the Patch Tester

Contact Dermatitis | Haptens | Patch Testing

Edition #2
March 2020

In this issue

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

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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 second 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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ACKNOWLEDGEMENTS

Production Editors: David Niklasson & Steve Lee

ICDRG presents updated Baseline Series

As reported in "Dermatitis" of January/February 2020, Volume 31, Issue 1, pages 5 to 7, the International Contact Dermatitis Research Group has announced a revision to their Baseline Series.

The first such Series was developed no less than 23 years ago, in 1997, and comprised just 20 haptens. This was revised in 2011 to encompass 32 haptens, and that panel has been used ever since. Now in 2020 the new composition has been revised down to 29 haptens. The reason for the reduction, (in contrast to the almost inevitable inflation of numbers in every other walk of life), is due to the changes in the occurrence of these haptens and the consequent reduction in the prevalence of clinical sensitivity, falling below the threshold of at least 0.5% in all tested individuals.

The ICDRG collected data from 13 PT centres on 4 continents during 2012 to 2016. In addition, there were several multi-centre studies with the specific purpose to investigate sensitisation rates for several of the constituent haptens of the previous Series.

As a consequence, the new ICDRG Baseline Series now comprises the haptens stated in the list to the right. Text in bold indicates changes to the Series.

It is highly likely that at least some if not all of these changes (additions, deletions and changed concentrations) will in due course become incorporated into other Baseline Series

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

* Chemotechnique are now developing the new hapten concentrations for #5 and #16.

#	Hapten Name	Concn.	Chemo. Art. No.
1	p-PHENYLENEDIAMINE (PPD)	1.0%	P-006
2	4-tert-Butylphenolformaldehyde resin	1.0%	B-024
3	Budesonide	0.01%	B-033B
4	Carba mix	3.0%	Mx-06
5	**MCI/MI** (aqua)	**0.215%**	*
6	Cobalt(II)chloride hexahydrate	1.0%	C-017A
7	COLOPHONIUM	20.0%	C-020
8	Compositae mix II	5.0%	MX-29A
9	DIAZOLIDINYL UREA	2.0%	D-044A
10	Epoxy resin, Bisphenol A	1.0%	E-002
11	FORMALDEHYDE (aqua)	2.0%	F-002B
12	Fragrance mix I	8.0%	Mx-07
13	Fragrance mix II	14.0%	Mx-25
14	IMIDAZOLIDINYL UREA	2.0%	I-001A
15	LANOLIN ALCOHOL	30.0%	W-001
16	**Mercapto mix**	**3.5%**	*
17	METHYLDIBROMO GLUTARONITRILE	0.3%	D-049A
18	Peru balsam	25.0%	B-001
19	N-Isopropyl-N-phenyl-4-phenylenediamine (IPPD)	0.1%	I-004
20	Neomycin sulfate	20.0%	N-001
21	Nickel(II)sulfate hexahydrate	2.5%	N-002B
22	Paraben mix	16.0%	Mx-03C
23	**Phenol formaldehyde resin (PFR2)**	**1.0%**	**P-005**
24	Potassium dichromate	0.5%	P-014A
25	QUATERNIUM-15	2.0%	C-007B
26	Sesquiterpene lactone mix	0.1%	Mx-18
27	**Textile dye mix**	**6.6%**	**Mx-30**
28	Thiuram mix	1.0%	Mx-01
29	Tixocortol-21-pivalate	0.1%	T-031B

ACD from Propolis

by *Gunnar Nyman, MD*
Gothenburg, Sweden

Propolis, or bee glue, is produced by honey bees together with honey, bees wax, royal jelly and bee bread. Bee pollen can also be collected from bee hives, but are actually not produced by bees, but just collected and stored. Besides those products, the most important function of bees for humans is that they are of greatest importance for pollinating plants, thereby mandatory for much of global agriculture and food production. Bees are indeed fascinating insects!
Propolis is a lipophilic substance manufactured by bees from resinous material from living plants around the hive, mixed with beeswax and ß-glycosidase from the bee's saliva. It is used by the bees for gluing and sealing cracks in the bee-hive. It has antimicrobial effects and is thus used as a protective material, guarding the colony against infections, e.g by covering the walls of the entrance of the hive (from Greek *pro-* in front of, *-polis* town). The bees also use it for embalming killed intruders and dead bees within the hive. In Central Europe, poplar buds (*Populus* spp.) are the most important source of plant material for propolis, but that might differ depending on what plants are growing in the vicinity of the hive. Interestingly, manufacuring of propolis is only known from the Western (European) honeybee (*Apis mellifera* species, several subspecies), while tropical honeybees (several *Apis*-species) and African *Apis mellifera* make no use of propolis.

