US Pediatric Contact Dermatitis Registry Providers**
   by Alina Goldenberg, et al
   in Dermatitis, July/August 2015, Volume 26, Issue 4, Pages 184-188.
10. **Patch Testing in Children from 2005 to 2012: Results from the North American Contact Dermatitis Group**
    by Kathryn Zug, et al
    in Dermatitis, Nov/Dec 2014, Volume 25, Issue 6, Pages 345-355.

Allergic Contact Dermatitis caused by Hydroperoxides of Limonene and Dose Response Relationship – a Repeated Open Application Test (ROAT) Study

by *Niels H Bennike, et al.*

in **Contact Dermatitis, April 2019, Volume 80, Issue 4, Pages 208-216.**

You may be wondering why we are writing about this article that is now 12 months since publication in Contact Dermatitis journal. However, this article has just been voted by ESCD as the best paper of 2019 – so we believe it is worth a revisit by Dermatologists, especially since it was published before The Patch Tester started in September 2019.

The purpose of the study was to determine the clinical relevance of a positive or doubtful patch test reaction to 0.3% Lim-OOH in petrolatum (Chemotechnique; L-005), as well as the elicitation threshold and the dose-response relationship. This was deemed useful because of the high proportion of weak positive and doubtful patch test reactions previously reported.

In brief, the conclusion reached by the study was that positive PT reactions are clinically relevant and even doubtful reactions can be of clinical relevance.
No surprises there then!

Oxidised limonene 3% pet., with a stable and standardised content of the main allergenic hydroperoxides of limonene (Lim-OOHs) of 0.3%, has been commercially available as the patch test preparation “Hydroperoxides of Limonene 0.3% pet.” from Chemotechnique (Vellinge Sweden) since 2012. High prevalence of contact allergy to Lim-OOHs 0.3% pet. has been reported in consecutive dermatitis patients referred for patch testing, both in an international multicentre study with 5.2% of patients positive overall, and lately in patch test clinics across Europe with 2.5% to 5.3% positive reactions. In most of these investigations, a high proportion of weak positive as well as doubtful and/or irritant patch test reactions to Lim-OOHs 0.3% pet. have been reported, which has caused some concern about the nature and clinical relevance of positive reactions.

ROAT testing was performed during 7 months in 2017/8 at Sahlgrenska University Hospital in Gothenburg Sweden. The investigators used simulated hydro-alcoholic leave-on cosmetic product containing Lim-OOHs at three different concentrations. The highest concentration was based on the known concentration of limonene determined by chemical analysis in leave-on cosmetic products intended for non-occlusive use.

In recent years, Lim-OOHs present in oxidised limonene have emerged as a very frequent cause of contact allergy in consecutively patch tested dermatitis patients. Although several possible sources of exposure to oxidised limonene exist, cosmetic products labelled to contain limonene are by far the most common sources of exposure causing allergic contact dermatitis in patients with positive patch test reactions to Lim-OOHs 0.3% pet.

The results showed that all patients with currently positive patch test reactions to standard Lim-OOHs 0.3% pet. and 15% (2 of 13) patients with currently doubtful patch test reactions at D3/4 or D7, developed allergic contact dermatitis when exposed daily to realistic doses of oxidised limonene. This substantiates the clinical relevance of a positive patch test reaction to standard Lim-

OOHs 0.3% pet. and further indicates that some patients with only doubtful patch test reactions have a weak but clinically relevant allergy. Note that no reactions, either allergic or irritant, were observed in the control group of subjects.

It is well-known that patch test reactivity can vary over time, and reactivity can be regained later. Importantly, 3 of the 4 participants with weak positive patch test reactions to Lim-OOHs 0.3% pet. and current negative confirmatory patch test results with Lim-OOHs 0.3% pet. did, in fact, have at least doubtful patch test reactions to one of the two highest concentrations of Lim-OOHs in the dilution patch test series.

Overall, the dose-response relationship in patients with contact allergy to Lim-OOHs 0.3% pet. following both single patch test exposure and repeated exposure in the ROAT, resembles that of other well-established fragrance contact haptens such as cinnamal, isoeugenol and hydroxyisohexyl-3-cyclohexene carboxaldehyde (Lyral).

In conclusion, patients with positive patch test reactions to Lim-OOHs 0.3% pet. develop allergic contact dermatitis when exposed to realistic doses of Lim-OOHs in a simulated leave-on cosmetic product. Furthermore, doubtful reactions to this preparation can be of clinical relevance in some patients.

As always, for further information please read the original article in Contact Dermatitis journal.

Dear Reader, if you have any particular article or book or website that you would like to have reviewed in a future issue of The Patch Tester, then please contact the Editor here.

Relative Prevalence of Contact Allergens in North America in 2018

by Andrew Scheman, et al.

in **Dermatitis, March/April 2020, Volume 31, Issue 2, Pages 112-121.**

The American Contact Dermatitis Society's Contact Allergen Management Program (CAMP) database was developed to provide patients with safe alternative products free of selected haptens. However, the Database also records valuable information including the frequency of hapten searches for patients.

Data from the CAMP database were analysed throughout 2018. The number of searches performed for a specific hapten serves as a measure of the number of positive patch test reactions, which in turn indicates the relative prevalence of sensitivity for each hapten. There are of course arguments that a search for information does not automatically correlate 100% with the number of positive results for that hapten, and there is also great dependency on the range of haptens tested by that practitioner, and on their patients. Nevertheless, the number of requests for information on alternative products serves as a good indication of the relative prevalence of sensitivity to that hapten.

