the Patch Tester

Contact Dermatitis | Haptens | Patch Testing

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THE ALLERGIST ISSUE

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

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CONTENTS

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 eighteenth issue comprises forty 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:
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3 What’s New in Patch Testing

5 Hot Topic
Why allergists should Patch Test

14 Hapten of the Year
Sulphites

18 Literature Review
p.18 Results of Patch Testing to Botanicals: Review of the Mayo Clinic Experience over 2 Decades (1997-2017)

p.22 Piloting Photographic Photonic Patch Testing: Pioneering Equitable Diagnosis of Contact Dermatitis

p.24 Patterns of simultaneous contact allergies in patients with contact sensitisation to oxidised Linalool and oxidised Limonene

p.28 The Contribution of Metal Allergy to the Failure of Metal Alloy Implants, with special reference to Titanium: Current knowledge and controversies

p. 32 Contact Allergy in African Countries: A review of published Patch Test Studies

p.34 Frequency and Relevance of Contact Allergy in Dental Patients

37 Website Review
European Academy of Allergy and Clinical Immunology (EAACI)

40 Congresses & Exhibitions
Upcoming events for Dermatology & Allergy Professionals

The possible risks of over-regulating haptens in European Union

The Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) plays a vital role in proposing regulations aimed at harmonising standards within the European Union (EU). While regulatory harmonisation is generally beneficial, there are concerns regarding its potential negative impact on the availability of patch test haptens in the EU. Today haptens are typically made available throughout the EU as unlicensed medicines in accordance with national interpretations of the Article 5 of the Directive 2001/83/EC. With the harmonised regulations as proposed by the CMDh, once implemented nationally, that availability of patch test haptens may be greatly adversely affected.

Within the EU there is currently one member state (Germany) where national regulations are similar to those proposed by the CMDh, and as a consequence of the implementation of their regulations, the accessibility of haptens in Germany has become significantly reduced so that now only approximately 110-120 haptens are currently available out of a possible total of over 500 that are commercially available elsewhere. This has of course had the effect of severely limiting the possibility of providing patients with a correct diagnosis.

4 What's New in Patch Testing?

CMDh's proposed patch test hapten regulation for the entire EU introduces heightened regulatory requirements, which results in prolonged timelines and increased costs for the manufacturer, or their local distributor, caused by obtaining regulatory clearance. Furthermore, compliance with CMDh's regulatory standards will pose significant challenges, as meeting the rigorous regulatory requirements will be financially prohibitive especially for the introduction of emerging new haptens, which will therefore limit if not totally prevent the development of new patch test haptens such as for emerging haptens.

Compliance by manufacturers such as ourselves with CMDh's new allergen regulations may necessitate changes to manufacturing processes, sourcing of raw materials, and supply chain logistics for hapten products, as well as increased administration and increased costs. These would in turn lead to price increases as well as disrupt existing supply chains, resulting in delays or shortages in product availability. Ultimately our concern is that healthcare providers reliant on uninterrupted access to a broad range of haptens may face restrictions in maintaining excellence and continuity of care for patients with contact allergies.

While regulatory harmonisation efforts by CMDh aim to enhance safety and standardisation across the EU, there are concerns regarding the potential negative repercussions on the availability of haptens for contact allergy diagnosis. Addressing these concerns necessitates striking a balance between regulatory stringency and ensuring continued access to essential diagnostic tools.

Collaborative efforts involving regulatory authorities, manufacturers such as ourselves at Chemotechnique, and national and international contact dermatitis societies are essential to mitigate the adverse effects of increased regulation, and thereby uphold the integrity of contact allergy diagnosis within the EU, so that the unfortunate situation that has developed in Germany does not occur throughout the EU countries.

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.

Why Allergists should Patch Test

On 31st May to 3rd June 2024 is the European Academy of Allergy and Clinical Immunology (EAACI) 2024 annual congress, to be held in Valencia Spain. Chemotechnique will be present in the trade exhibition in order to bring to the Allergy Specialists of Europe, and many other corners of the world, knowledge, information, expertise, experience, and the essential products of patch testing to identify contact allergens.

Allergy is one of those clinical specialities that crosses over into the traditional territory of several other specialities, besides Immunology, also Paediatrics, Respiratory Medicine, Oto-Rhino-Laryngology, Gastro-Enterology, and of course Dermatology.

In fact, the interaction between Allergy and Dermatology is so great that in some countries such as Germany, Austria and Switzerland, Dermatology is a combined speciality with Allergy.

EAACI themselves have a Dermatology Interest Group, which holds bi-annual congresses in close cooperation with the European Society for Contact Dermatitis (ESCD). Their most recent joint event was the Skin Allergy Meeting (SAM) of March 2021 held online due to the COVID pandemic. We are overdue the next such SAM event.

Another example of the great degree of overlap between Allergy and Dermatology is the very recent joint position statement by several allergy and dermatology organisations entitled "The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of Urticaria".