Propolis has been used since ancient times, described in old Egyptian sources and mentioned by Aristoteles as a cure for bruises and sores. It is nowadays used in "natural" remedies and biocosmetics, and is often an impurity in beeswax. Depending on how well refined or how chemically treated the beeswax is, it contains different amounts of propolis.
Propolis can cause contact allergy, and is rather common as a contact allergen in many European countries, especially in central and eastern Europe. Frequencies of 3-7% positive reactions have been recorded among dermatitis patients. Main haptens in propolis are considered to be caffeic acid and its derivatives, but also isoferulates, flavonoid aglycones and free aromatic acids. Several of these are also known to occur in *Myroxylon pereirae* resin

The author presenting a batch of Propolis hapten

(Balsam of Peru). It has earlier been shown that there is a high number of concomitant reactions between propolis and fragrances or plant substances.
Beeswax and propolis are thus different products though they are sometime referred to as the same thing. As natural products, beeswax and propolis are not chemically defined, but they share common elements. The possible variation of composition is a problem, and if this variation has relevance for patch test reactions is hitherto not investigated.

Since 2019, propolis is part of the European baseline series. This means that it will be tested on a bigger scale, and we will learn more about frequencies of contact allergy, relevance and variations in test results. Positive test reactions can be of importance for patients using different "natural remedies" and cosmetics containing propolis, honey or beeswax, since the latter can be contaminated with propolis. Another group of patients at risk for contact allergy to propolis is musicians playing stringed instruments, as the varnish used for treating the surface of the instruments often contain propolis. From the view of occupational dermatitis, beekeepers are at risk as well as people involved in manufacturing the topical products mentioned above, and also producers of stringed instruments.

Hydroperoxides of Limonene

Derived from articles:
- "Limonene Hydroperoxides by A. de Groot
  in "Dermatitis", Volume 30, Issue 6, pages 331-335, November/December 2019
- "Fragrances – Contact Allergy and other Adverse Effects" by A. de Groot
  in "Dermatitis", Volume 31, Issue 1, pages 13-35, January/February 2020

More than 160 different fragrance chemicals have been reported to cause contact allergy or ACD, though only 36 fragrances have shown positive results in routine testing. The most frequent sensitisers are linalool and limonene hydroperoxides, along with HICC, treemoss and oakmoss absolute, isoeugenol, cinnamyl alcohol and cinnamal.

The linalool and limonene are most frequently present in a wide range of cosmetics and household products, but limonene is also present in industrial degreasing agents, hand-cleansers, solvents, tobacco-substitute products, therapeutic transdermal delivery systems, etc. Limonene is also found naturally in various fruits and oils, including lemon, orange, grapefruits, Eucalyptus trees, other trees, shrubs, crops and grasses. For example, a 2015-6 investigation in Denmark found limonene in 49% of 5,588 fragranced cosmetic products. Note though that the threshold for notification of presence may be set too high and compliance by manufacturers is also not absolute, so the real-life occurrence is most probably considerably higher than half of cosmetic products. Limonene has also been demonstrated in 675 non-cosmetic consumer products in Denmark, and in 78% of 46 domestic and occupational products in Denmark, UK, Germany and Italy.
So, it is true to say limonene is almost ubiquitous in cosmetics and very common indeed in household products. Avoidance will therefore not be easy!

Limonene has three forms, the isomers D-limonene (R)-limonene, (+)-limonene, L-limonene, (-)-limonene, and their mixture DL-limonene (dipentene).

However, it is not so much limonene as a sensitiser but the hydroperoxides of limonene formed when limonene is oxidised by exposure to oxygen in the air.

Patch testing of suspected sensitised patients to limonene gives only a rare positive reaction, whereas testing with limonene hydroperoxides in various concentrations gives a much greater rate of positive reactions in suspected sensitised patients. Seven studies have found a prevalence of between 2.5% and 9.4% amongst test subjects screened for sensitivity, with a median of 5%. Note however that a significant proportion of these positive reactions may be dubious/weak reactions (up to 17% of positives) and irritant reactions (up to 9.8% of positives) have been observed, so a positive reaction may not mean sensitisation *per se*. Note also that up to 8% of positive reactions are late responses, so would be missed if not read at Day 7.

From 2011 to the present, nearly all investigators have used limonene hydroperoxides, because this material had been proven to be more suitable for patch testing than oxidised limonene.

A relevant fact is that it is only recently that limonene and limonene hydroperoxides for patch testing have become reliably commercially available. The chemistry involved in the production of such limonene hydroperoxides for use in patch testing is exceptionally difficult due to the unstable properties of not only limonene but also the oxides and hydroperoxides, which each in turn degrade to other substances, some of which are also potent sensitisers. Clinically, the most important sensitiser is limonene-1-hydroperoxide.