The CAMP database is an online and freely accessible application developed by ACDS that permits professional members to generate a list of alternative products for patients. Obviously, the product names are most relevant for the American market, and so may not be the same as in the rest of the world.

Overall there were 32,220 total new patient searches, conducted by 927 different users across North America during 2018. The 2018 CAMP data showed that many of the prevalent haptens in North America are not currently in any contact allergy screening series. These data strongly indicate that testing only to an 80-item screening series, such as the North American Comprehensive Series of 80 haptens, will not provide adequate care for many patients with contact allergy.

The most prevalent haptens were fragrance mix, nickel, balsam of Peru, MCI/MI, and cobalt.

See table A for the prevalence of each of the different haptens ranked from highest to lowest. This table also show which haptens are in the North American 80 Series and in the T.R.U.E. Test series respectively.

The ACDS Core Series consists of 80 haptens. The CAMP data indicate that 81 haptens had more than 300 searches in 2018; however, a number of these are not on the ACDS Core Series, therefore all of these other haptens should be considered for inclusion in the North American Standard Series. Currently it is clear that at the very least these important haptens need to be patch tested in addition to the limit of 80 haptens allowed based on date of service.

It is important to note that some of these haptens were unexpectedly prevalent, and this was only discovered by testing to an even wider range of haptens than in the North American 80 Series.

From 2008 to 2015, 172 new haptens were identified, and these haptens would not have been identified if only limited patch testing panels were used.

Hapten	n	%	NAC-80	TRUE TEST	Hapten	n	%	NAC-80	TRUE TEST
Fragrance mix I	8833	27,4%			Imidazolidinyl urea	611	1,9%		
Nickelsulfate hexahydrate	6319	19,6%			Tea tree oil	608	1,9%		
Peru Balsam	6196	19,2%			Benzocaine	567	1,8%		
MI / MCI	4157	12,9%			Benzalkonium chloride	566	1,8%		
Cobalt(II)chloride hexahydrate	3893	12,1%			Budesonide	563	1,7%		
FORMALDEHYDE	3596	11,2%			n,n-Diphenylguanidine	547	1,7%		
MDBG	3522	10,9%			Epoxy resin	525	1,6%		
Gold sodium thiosulphate	3447	10,7%			Benzyl salicylate	520	1,6%		
METHYLISOTHIAZOLINONE	3366	10,4%			LANOLIN ALCOHOL	513	1,6%		
Polyethylene glycol	3326	10,3%			DMDM HYDANTOIN	511	1,6%		
IPBC	3217	10,0%			Cocamide DEA	503	1,6%		
Neomycin sulfate	2666	8,3%			Carmine	471	1,5%		
p-PHENYLENEDIAMINE (PPD)	2602	8,1%			Tocopherol acetate	467	1,4%		
PROPOLIS	2481	7,7%			Ammonium persulphate	452	1,4%		
Bacitracin	2226	6,9%			Benzyl alcohol	446	1,4%		
Fragrance mix II	2154	6,7%			Cinnamyl alcohol	416	1,3%		
Carba mix	2131	6,6%			Glyceryl thioglycolate	415	1,3%		
QUATERNIUM-15	1854	5,8%			Black rubber mix	412	1,3%		
THIMEROSAL	1851	5,7%			Lidocaine	393	1,2%		
CPB	1832	5,7%			Phenoxyethanol	391	1,2%		
Hydroperoxides of Linalool	1807	5,6%			Benzophenone-3	385	1,2%		
Amerchol L-101	1617	5,0%			Mercaptobenzothiazole	382	1,2%		
Potassium dichromate	1599	5,0%			Ethyleneurea formaldehyde mix	379	1,2%		
Glutaraldehyde	1558	4,8%			Hydrocortisone-17-butyrate	372	1,2%		
Disperse Blue 106	1519	4,7%			Clobetasol-17-propionate	366	1,1%		
2-BROMO-2-NITROPROPANE-1,3-DIOL	1446	4,5%			Mercapto mix	362	1,1%		
Cinnamic aldehyde	1379	4,3%			Octyl gallate	361	1,1%		
Benzoyl peroxide	1297	4,0%			Sequiterpene lactone mix	351	1,1%		
Amidoamine	1276	4,0%			L-Carvone	335	1,0%		
Dimethylaminopropylamine	1179	3,7%			Lyral	327	1,0%		
DECYL GLUCOSIDE	1164	3,6%			Sorbitan sesquiolate	320	1,0%		
Hydroperoxides of Limonene	1141	3,5%			Laury! glucoside	313	1,0%		
Compositae mix	1093	3,4%			Chlorhexidene digluconate	295	0,9%		
OAPDMA	1091	3,4%			Ethyl cyanoacrylate	276	0,9%		
Colophony	1087	3,4%			TSF Resin	274	0,9%		
Thiuram mix	1073	3,3%			Textile dye mix	265	0,8%		
Paraben mix	987	3,1%			Caine mix	259	0,8%		
Tixocortol-21-pivalate	978	3,0%			Dibucaine	198	0,6%		
Disperse orange 3	847	2,6%			Propyl gallate	197	0,6%		
2-Hydroxyethyl methacrylate	808	2,5%			Triethanolamine	196	0,6%		
Diazolidinyl urea	804	2,5%			CHLOROXYLENOL (PCMX)	196	0,6%		
Ethylenediamine dihydrochloride	731	2,3%			Desoximetasone	191	0,6%		
Ethyl acrylate	714	2,2%			Parthenolide	189	0,6%		
Benzoic acid & benzoates	698	2,2%			TRICLOSAN	188	0,6%		
Methyl methacrylate	693	2,2%			Mixed dialkyl thiourea	159	0,5%		
Benzophenone-4	660	2,0%			Amyl cinnamaldehyde	47	0,5%		
p-tert-Butylphenol formaldehyde resin	646	2,0%			Jasmine absolute	145	0,5%		
Dodecyl gallate	632	2,0%			Isoeugenol	44	0,4%		
YLANG-YLANG OIL	626	1,9%			SORBIC ACID	137	0,4%		
Shellac	613	1,9%			Peppermint oil	129	0,4%		