This update and revision of the international guideline for urticaria is a joint initiative of several organisations:

- The Dermatology Section of the European Academy of Allergology and Clinical Immunology (EAACI)
- The Global Allergy and Asthma European Network (GA²LEN) and its Urticaria and Angioedema Centers of Reference and Excellence (UCAREs and ACAREs)
- The European Dermatology Forum (EDF; EuroGuiDerm)
- The Asia Pacific Association of Allergy, Asthma and Clinical Immunology;

with the participation of 64 delegates of 50 national and international societies and from 31 countries. This guideline was acknowledged and accepted by the European Union of Medical Specialists (UEMS).

As a contribution to Chemotechnique's participation at the 2024 EAACI Congress in this 18th issue of the Patch Tester e-mag published online shortly before the congress, we will raise the question of

"Why Allergy Specialists should do Patch Tests?"

In a single sentence...
Allergists should be able to offer and utilise patch test because patch tests enable the identification of primarily chemical substances that cause Allergic Contact Dermatitis, which is a very significant proportion of the symptoms of allergy amongst patients managed by Allergy Specialists.

Type I or Type IV; Allergy or Dermatology – is it really that simple??
In 1963 the British immunologists Gell and Coombs proposed a classification of allergic reactions. The Gell and Coombs's classification, as it is still known, became the absolute reference for defining the pathogenesis of allergic reactions, including drug reactions.
Essentially, their classification defined the four types of allergy:

Type I: Immediate IgE-mediated reactions; classically caused by foreign biological materials such as pollens (trees, grasses and weeds), house dust mites (HDM), mould spores, cockroaches, animal dander, saliva and urine (e.g. cats, dogs, hamsters, guinea pigs), insect venoms (e.g. bees, wasps, ants), foods (e.g. peanuts, tree nuts, milk, eggs, fish, shellfish, soy, wheat, fruits, vegetables), latex (e.g. gloves, balloons and condoms) and drugs (e.g. penicillin and other beta-lactam antibiotics, serums and vaccines causing primarily respiratory and GI and dermal conditions such as Rhinitis, Asthma, and Eczema, etc).
Traditionally the realm of the Allergy Specialist and their use of mainly Skin prick Tests (SPT) and s-IgE tests to identify the problem biological allergens that cause the IgE-response and the subsequent symptoms.

Type II: Antibody-mediated cellular cytotoxicity reactions; these are typically drug-induced reactions considered a cause of allergic cytopenia, but are also involved in several auto-immune diseases,

such as such as immune thrombocytopenia, autoimmune haemolytic anaemia (AIHA), autoimmune neutropenia, Biermer's disease, Goodpasture syndrome, haemolytic disease of the foetus and the new-born (erythroblastosis fetalis), myasthenia gravis, pemphigus and transfusion reactions involving mismatched blood types.

Type III: Immune complex-mediated reactions; these include the acute phase of hypersensitivity pneumonitis (extrinsic allergic alveolitis), drug-induced vasculitis, serum sickness and Arthus reaction. They are also associated with several autoimmune diseases, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and post-streptococcal glomerulonephritis.

Type IV: Cell-mediated reactions; classically caused by low-molecular weight chemicals acting as haptens, penetrating the dermis, binding with dermal proteins, to form allergens, and causing Allergic Contact Dermatitis. This is classically the area of expertise and the domain of the Dermatologist, and their use of patch tests to identify the problem chemical substances that trigger the Type IV reaction.

Although our knowledge and understanding of the immune system has dramatically exploded in the past 60 years since then, the classification remains essentially unchanged. In that long-ago era when the classification was proposed, many critical aspects, such as the pivotal role of T-lymphocytes in immune responses, MHC restriction or the cytokines to give only a few examples, were not recognised or even suspected.

Despite the widening gap between our currently expanding knowledge on the immune system and the simplified and mechanistic classification established by Gell and Coombs, this classification is still in use, though it is obvious that many hypersensitivity reactions cannot be explained in this context.

The question must therefore be asked, is whether it is still valid or should be updated and expanded to encompass all the established facts and current knowledge of the science and clinical practice of allergy.

For those practitioners who still follow the Gell & Coombs classification, the Type IV cell-mediated reaction that can occur in response to contact with certain haptens/allergens results in the clinical condition of Allergic Contact Dermatitis. For a review of the evaluation and management of Type IV hypersensitivity reactions, highlighting the role of the inter-professional team in improving care for patients with ACD see the very recent article entitled "Type IV Hypersensitivity Reaction".