Dose-finding studies in Spain and UK have indicated that the ideal concentration of limonene hydroperoxides for patch testing is 0.3%, but this finding is by no means definitive. Both investigator groups advised to use 0.3% preparation for screening, and the UK authors suggested to add limonene hydroperoxides 0.3% petrolatum to the British Baseline Series.

Recently the ESCD has proposed and recommended to test limonene hydroperoxides in addition to the European Baseline Series, with 0.3% and 0.2%.

It is very important to realise that 70% of sensitisations to limonene were not detected by positive reactions to the indicators of fragrance allergy; *viz*: Fragrance Mix I and II, and *M. pereirae* and Colophonium. Therefore, unless limonene is specifically tested for as a consequence of the clinical history, then the sensitisation could well be missed from the diagnosis.

The authors of a rare study on limonene sensitivity in USA suggested that "patch testing to the hydroperoxides of limonene (and linalool) should be performed in all patients with suspected fragrance allergy".

De Groot concludes his paper on "Limonene Hydroperoxides" with the statement…
"Limonene hydroperoxides seem to be a frequent cause of contact allergy and likely also of allergic contact dermatitis in Europe and probably also in the United States. Testing of limonene hydroperoxides 0.3% and 0.2% in petrolatum (available at http://chemotechnique.se) in all patients suspected of having contact dermatitis or, when preferred, in patients suspected of having fragrance allergy, will reveal a considerable number of sensitisations, a large percentage of which may not be picked up by the fragrance markers in the baseline series….".

Chemotechnique uniquely manufacture and offer three different patch test preparations of Limonene and Limonene hydroperoxides:

•	L-006C	D-Limonene	3%	petrolatum
•	H-032A	Hydroperoxides of Limonene	0.3%	petrolatum
•	H-032B	Hydroperoxides of Limonene	0.2%	petrolatum

Safety Data Sheets and Hapten Information Sheets for each of these haptens are available as downloads from the Chemotechnique website at www.chemotechnique.se

ACD from Cigarette Smoking

by *Anne Herman, et al.*
in **Contact Dermatitis. Volume 81, Issue 6, pp 473-4, December 2019.**

ACD to cigarette smoking is an exceedingly rare event, with only 10 cases reported to date, but it is nonetheless intriguing. Two of those cases were of airborne CD.

In the single case reported by the authors, the patient exhibited ACD on the fingers due to direct contact with cigarettes, as well as facial eruptions including two lines of brownish pigmentation on and above the upper lip, that was most likely due to the airborne tobacco smoke.

The 54-year old man had a 3-year history of itchy erythema and vesicles on his second and third fingers, which gradually worsened despite topical corticosteroid treatment.

The patient had smoked 40 cigarettes a day for 30 years. That is no less than almost 440,000 cigarettes (brand Winston XS Caster One 100's). Obviously, the risk of lung cancer and all the other medical conditions caused by cigarette smoking failed to deter the patient, but the development of faint lines of facial pigmentation, plus the ACD on two fingers tipped the scales and motivated him to quit, cold.

Various patch tests were performed on the patient, using tobacco leaves and components of unsmoked cigarettes and smoked cigarettes, alongside the Japanese Baseline Series and a metal series.

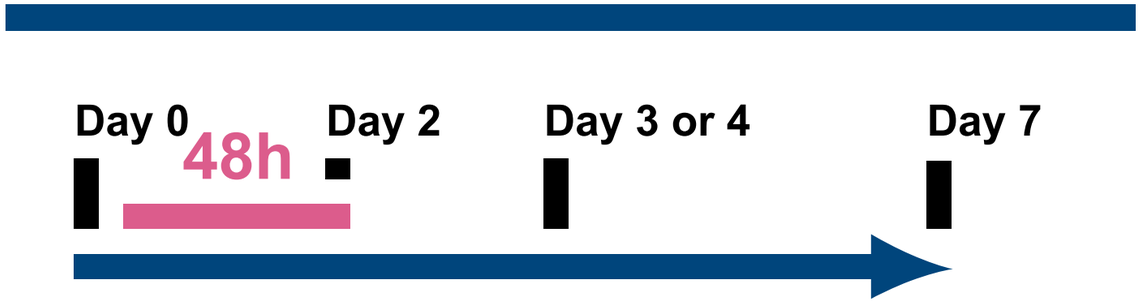
Positive reactions were obtained to unsmoked and smoked tobacco leaves and to the filter of the cigarettes. The patch test reactions to the smoked leaves was much stronger than to the unsmoked leaves. Patch tests to nicotine (in various formulations and concentrations) and to vanilla beans were negative.

After receiving the PT results and the recommendations of the doctor, the patient quit smoking and continued with the local steroid to the affected fingers.

Within a month, the fingers had improved, and the lip eruptions disappeared spontaneously without treatment, suggesting that the latter was indeed airborne contact dermatitis due to cigarette smoke.