The haptens below are comstituents of the NAC-80 (blue) Series and the T.R.U.E Test (pink), but are not amongst the Top 100 haptens of the CAMP Database.

Disperse Yellow 3	ETHYLHEXYL SALICYLATE	ISOPROPYL MYRISTATE
Fusidic acid sodium salt	2-n-Octy-I 4-isothiazolin-3-one	POLYSORBATE 80
2-tert-Butyl-4-methoxyphenol (BHA)	ISOAMYL p-METHOXYCINNAMATE	

Quinoline mix
Bronopol

Table A. The Top 100 haptens in the CAMP Database.

This really would seem to be a case of “the more you look, the more you will find”.

Overall, it has been estimated that an 80-item patch testing series will detect up to only 70% of clinically relevant sources of contact allergy.

On the other hand, there are a number of haptens with very few searches which are currently included in the ACDS Core Series including chlorhexidine, ethyl cyanoacrylate, TSF Resin, dibucaine, chloroxylenol, desoximetasone, mixed dialkyl thioureas, sorbic acid, triamcinolone, BHA, cetylstearyl alcohol and PCMC.

Notably, 16 (46%) of the top 35 most prevalent CAMP haptens are not on the T.R.U.E. Test series including MI, PG, IPBC and propolis.

Particularily for fragrance mix I and balsam of Peru, the T.R.U.E. Test demonstrated substantially lower rates of prevalence compared with other screening series, as has been previously reported. These results suggest that the T.R.U.E. Test may have a lower sensitivity for picking up fragrance allergy. This is of great significance because fragrance is one of the most prevalent haptens and so identification of fragrance allergy is an extremely important function of any screening series.

In contrast, gold sodium thiosulphate, PPD, Quaternium 15, thimerosal, carba mix, bronopol and tixocortol pivalate were found to be more than five ranks more prevalent for the searches that use the T.R.U.E. Test. This may mean that the T.R.U.E. Test may be yielding a number of false positive reactions for these haptens.

It is notable that Amerchol L101 seems to be much more sensitive in identifying lanolin allergy than wool alcohol, which is the hapten currently available in the T.R.U.E. Test series.

More importantly 16 (46%) of the top 35 most prevalent haptens in CAMP are not found in the T.R.U.E. Test series; including MI, PG, IPBC, propolis, fragrance mix II, CPB, linalool HP, Amerchol L101, glutaraldehyde, cinnamic aldehyde, benzoyl peroxide, amidoamine, decyl glucoside, limonene HP, Compositae mix, and OAPDMA. This confirms what other studies have found, that testing to this series alone might fail to detect relevant haptens.

In conclusion, the CAMP database provides information on the relative prevalence of haptens from both community and academic medical practices across the entirety of North America. These data are of great importance in the design of patch test screening series, and clearly document the medical necessity of comprehensive patch testing to haptens beyond even an 80-item screening series.

As always, for full information please read the original article in Dermatitis journal.

Indium and Iridium: two rare earth metals with a high rate of contact sensitisation

by *I Terrani, et al.*

in **Contact Dermatitis, Accepted for publication, April 2020, Volume 82, Issue 4.**

Humans are exposed to a variety of metals on a daily basis, and nickel is the most frequent sensitising contact hapten. Currently little is known with regard to the frequency of sensitisation to indium and iridium. This retrospective study evaluated the prevalence of indium and iridium sensitisation and also evaluated the optimal patch test conditions.

364 patients were patched tested at the Allergy Unit of the University Hospital of Basel Switzerland. Pure metals, metal chlorides and metal sulphates were applied in petrolatum or water in Chemotechnique IQ test chambers for two days. Reactions were read twice, at D2 and between D4 and D7.

11 patients reacted to indium salts (3%) 13 to iridium salts (3.6%) and one reacted to both salts. None of the reactor patients reacted to pure metals. 19 of the 23 patients who reacted to indium or iridium showed concomitant positive reactions to other metals, mainly nickel and palladium.

In conclusion this retrospective clinical study provides insight into prevalence and test conditions of two rarely tested metal haptens in this larger patient cohort. A considerable number of iridium or indium positive subjects had co-sensitisation to other metals.