The authors consequently recommend that smokers presenting with a refractory itchy eruption on both the fingers and face and especially the upper lip, be considered as candidates for patch testing for tobacco, due to possible allergic contact dermatitis to cigarette tobacco and airborne contact dermatitis due to cigarette smoke.

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.



The final Patch Test Read

by H.M. Cantwell *et al.*
in **Dermatitis, Volume 31, Issue 1, pages 42-52, January/February 2020.**

Guidelines from the ESCD suggest that patch test evaluations be performed on at least 2 days, with a preference for Day 2 (i.e. after 48 hours after application on Day 0) and again on Day 3 (72 hours) or Day 4 (96 hours) and again on Day 7 (168 hours).

The North American Contact Dermatitis society recommends readings at 48 hours (2 days) and at 72 to 168 hours (Day 3 to Day 7).

Those two recommendations leave a fair amount of leeway and individual choice for the individual Dermatologist and individual patient. The major question is when exactly to perform the final reading, classically on Day 4/5 or on Day 7.

The authors of the article are based at the Mayo Clinic in Rochester USA, so speak from experience and with authority.

They retrospectively studied 42,438 individual reactions to 494 allergens in 411 patients over 10 years at the Mayo Clinic.

The Clinic currently routinely tests on Day 3 for their first reading, and then on either Day 5 or Day 7 or both Day 5 and Day 7, depending on the hapten in question.

Some interesting facts and figures emerged from the investigation:

- 142 allergens (72.8%) had different reactions on Day 5 than on Day 7 or later
- Early reactors were 131 allergens (67.2%), which tested positive on Day 5 but were negative on Day 7 or later
- Delayed reactions, i.e. positive on Day 7 but negative on Day 5) occurred with 58 allergens (29.7%).
- These delayed reactors were most usually metals or metal alloys (27 allergens, 46.5%) but also included various acrylates.
- The metal alloys included compounds with nickel, copper, cobalt and mercury.
- However, some metals were early reactors on Day 5 but negative on Day 7.
- Delayed reactions were also occasionally seen with Fragrances, Preservatives, Topical Antibiotics, but not with Corticosteroids or PPD.

The authors recommendations were:

- When patch testing for metals or metal alloys or metal-based substances then readings on both Day 5 and Day 7 are warranted.
- Also, for acrylates, such as are used in dental products, nail cosmetics and in printing products, then reading on both Day 5 and Day 7 is recommended.
- Similarly, for antibiotics such as bacitracin and neomycin, readings on both Day 5 and Day 7 are recommended.
- For testing with Corticosteroids or PPD, then a Day 5 reading is adequate.
- No recommendation is made for other types of haptens; which were not included in this study.
- “Our current findings suggest that readings on both Day 5 and Day 7 or later would have the highest yield for evaluating allergy to metals, acrylates, some preservatives and topical antibiotics”.

There are obviously some fundamental implications that follow from these recommendations.

1. Multiple factors must be considered when designing a patch test schedule, including patient convenience, clinical setting, staff availability, haptens tested, but most importantly must be test efficiency & clinical reliability.

2. When a patient is being tested with any of the following haptens then there should be not only a reading on Day 5 (to cover other haptens) but also an additional (third) reading on Day 7, for metals, acrylates, some preservatives and topical corticosteroids.

3. Practically, if running a PT clinic that operates only Monday to Friday then this greatly restricts the days when the PT procedure can be started.

Day >>	0	1	2	3	4	5	6	7	8	9
Start Monday >>	M	T	W	T	F	S	S	M	T	W
Start Tuesday >>	T	W	T	F	S	S	M	T	W	T
Start Wednesday >>	W	T	F	S	S	M	T	W	T	F
Start Thursday >>	T	F	S	S	M	T	W	T	F	S
Start Friday >>	F	S	S	M	T	W	T	F	S	S
Start Saturday >>	S	S	M	T	W	T	F	S	S	M