Prevalence of Contact Allergy to Metals: Nickel, Palladium and Cobalt, in Southern Sweden from 1995 to 2016

by *Lisbeth Comstedt, et al.*

in **Contact Dermatitis, April 2020, Volume 82, Issue 4, Pages 218-226.**

Metal allergy has for a long time been and still is the most frequent contact allergy. Among the metals, nickel is the most common contact hapten, with a prevalence of 10% to 20% amongst women in the general population in Europe. In 1990 the first national nickel regulation in Sweden came into force, regulating the content of nickel in earrings and piercing posts. The first European nickel directive was later adopted in 1994 and came into force in 2001. The directive limited the rate of nickel released from products intended to come into direct and prolonged contact with the skin. In 2004 the directive was revised and the limit for post assemblies used in pierced holes was lowered. The directive is since 2009 part of the registration, evaluation, authorisation and restriction of chemicals (REACH) regulation.

Nickel is still to be found in cheap watches, jewellery, sewing materials, zippers, buttons, belt buckles, coins, etc.

Nickel sulphate hexahydrate (NiSO4) is the most common nickel salt used when patch testing for nickel. In the European Baseline Series, NiSO4 is tested at 5% w/w in petrolatum.

Palladium is today used primarily as industrial catalysts in cars, dental appliances and jewellery. Dental appliances are the main source of sensitisation.

Palladium is not routinely tested for, such as in the European Baseline Series, though it is present in various Dental Series from manufacturers of patch test haptens. Patch testing with palladium chloride (PdCl2) has been the standard test since the 1990's but recent research shows that sodium tetrachloropalladate (Na2PdCl4) is a better test salt for detecting palladium sensitisation.

Cobalt does not belong to the same group in the Periodic Table as nickel and palladium, but co-exists with nickel in nature, which is why it is present in many nickel alloys. Today, cobalt without nickel is used in many different consumer articles, such as electronic devices (notebook computers!), magnetic materials, jewellery, dental alloys, and in pigments used in cosmetics and leather.

Cobalt chloride (CoCl2) is used to test for sensitivity to cobalt metal.

The purpose of the study was to determine the prevalence of sensitisation to these three metals, and to assess the impact of the REACH directive.

The study was based on 18,306 patients patch tested in 1995 to 2016 for one or more of these metals at Skåne University Hospital, Malmö, Sweden.

Below are a dozen more interesting observations that the authors elicited from the results of their study:

- Intensity of reaction to nickel sulphate varies over time.
- Concomitant reaction to either palladium or cobalt is common in persons who patch test positive to nickel.
- Notes from a separate study in 2019 suggest that isolated reactions to Na2PdCl4 can be false positive in aluminium-sensitised persons due to contaminating aluminium from aluminium patch test chambers.
- Overall reactions to palladium chloride and to cobalt chloride decreased together with the decreasing prevalence of nickel allergy.
- As cobalt is often found in nickel alloys makes it possible to be sensitised to both metals simultaneously.
- Individuals with nickel allergy were approximately 36 times more likely to have palladium allergy compared to individuals who were not allergic to nickel.
- The prevalence of palladium sensitisation, which was found (in this study cohort) to be approximately 10% and was stable over 8 years (2009-2016). Other studies in Europe and USA have found a prevalence of 5.3% to 13% in their test cohorts.
- The retained high prevalence of nickel allergy in the older age groups remained stable, probably due to exposure and sensitisation to nickel prior to when the nickel directive came into force.
- The greatest reduction in nickel sensitisation (in this study cohort), as a result of the increasing regulation of its usage, is in the youngest female age group, reducing from 33.4% in 1995-1999 to 19.4% in 2012 to 2016.
- There are still items in the market (in Sweden, for various reasons including personal importation) that release too much nickel (>0.5µg/cm^2/per week) causing the prevalence of nickel sensitisation (in the study cohort) to remain high at 19.1% amongst young females.
- Prolonged contact is defined as 10 minutes for 2-3 occasions within 2 weeks, or 30 minutes on 1 occasion within 2 weeks. Therefore, the regulations do not cover nickel release from objects meant to have short contact with the skin.
- Nickel ions have been shown to accumulate in the skin after even a brief contact, therefore new regulations might be needed to reduce the exposure further and thereby reduce the still significant nickel sensitisation.

By way of conclusion, the authors stated that allergy to nickel has decreased in southern Sweden amongst young patients, both men and women, age 6 to 30 years, suspected to have contact dermatitis. Today the prevalence of nickel allergy amongst younger female is 19.1%, which still makes it the most common contact allergy. The REACH regulation seems to have had a beneficial impact on the decrease in nickel allergy, but further steps may be necessary to further reduce sensitisation.

Note that the various patch test haptens mentioned above are available from Chemotechnique, as follows:

Art. no	Hapten	Conc. Veh.	Formula
N-002	Nickel sulphate hexahydrate	5.0% pet	NiSO4
P-001	Palladium chloride	2.0% pet	PdCl2
S-017	Sodium tetrachloropalladate	3.0% pet	Na2PdCl4
C-017	Cobalt chloride	0.5% pet	CoCl2

In addition, Chemotechnique offer Spot Tests for nickel (NT) and for cobalt (CoT), to identify items such as jewellery that contain either of those two metals.

As always, for further information, read the original article in Contact Dermatitis journal.

A Survey of Members of ESCS on Contact Dermatitis and the EU project "Standerm" to Identify allergens tested in Cosmetic Series across Europe

by *Emma Horton, et al.*

in **Contact Dermatitis, March 2020, Volume 82, Issue 3, Pages 195-200**

There is currently no agreed cosmetic series for use across Europe.