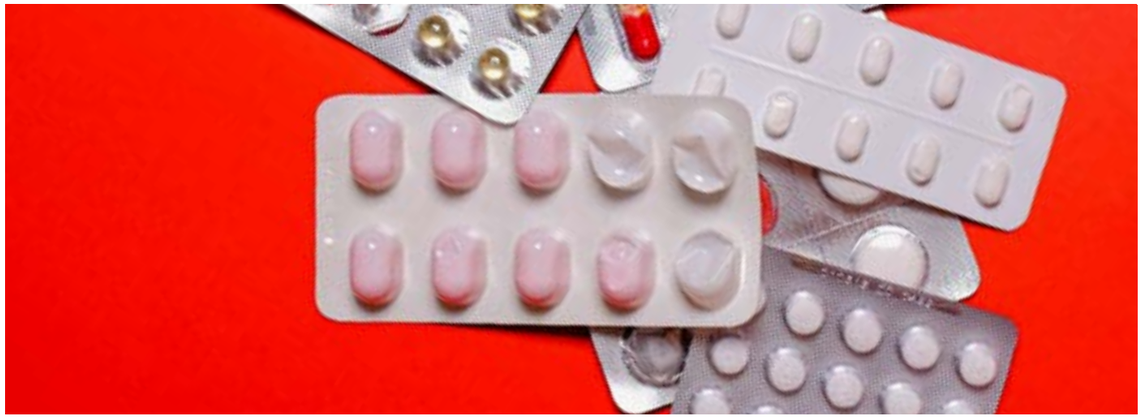
In fact, the table above shows that for patients being tested with metals or acrylates or some preservatives or topical antibiotics then it is only possible to start the PT procedure (apply the haptens) on a Friday, so that the first reading can be made on Monday (Day 3) and the second reading on Wednesday (Day 5) and the third reading on Friday (Day 7).

All other start days (Mondays, Tuesdays, Wednesdays and Thursdays) mean that one or the other readings cannot be made on Day 3 or Day 5 or Day 7.

So then compromises will have to be made, with a consequent reduction in test efficiency and therefore also clinical reliability.

Anybody want to run their PT clinic on a Saturday morning?
Perfect for Patch Testing those late reactors!!

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



Occupational Allergic Contact Dermatitis from Systemic Drugs

by Lisbeth Gilissen*, et al*
in **Contact Dermatitis. Volume 81, issue 6, pp 24-30, January 2020.**

Health-care workers (HCW) and pharmaceutical industry workers are at risk of developing occupational allergic contact dermatitis (OACD) from systemic drugs and drug intermediates encountered on their workplace. Whilst most of such occurrences of OACD are truly contact-derived, some cases are undoubtedly a result of airborne sensitisation, even with contact sensitisation. The lesions most commonly occur at the site of contact (most usually the hands) however airborne reactions from powered drugs, droplets or vapours are not uncommon. Severity may be severe, with generalised systemic reactions, due to inhalation or transcutaneous absorption.

The authors investigated cases for a period of 19 years up to 2019, encompassing 9,780 patients. These subjects were patch tested with at least the European Baseline Series, though sometimes with additional Series and other relevant potential haptens.

Patch test readings were taken on Day 2 and Day 4, and in accordance with ESCD guidelines.

The patch test haptens and patch test chambers that were used by clinicians throughout the 20-year period of this study were from several manufacturers.

Of 1,248 HCW examined in the Leuven clinic, 201 (16.1%) suffered from OACD.
Typically, the HCW most at risk are physicians, nurses, dentists, physiotherapists, pharmacists, pedicurists and veterinarians. Within the pharmaceutical industry, then chemists and other workers involved in the actual manufacturing process are most at risk.The occupations of those diagnosed with OACD were the following:

• Nurses	104/201	52%
• Chemists	53/201	26%
• Dentists	11/201	55%
• Physiotherapists	11/201	55%
• Physicians	17/201	8%
• GPs	4/201	2%
• Veterinarians	1/201	0.5%

Seventy-five percent of patients diagnosed with OACD were female, (151/201), though this most probably represents the proportion of females in these occupations.

Of these 201, for 26 (13%) the dermatitis was caused by skin contact with a systemic drug, 19 nurses and 5 chemists, one physician and one veterinarian. In total, 45 positive patch test reactions to 20 different systemic drugs were found.

The most commonly encountered sensitisers were (respectively) tetrazepam (24.4%), ranitidine hydrochloride (11.1%) and zolpidem (8.9%). However, these figures are dependent on the usage of various drugs by the HCWs and on the chemicals manufactured by the local pharmaceutical industry, that were seen by this tertiary referral centre for Belgium.

As much as 13% of OACD in HCWs was attributable to systemic drugs, and the most affected professional group were nurses.

Other occupation-related sensitisers for HCWs are rubber gloves, metallic objects (especially nickel), cosmetics, antiseptics and disinfectants, and ingredients of topical pharmaceutical products.

A very important observation from the period of the study (2001 – 2019) is that the great majority of cases were diagnosed between 2008 and 2011, after which the prevalence of patients with OACD from drugs decreased, to zero from 2015. It is believed that this reduction in incidence is a consequence of increased knowledge and awareness leading to an increase in prevention measures such as the use of appropriate ventilation systems, and the increased use of Personal Protective Equipment such as masks and gloves.