There are significant variations between centres across Europe on the haptens considered to be of importance in screening for allergy to cosmetics.

One of the main outcomes of the European surveillance system on contact allergy from September 2016 was to develop a recommended European Cosmetic Series.

Of the 13 countries surveyed, only Belgium, Finland, Germany and the UK had nationally agreed series to screen for cosmetic allergy.

For details of which haptens are included in which national cosmetic series, and other hapten information, please see the original article.

The variation from country to country may be due to the cost, or a combination of other factors such as prevalence, product brands, etc. A European standard Cosmetic Series should take into consideration these factors.

It should be noted that manufacturers of patch test haptens have their own recommendations for Cosmetic Series.

The Cosmetic Series as recommended by Chemotechnique is shown alongside.

Information on each hapten is available online at www.chemotechnique.se

Further information is at:
https://www.chemotechnique.se/products/series/cosmetic-series/

Position	Art. no	Hapten	Conc. Veh.
1.	I-003	ISOPROPYL MYRISTATE	20.0% pet
2.	A-004	Amerchol L-101	50.0% pet
3.	T-016	TRIETHANOLAMINE	2.0% pet
4.	P-013	POLYSORBATE 80	5.0% pet
5.	S-004	SORBITAN OLEATE	5.0% pet
6.	B-022	2-tert-Butyl-4-methoxyphenol (BHA)	2.0% pet
7.	D-006	BHT	2.0% pet
8.	O-002	Octyl gallate	0.25% pet
9.	T-014	TRICLOSAN	2.0% pet
10.	S-003	SORBIC ACID	2.0% pet
11.	C-008	p-CHLORO-m-CRESOL	1.0% pet
12.	C-010A	CHLOROXYLENOL (PCMX)	0.5% pet
13.	T-007	THIMEROSAL	0.1% pet
14.	I-001A	IMIDAZOLIDINYL UREA	2.0% pet
15.	H-003	METHENAMINE	2.0% pet
16.	C-005	CHLORHEXIDINE DIGLUCONATE	0.5% aq
17.	Mx-03C	Paraben mix	16.0% pet
18.	P-008	PHENYL MERCURIC ACETATE	0.01% aq
19.	C-006	CHLOROACETAMIDE	0.2% pet
20.	H-002	Hexahydro-1,3,5-tris-(2-hydroxyethyl)triazine	1.0% aq
21.	C-015	Clioquinol	5.0% pet
22.	E-005	Ethylenediamine dihydrochloride	1.0% pet
23.	A-002	HYDROABIETYL ALCOHOL	10.0% pet
24.	P-011	PHENYL SALICYLATE	1.0% pet
25.	H-014C	BENZOPHENONE-3	10.0% pet
26.	S-005	SORBITAN SESQUIOLEATE	20.0% pet
27.	P-019A	PROPYLENE GLYCOL	5.0% pet
28.	S-006	STEARYL ALCOHOL	30.0% pet
29.	C-003	CETYL ALCOHOL	5.0% pet
30.	B-010B	BENZYL SALICYLATE	10.0% pet
31.	B-015A	2-BROMO-2-NITROPROPANE-1,3-DIOL	0.25% pet
32.	S-002	Sodium-2-pyridinethiol-1-oxide	0.1% aq
33.	C-018	COCAMIDOPROPYL BETAINE	1.0% aq
34.	B-008B	BENZYL ALCOHOL	10.0% sof
35.	C-009B	MI/MCI	0.02% aq
36.	B-028	t-BUTYL HYDROQUINONE	1.0% pet
37.	H-016	DROMETRIZOLE	1.0% pet
38.	P-021	PROPYL GALLATE	1.0% pet
39.	D-042	DODECYL GALLATE	0.25% pet
40.	C-007A	QUATERNIUM-15	1.0% pet
41.	P-025	PHENOXYETHANOL	1.0% pet
42.	D-044A	DIAZOLIDINYL UREA	2.0% pet
43.	T-036	TOCOPHEROL	100%
44.	D-047A	DMDM HYDANTOIN	2.0% aq
45.	D-049E	METHYLDIBROMO GLUTARONITRILE	0.5% pet
46.	T-035B	Tea Tree Oil oxidized	5.0% pet
47.	I-008C	IODOPROPYNYL BUTYLCARBAMATE	0.2% pet
48.	D-053	3-(Dimethylamino)-1-propylamine	1.0% aq
49.	L-004	LAURYL POLYGLUCOSE	3.0% pet
50.	P-036	Peppermint oil	2.0% pet
51.	S-015	SHELLAC	20.0% alc
52.	T-037B	TOCOPHERYL ACETATE	10.0% pet
53.	T-024B	Turpentine oil oxidized	0.4% pet
54.	M-035B	METHYLISOTHIAZOLINONE	0.2% aq
55.	Mx-10B	Musk mix	3.0% pet
56.	O-005	OLEAMIDOPROPYL DIMETHYLAMINE	0.1% aq
57.	D-065	DECYL GLUCOSIDE	5.0% pet
58.	E-027	ETHYLHEXYLGLYCERIN	5.0% pet
59.	S-011	SODIUM METABISULFITE	1.0% pet
60.	Mx-28B	Gallate mix	1.0% pet
61.	C-056	CETEARYL GLUCOSIDE	5.0% pet
62.	P-042	PANTHENOL	5.0% pet
63.	P-043	POLYAMINOPROPYL BIGUANIDE	2.5% aq

Safety Checks in Patch Testing
5 Hurdles in the Patch Testing Obstacle Course

By Gabriela Poole, et al

in **Dermatitis, March/April 2020, Volume 31, Issue 2, Pages 89-98**

A very interesting and rather unusual article that describes the practicalities of patch testing in order to achieve a reliable result.

Patch testing is an important diagnostic tool in the diagnosis of allergic contact dermatitis.

Pre-prepared haptens are available e.g. T.R.U.E. Test, but are limited to 36 haptens. Therefore, many patch test clinics prepare patches manually from commercially available haptens, to allow testing of more haptens, specialised series, and customisation to the individual patient.

Commercial sources of haptens are usually readily available, as well as chemicals from the individual patient.

Each clinic will determine their own patch testing capabilities, depending on available staff, the special interests of the individual Dermatology Specialist, the patient load, and the type of patients encountered. This may range from a standard series of perhaps 30 haptens, up to several different Series and perhaps 200 or more different haptens. This particular clinic of the authors is based in USA, and is dedicated to solely patch testing, and has a staff of 11 professionals; so it is by no means typical of all Dermatology practices.

In accordance with the scope and detail of their practice, the authors have instituted various patch testing safety check points which they trust other practitioners will find useful in their own practices to combat error and ensure high quality of testing and patient care.

Accuracy in patch testing is critical for correct hapten identification. This multi-step process is prone to error, and the risk increases with more staff involved (physicians, residents, fellows, technicians, nurses), antigens and patients. Standardised safety check points increase efficiency, consistency and safety.

In this article, the USA-based authors outline workflows that have been developed over 20 years of experience, that maximise productivity and communication among team members, and minimise system errors.

They organise patch safety into five key hurdles or steps and outline the specific safety procedures of each step via the use of checklists, easy visual cues, and double verification.

Its inportant to monitor your hapten inventory

The five hurdles are the following:

1 Inventory
- Stocking sufficient haptens
- Maintaining chemical viability through appropriate storage
- Systematising correct antigen identification

2 Patch preparation
- Consistent order communication
- Standardising conformation and numbering of patches
- Accurate placement of haptens on patches

3 Application
- Maximising patch contact with suitable skin on patient
- Minimising risk of interference with patch test reactions

4 Documentation
- Accurate maps
- Avoiding frame-shift mis-reads

5 Education
- Promoting patient partnership
- Hapten avoidance

Having all team members consistently use the same workflow maximises productivity and minimises human error risk.

Below are stated just some of the many notes and tips and recommendations from the authors; but for further information, please read the original article.

Stocking Sufficient Haptens

• Consider delivery lead times from your commercial supplier of commercially manufactured haptens.
• Consider timing of production of any own-manufactured haptens.
• Accurate labelling and cross-referencing of haptens.
• Tracking expiration dates (including on product arrival).
• Efficient ordering of exhausted syringes/bottles, or of entirely new haptens.
• Reserve stock.

Maintaining Chemical Viability

• Appropriate storage, at 2-8*C for most haptens, but acrylates & isocyanates and other highly volatile haptens may be maintained at -20*C.
• Preparation of pre-made patches, maximum 2 weeks before use, but not for volatile or labile haptens.
• Cap the syringes, and pull back slightly to prevent leakage.

Systematising Correct Hapten Identification

• On receipt from supplier, check hapten identification and concentration and vehicle and expiry date. Record information in an Excel database.
• Organise into a working Series or into a reserve stock.
• Try to avoid duplicate testing, such as using one hapten that occurs in 2 different series. Keep that hapten syringe or vial in its home series, usually the most frequently used series. In the other series, place a dummy object such as a wooden spatula with a note stating where the syringe/bottle will be located in the other series.
• When loading the patch test chamber strip with a hapten that occurs in another series that is also being applied to the patient, then place coloured paper note in the appropriate chamber, to indicate the avoided duplication and to minimise the risk of misplacement of the hapten.

Patch Preparation

• It is not uncommon for the physician to order changes (additions or deletions of specific haptens or even series) during the initial visit or at the second visit. Any new orders must be communicated very clearly to the technician/nurse, in a standardised and recorded manner.
• The technician/nurse must correspondingly record their compliance.

Standardising Patch Creation

• Accurate identification and labelling of chamber strips is absolutely crucial. This can be done directly on the chamber strip or possibly on the overlying adhesive tape. For example; “Perfume #1” or “Cosmetic #3”.
• Pre-made patches/chamber strips should be labelled with the date of preparation.
• Trays are available from patch test suppliers that aid the creation of the chamber strips, and the labelling.
• A form is created and annotated for each chamber strip, showing what haptens are located where – these forms are standardised for each series.
• Be very careful with the mirror imaging of patch chamber strip preparation. Whilst being prepared, the top left chamber becomes the top right chamber on the patient, and so on.
• Ensure the chamber strips are applied right way up.
• Volatile haptens are added to the chamber strip only immediately before application to the patient.

Accurate Placement of Antigens on the Patch

• It is of paramount importance that the correct antigen be placed into the correct patch test chamber site on the correct chamber strip. Although this is obvious and might seem straightforward, it is prone to error without appropriate safety checkpoints.
• For all patches using petrolatum-based haptens, approximately one third of the chamber area is covered with hapten.
• Note that manufacturers recommend that a ribbon of the petrolatum is run from one corner to the diagonally opposite corner. (That is approx. 20 mg).
• Note that manufacturers recommend one drop of the liquid hapten.