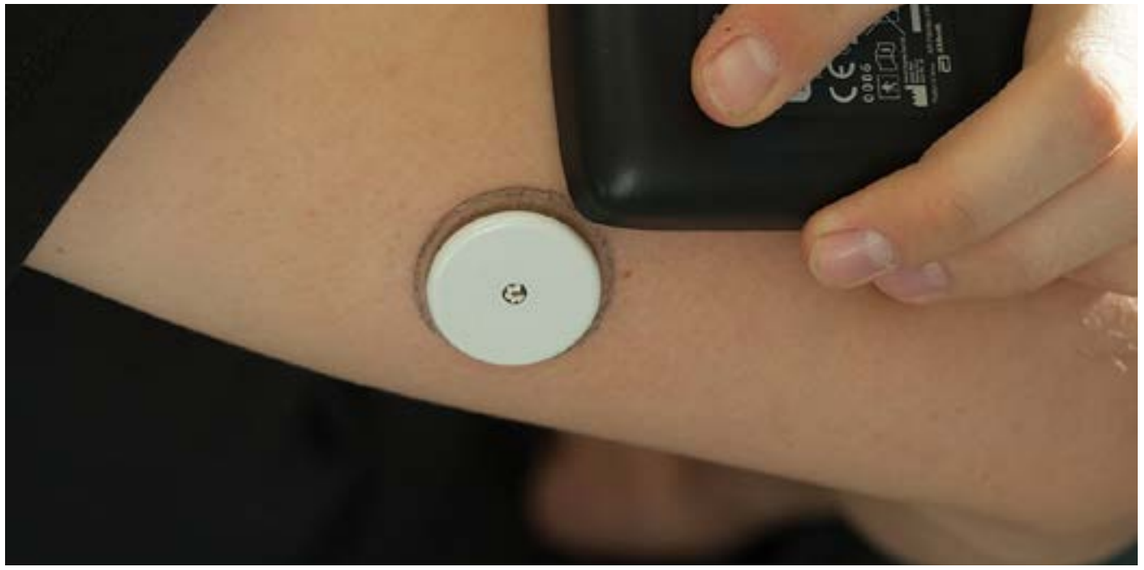
This decreasing trend stresses the importance of close monitoring, preventive and protecting measures during manufacturing, and changes in the administration methods, all in order to avoid skin contact and inhalation of sensitisers.

OACD due to exposure to systemic-acting drugs is certainly overlooked and under-diagnosed, as attention is preferentially given to sensitisation to soaps, antiseptics, disinfectants, and gloves. Therefore, the results of this retrospective analysis probably underestimate the actual incidence of sensitisation.

The authors suggest that Dermatologists, when confronted by HCW or pharmaceutical manufacturing worker with hand and/or airborne dermatitis, firstly exclude reactions to gloves and disinfectants, then should ask proactively for further information on the pharmaceuticals that may be involved from their occupation. If the patient history is unhelpful then it might be useful to test with a Drug Series, such as the one suggested by Chemotechnique Diagnostics. Other medications can be tested separately if they are available commercially as patch test haptens, or with medications supplied by the patient.

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

Note that the Chemotechnique Cutaneous Adverse Drug Reaction Series comprises 32 haptens, with product code CAD-1000, and is stated in detail on the Chemotechnique website at: https://www.chemotechnique.se/products/series/cutaneous-adverse-drug-reaction-series/



IBOA from Insulin Sensors and Sets

by Mami Miyakawa, *et al*

in **Contact Dermatitis, Volume 81, issue 6, pp 105-111, February 2020.**

As reported in the Patch Tester 1st edition from December 2019, the “Freestyle” glucose sensor has caused many cases of ACD, and IBOA has been identified in this sensor as one of the culprits.

The authors investigated the presence of IBOA in other commercial devices used by diabetic patients; namely the “Enlite” sensor and the “Paradigm MiniMed Quick-set”, both manufactured by Medtronics of USA.

The “Freestyle Libre” is manufactured by Abbott.

The glucose sensor “Enlite” is a medical device developed as a continuous glucose monitoring system for diabetes patients. It may be worn, on the skin, for up to 6 days. It consists of a catheter with adhesive film for attachment to the skin, and two transmitter units.

The first transmitter (“Guardian Connect”) is reusable and rechargeable, and is connected to the sensor, and sends data to (most usually) a smartphone device.

The second transmitter unit (“Guardian 2”) connects to the sensor and sends data to an insulin pump (“MiniMed”). This insulin pump is connected to the skin with an infusion set (“Paradigm MiniMed Quick-set, or similar).

Five patients in 3 clinics in Belgium and Sweden who had reacted to one or the other of these devices, were subsequently patch tested for IBOA and baseline series and other series, as well as components of the devices.

Gas chromatography and mass spectrometry analyses were also performed on alcohol or acetone extracts of various components of the devices, including the adhesive patches, the plastic material, and the glues used. Technical details are provided in the original article.