Maximising Patch Contact with Suitable Skin on the Patient

• Before the appointment, the patients are counselled to not apply lotion or creams for 24 hours.
• Tape should be used, and should extend beyond the edges of the chamber strips, without overlying the tape of other patches/chamber strips.
• Note that some commercially available patch test units are more adhesive than others, and some types of patch test units are more rigid or more flexible than others.
• Outline patch tests with surgical marker, especially if there is a risk of dislodgement due to body movement.

Minimising Risk of Interference with Patch Test Reactions

• Patients are counselled to avoid harsh sunlight and exercise for the week of the test.
• Patients should discontinue oral prednisolone and immunosuppressive drugs up to 1-2 weeks before testing, under guidance of their physician.
• Steps are taken to minimise the risk of reacting to the testing materials themselves: for example: use a hypoallergenic tape such as Scanpor. Some patients will react to the adhesive of the chamber strips, but not to the adhesive of other brands of chamber strips. Some patients, especially prepubescent patients, may react to the aluminium in Finn Chambers, so the authors use IQ Ultra or IQ Ultimate chambers from Chemotechnique.

Accurate Maps

• Many clinics photograph instead of drawing maps of the chamber strips on the patient; some do both for safety’s sake. The authors prefer hand-drawn maps.

Avoiding Frame-Shift Mis-reads

• At the second visit, the patches are removed in a systematic manner.
• First remove the outer Scanpor tape.
• Then confirm the chamber strips are still correctly located and so have not moved since their application (the previously drawn outline will confirm this).
• After the chamber strips are one by one removed then the test sites can be marked with ticks between the sites.
• Take photographs of the test sites, both distant and close-up.
• Evaluation of test site reactions is the prerogative of the physician.
• Results must be carefully documented.

Promoting Patient Partnership

• Both the Physician and the technician/nurse counsel the patients on their restrictions during their week of testing; it really must be a low-key week.

Hapten Avoidance

• With contact dermatitis, the best treatment is hapten avoidance, temporarily supplemented if necessary by symptomatic treatment, such as topical steroids.
• Identification of the problem contact hapten is therefore extremely important.
• Recommendations for hapten avoidance must also be accurate and reliable.
• Problem products in the patient’s household must be accurately identified, product by product if necessary.
• Alternative products to the identified problem products must be recommended.

Effect of Patch Testing on the Course of Allergic Contact Dermatitis and Prognostic Factors That Influence Outcomes

by *Pinar Korkmaz, et al.*

in **Dermatitis, March/April 2019, Volume 30, Issue 2, Pages 135 – 141.**

In this third issue of The Patch Tester, this is a second “older” article, from March/April 2019, but is included here by virtue of it having been voted by ACDS as the 2nd place runner-up in the Dermatitis journal “Article of the Year 2019”. The topic of the article is also very relevant to The Patch Tester as it underlines the importance of patch testing to the management of patients with Allergic Contact Dermatitis.

The researchers based in Ankara Turkey wished to study the effect of patch testing on the severity of the contact dermatitis, the QoL and Dermatology Life Quality Index (DLQI) of the patients, and various other associated factors. The Investigator Global Assessment scale (IGA) was used to quantify disease severity.

They recruited a total of 51 patients in their test group and a matched cohort of controls.

The European Baseline Series was tested, using Chemotechnique haptens, supplemented with special series and patient-supplied products when indicated.

The most common positive patch test reactions in the ACD group were as follows:

Art. no	Hapten	RPPT
N-002A	Nickelsulfate hexahydrate	23,5%
P-014A	Potassium dichromate	19,6%
C-017A	Cobalt(II)chloride hexahydrate	13,7%
Mx-01	Thiuram mix	11,7%
Mx-25	Fragrance mix II	11,7%
P-006	p-PHENYLENEDIAMINE (PPD)	11,7%
N-001	Neomycin sulfate	9,8%
Mx-07	Fragrance mix I	7,8%
C-009A	MI / MCI	7,8%

Twenty-five patients in the ACD group (49%) had more than one hapten positivity. Of these 25 patients, 56% had 2 haptens, 32% had 3 haptens and 12% had 4 haptens.

Occupational relevance was noted in 23 (56%) of patients. The most common occupations involved were construction workers, hairdressers and food industry workers.

Potassium dichromate, thiuram mix and PPD were the most frequently encountered relevant occupational haptens.

The ACD patients were all advised, both verbally and in writing, of their specific problem hapten or haptens, and given information on avoidance and alternative products.

At 6 months follow-up of the ACD group of 51 patients, 27 (52.9%) reported total clearing of their lesions, whereas 9 (17.6%) reported partial clearing, and 7 (13.7%) reported no change in the severity of the lesions. 8 (15.7%) reported the lesions had become worse.

Recall of problem haptens at 6 months was shown by 38 (74.5%) of patients. Twenty-four patients (63%) recalled the name of the haptens, and 14 patients (37%) recalled the substance group. Of all, 84% of the female patients and 64% of the male patients recalled the haptens, though this recall was independent of age and educational background. There was a strong correlation between hapten recall and the improvement in the DLQI scores.

The greater the number of problem haptens then the lesser the recall rate, as would be expected.

Similarly, the greater the number of problem haptens then the greater the difficulty to implement effective hapten avoidance, and therefore the smaller improvement in IGA and DLQI scores.