Four of the patients reacted to IBOA, whilst the fifth reacted to Colophonium (or its derivative glyceryl rosinate), but not to IBOA.
Three of them also reacted to the adhesive part of the sensor or infusion set.
The original article details each patient case.

On chemical analysis, in the extract of the two “Enlite” Sensors that were examined (with the adhesive patches removed), IBOA was found in a concentration corresponding to 10 µg per sensor. No IBOA (<1 µg/patch) could be demonstrated in the extract of the two adhesive patches. In the separate extracts of the glue spots and the sensor prepared from a sensor from another batch, IBOA was found in both extracts at a concentration corresponding to an amount of 4 µg in the glue spots and 40 µg in the sensor.

The analysis of the plastic part of the “Paradigm MiniMed Quick-set” infusion set demonstrated the likely presence of small amounts of IBOA (<1 µg). No signs of IBOA were found in the extracts of the adhesive patches, even though these patches did cause sensitivity reaction in three patients, presumably because there was an insufficient concentration to be detected by chemical analysis.

Both the “Enlite” sensor and the “Paradigm” infusion set also appear to contain the photo-initiator hydroxycyclohexyl phenyl ketone, although this was not able to be confirmed by analysis of reference samples of that substance.

In this study, four of the five patients had been previous users of a “Freestyle Libre” sensor before wearing the “Enlite” sensor or insulin infusion set. Therefore, it is likely that the “Freestyle Libre” was the primary sensitiser to IBOA. Not only is the period of use prior to symptom appearance longer with “Freestyle Libre”, but also the concentration of IBOA is greater with the “Freestyle Libre”.

Interestingly, two of three patients with IBOA sensitivity showed a concomitant sensitivity to sesquiterpene lactone mix.

So although this is a small study, and gives no indication of the frequency of sensitisation, the results clearly indicate that the IBOA sensitivity problem exists not only with the “FreeStyle Libre” product but also with at least two other devices used by diabetic patients as potentially suitable alternative devices to the “Freestyle Libre”.

Another interesting point made by the authors was the lack of cooperation from the manufacturer of the “Enlite” and “Paradigm” devices; Medtronics. So perhaps it is time for the regulatory authorities at the highest level (such as EU and FDA) to require the manufacturers of such medical devices to fully disclose the chemical composition of their devices as an integral part of the registration process. That should encourage such manufacturers to find the best possible alternatives to known sensitising agents such as IBOA.

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

Note that IBOA is available as a commercially supplied patch test hapten from Chemotechnique, as product code I-109, which is presented at 0.1% concentration in petrolatum.

Patch Test reactivity to Aluminium Chambers

Letter to the editor, by Annica Inerot, et al.
in **Contact Dermatitis", Volume 82, Issue 2, p135, February 2020.**

Our Allergist/Immunologist colleagues will be well aware of the questions around the inclusion of aluminium hydroxide in the composition of the European-style allergen injection immunotherapy treatment sets used to desensitise allergic patients against various inhalant allergens. The purpose of the aluminium hydroxide is to form the physical matrix onto which the allergenic proteins of the vaccine are adsorbed, so that there is a slow release of those proteins over time for presentation to the patient's immune system. This is known as a depot injection treatment, as opposed to the bolus-type injection when the allergenic proteins are not coupled to such a matrix but are in simple aqueous or glycerinated solution. This is the USA-style of sub-cutaneous injection immunotherapy.

Without such a depot-effect there is a consequent greater risk of over-reaction to the injected allergenic proteins, resulting in local or even systemic adverse effects of oedema or urticaria or even anaphylaxis.

Other agents besides aluminium hydroxide can be and are used, such as calcium phosphate, but the great majority of such European-style commercial vaccines utilise aluminium hydroxide.
This may result in the creation of nodules (granulomas) at the injection site, and as 36 to 50 injections are required for the 3-year treatment course, and there are only two arms for injection, then this issue becomes important for the Allergist and their patient.

Not only allergen immunotherapy injections but also other injectable vaccines utilise aluminium hydroxide for this depot purpose. During the 1990's a mass vaccination program in Sweden on a new acellular pertussis vaccine was studied for its effect on causing itching nodules at the injection site. 645 of 76,000 vaccinated children (0.85%) developed these itching nodules. Not a high rate, and not a great clinical consequence, but nevertheless this report was apparently the first researched and documented report on the prevalence of possible aluminium sensitivity.

These 645 children were then offered a patch test to aluminium.
Of these, 352 of the 455 (77%) tested children gave a positive PT response to aluminium.

In addition, 211 asymptomatic siblings (who had also received the vaccine) were also patch tested for aluminium sensitivity, and of these 8% were aluminium sensitive, though asymptomatic.

This phenomenon of aluminium sensitivity is of course of particular interest to Dermatologists due to the ongoing use since decades of aluminium discs in some patch testing systems, when, paradoxically, the patient may be sensitive to the aluminium itself.