The most significant reductions in the IGA and DLQI scores were obtained in the patients who were able to avoid the haptens. Conversely, the IGA and DLQI scores of the patients whose contact with the problem haptens had continued had increased compared to their previous baseline.

All the above findings are in concordance with other previous studies.

Change of occupation was made by 8 patients (45.1%) of the 23 with occupation related ACD. 10 (43.4%) had continued working but with preventive measures, and 5 (21.7%) had continued working without any hapten avoidance. At the six-month follow-up visit, the IGA and DLQI scores of the patients who had changed their jobs were significantly lower (better) than those patients who had continued working at the same job with or without prevention. The IGA and DLQI scores of the patients who had worked without prevention were even higher than the baseline values. Most of the patients continued working in the same jobs because of personal financial considerations and/or inadequacy of workplace legal regulations in that country.

At the 6-month follow-up visit, 37 patients reported that they had benefited from patch testing (72.5%), 8 patients (15.7%) claimed that it was not beneficial, and 6 patients (11.8%) were uncertain about the benefit of the procedure. Although these uncertain patients had noticed the beneficial effect, they claimed that the necessity to check each item caused uneasiness and great difficulty in their lives. These results are very similar to the results obtained in previous studies in which 72% to 89% of patients were satisfied with the patch test procedure.

The information given about the patch test results and the necessary precautions to avoid products containing problem haptens was found useful by 94% of patients, which reflects the quantity and quality of the written and verbal information provided. This is therefore an essential part of any patch testing program.

In summary, although patch testing is expected to make a significant improvement in the quality of life of the patients, avoidance can be very difficult to achieve especially for patients who have a sensitivity to antigens that are abundant in the environment. In our study, 56.9% of the patients had succeeded in avoiding allergens, and these patients had the most significant improvement in IGA and DLQI scores.

For full information, please read the original article in Dermatitis journal.

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

THE AUSTRALASIAN COLLEGE OF DERMATOLOGISTS

Australian College of Dermatologists

www.dermcoll.edu.au

The ACD is the peak professional medical college accredited by the Australian Medical Council for the training and continuing professional development of medical practitioners in the speciality of dermatology.
Established in 1967, the ACD provides authoritative information about dermatology to government, the media, other health professionals and the general public. They are a not-for-profit organisation, based in Sydney, and with an in-house staff of no less than 17 persons. The college has 573 Fellows and 114 Trainee members, located throughout the 8 States and Territories of Australia, plus a score of overseas members. Note that New Zealand-based Dermatologists have their own national society, NZDSI, though they work closely with the college and the annual ACD congresses are well attended by NZ delegates.The vast majority of Australian Dermatologists are members of ACD.

The website offers clinical information for the general public, at
https://www.dermcoll.edu.au/a-to-z-of-skin/

AUSTRALASIAN SOCIETY FOR DERMATOLOGY RESEARCH
ASDR

Australasian Society for Dermatology Research (ASDR)

www.asdr.org.au

This is a rather lesser-known organisation than ACD, and is primarily intended for those Dermatologists interested in the latest research, and connection to equivalent international professional societies.
As such, the organisation covers the spectrum of dermatological conditions, of which Allergic Contact Dermatitis and Patch Testing are but a small corner.

Their objectives are to promote scientific research in the field, to provide a forum for interaction amongst professionals, and to investigate sources for research funding.

They usually have a congress associated with the annual congress of ACD, which was due to be held in Adelaide on 13th to 16th May 2020. However, that ACD Congress has been postponed till 9th to 13th April 2021. Therefore, the ASDR cancelled their congress for 2020. For information on congresses for several other Dermatology research organisations see the Congresses and Exhibitions feature on page 28.

Contact Dermatitis / Patch Testing

14th - 16th December 2020
ESCD Congress
Amsterdam, Netherlands
www.escd2020.com

19th to 23rd March 2021
American Academy of Dermatology
San Francisco, California
www.aad.org

Dermatology - International

5th – 6th October 2020
26th Asia-Pacific Dermatology Conference
Auckland New Zealand
www.dermatology.conferenceseries.com/asiapacific/

14th to 15th October 2020
World Dermatology Congress
Rome, Italy
www.dermatology.healthconferences.org/

28th October to 1st November 2020
EADV Congress
Vienna, Austria
www.eadvvienna2020.org

20th to 21st November 2020
Asia Pacific Combined Dermatology Research Conference
Tokyo, Japan
www.apc2020tokyo.jp

15th to 18th September 2021
Ibero-Latin American Congress of Dermatology 2020 (CILAD)
Madrid, Spain
www.cilad2020.org

22nd to 25th September 2021
European Society for Dermatological Research
Amsterdam, Netherlands
www.esdrmeeting.org

22nd to 25th September 2021
14th World Congress of Paediatric Dermatology
Edinburgh, Scotland
www.wcpd2021.com

10th to 13th November 2021
International Congress of Dermatology
Melbourne Australia
www.icd2021.com.au

Dermatology - National

30th September to 2nd October 2020
BSACI Annual Conference
Harrogate, United Kingdom
www.bsacimeeting.org

5th to 9th August 2020
New Zealand Dermatology Conference
Queenstown, New Zealand
sue@spconferences.co.nz

1st September 2020
100th Annual Meeting of the British Association of Dermatologists
Online digital congress only
https://badannualmeeting.co.uk
Online