This raises the intriguing question of whether the Dermatologist should incorporate in their Patch Test procedure that uses aluminium discs a Negative Control of an "empty" aluminium disc for each patient.

This concept has a directly comparable situation in allergy Skin Prick testing, when the Allergist will always, as standard practice, include a Negative Control of saline/glycerol solution when performing a Skin Prick Test. This should indicate any sensitivity to the "naked" test solution, without allergen. If the Negative Control is positive, then that would likely invalidate the test session or at least require

an assesment of the difference between the negative control and the test result.

There is also a similar situation with most of the laboratory-based *in vitro* diagnostic tests used to identify allergen specific IgE (s-IgE). Some but not all s-IgE assay systems utilise a cellulose solid-phase matrix, which unfortunately can lead to the production of s-IgE against the clinically irrelevant cross-reacting carbohydrate determinants (CCDs). So a positive s-IgE result can be due to not only allergen specific IgE but also to the presence of these CCDs. This can lead to an artificially high test-result for various allergens, and so possible false positive results. Only by excluding any CCDs such as cellulose from the assay process can a clean signal be obtained, untainted by any possible sensitivity to clinically irrelevant carbohydrate components.

The Danish author of this letter to the editor on aluminium sensitivity has now included aluminium in the Danish Baseline Series for patch testing of children.

It would be very interesting to investigate the prevalence of aluminium sensitivity in the general population, as well as in patients having undergone sub-cutaneous injection allergen immunotherapy.

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

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

Swedish Society for Dermatology and Venerology

www.ssdv.se - website in Swedish, but use Google Chrome to translate

The SSDV is a member of the ILDS and of NDA; and has within its own highly organised structure no less than thirteen different sections and interest groups, one of which is SKDG, the Swedish Contact Dermatitis Group. The work within the group covers contact dermatitis and other occupational and environmental skin diseases. This is done through research and development work, and the group submits comments on proposals from authorities and other organizations to its members.
SKDG is the Swedish equivalent of the European Environmental and Contact Dermatitis Research Group (EECDRG). The group was formed in 1996 and is managed by the chairman and secretary. The group is multi-disciplinary, as it has solid expertise in clinical work, allergology, epidemiology, chemistry and immunology. SKDG updates and provides on its website a list of all Swedish theses and review statements in the areas of contact dermatitis and contact allergy.
As the Nordic countries are often forerunners in the field of CD and regulation, then this would be a good source of information for all Patch Testers.

Nordic Dermatology Association

www.nordicdermatology.com

The NDA comprises five national dermatology associations, one for each of Sweden, Norway, Denmark, Finland and Iceland, with its main office in Uppsala Sweden. Founded in 1910, and with their own official journal Forum for Nordic Dermato-Venerology, (in English language), with reports on the latest dissertations and information on recent publications from Nordic Dermatologists. The NDA also organises a Nordic congress every 3 years, besides the congresses of the individual national societies and their own regional congresses and workshops. The online Forum includes sections on training, news, information on vacancies, and perhaps rather unusually, information from companies on their products and services for Dermatologists.

Contact Dermatitis / Patch Testing

~~**19th March 2020**~~
~~**ACDS 31st Annual Meeting**~~
~~Denver, Colorado, USA~~
~~*www.contactderm.org/meetings/acds-annual-meeting*~~
Cancelled

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

Dermatology - International

16th - 18th March 2020
Dubai Derma
Dubai. UAE
www.dubaiderma.com

~~**20th - 24th March 2020**~~
~~**American Academy of Dermatology**~~
~~Denver, Colorado, USA~~
~~*www.aad.org/member/meetings/am2020*~~
Cancelled

13th - 14th April 2020
15th International Conference on Dermatology and Cosmetic Medicine
London, UK.
www.dermatologymeeting.com

22nd - 25th April 2020
7th Continental Congress of Dermatology
Mexico City, Mexico
www.academiaderma.mx

29th - 30th April 2020
20th International European Dermatology Congress
Prague, Czech Republic
www.dermatology.conferenceseries.com/europe/

April 30th - 2nd May 2020
16th EADV Spring Symposium
Porto, Portugal
www.eadvporto2020.org

20th - 21st May 2020
2nd Edition of International Conference on Dermatology and Cosmetology
Tokyo, Japan
www.dermatology-conferences.com

6th – 9th June 2020
EAACI European Academy of Allergy & Clinical Immunology.
London, United Kingdom
www.eaaci.org/eaaci-congresses/eaaci-2020

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

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

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

Dermatology - National

16th to 19th May 2020
Australasian College of Dermatologists ASM
Adelaide, Australia
www.acdasm.com

27th to 29th May 2020
SSVD Spring Meeting 2020
Västerås, Sweden
www.ssdv.se

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