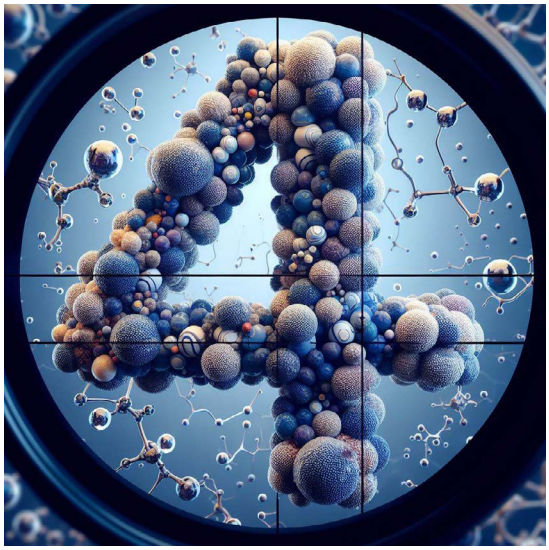
As a very large step in the recognition of the complexity of allergic hypersensitivity reactions and the ever-increasing extent of knowledge, EAACI has very recently published a position paper entitled "Nomenclature of allergic diseases and hypersensitivity reactions: Adapted to modern needs: An EAACI position paper" . This has been written by 40 leading Allergy Specialists from around the world. In this article, the four hypersensitivity reactions originally described by Gell and Coombs have been extended into nine different types comprising antibody (I-III), cell-mediated (IVa-c), tissue-driven mechanisms (V-VI) and direct response to chemicals (VII).

- Types I-III are linked to classical and newly described clinical conditions.
- Type IVa-c are specified and detailed according to the current understanding of T1, T2 and T3

responses.

• Types V-VI involve epithelial barrier defects and metabolic-induced immune dysregulation

• Type VII are direct cellular and inflammatory responses to chemicals.



It is notable that several combinations of mixed types may appear in the clinical setting.

EAACI will shortly publish a follow-up statement on the clinical relevance of the current approach for allergy practice, aiming at showing the relevance in clinical practice where various endotypes can overlap and evolve over the lifetime.

Allergen or Hapten?
Then we come to the thorny question of allergen or hapten. At Chemotechnique we are very firm believers in the concept that Contact Allergy is the result of specific immune responses caused by haptens. Unlike allergens (such as pollens and animal proteins) causing other forms of allergy (Gell & Coombs Type I, IgE-mediated), the culprits of Contact Allergies, haptens, are not antigens by themselves. Haptens are typically small, chemically reactive molecules with low molecular weight, which need to penetrate the horny layer of the skin in order to conjugate with epidermal and dermal proteins, thereby forming “hapten-carrier complexes” with antigenic properties capable of causing contact allergy.

This topic has been covered in greater depth on a previous issue of **The Patch Tester; issue #15 of June 2023**.

Classically, an allergen is a biologically derived substance most usually comprising of or including proteins. These allergens elicit an immune response by activating specific immune cells, such as T lymphocytes, B lymphocytes and mast cells, leading to the production of allergen-specific antibodies (primarily s-IgE) and the release of inflammatory mediators such as histamine, tryptase and others, in the so-called Allergic Cascade.

ACD or AD?
Allergic Contact Dermatitis (ACD) and Atopic Dermatitis (AD) have very similar clinical presentations and may even overlap concurrently in the same patient. Patients with either condition may appear before either a Dermatology Specialist or an Allergy Specialist, but neither type of Specialist can afford to ignore or underplay the significance of signs and symptoms that do not fall entirely within their theoretical domain.

Allergic Contact Dermatitis (ACD) is a Type IV delayed cutaneous hypersensitivity or cell-mediated immune reaction to small-molecular-weight chemicals, which act as haptens. To date, more than 3,000 chemicals have been described to cause Allergic Contact Dermatitis in humans. ACD begins with a sensitisation phase, in which these small molecules pass through the stratum corneum and

are processed by Langerhans cells in the epidermis. Antigen-coupled Langerhans cells then leave the epidermis and migrate to the regional lymph nodes via the afferent lymphatics and present this antigen to naïve CD4+ T cells. These T cells proliferate into memory and effector T cells, which are capable of inducing ACD after repeat exposure to the allergen. This elicitation phase has a latency period that corresponds to the travel time for Langerhans cells to present the allergen to T cells plus the time for these T cells to proliferate, secrete cytokines, and home with other inflammatory cells to the site of contact. A contact allergic reaction normally appears 12 to 72 hours after exposure in a previously sensitised individual.

Allergic Contact Dermatitis (ACD) has a wide spectrum of presentations that often imitate or overlap with other cutaneous eruptions. Differential diagnoses to consider include infections, skin lymphoma-malignancies, inflammatory dermatoses, nutritional deficiencies, and mechanical causes of tissue damage. There are strong clues to the diagnosis of ACD, such as pruritus, localisation to the area of skin contact with the hapten, recurrence with repeat exposures, and supportive skin biopsy histology.

Allergen avoidance, which might include dietary restriction, is the definitive treatment for ACD. This presupposes of course a reliable identification of the problem haptens/allergens. Epicutaneous patch testing remains the gold standard for diagnosing ACD and the identification of the problem haptens.

The estimated prevalence of ACD in children within the general population is 16.5%. However, less than 10% of patch testing (the current gold standard for diagnosis of ACD) is performed on children. ACD is under-diagnosed, due in part to the comparatively low incidence of patch testing to identify ACD and the causative haptens, particularly in children.

Atopic Dermatitis (AD), also known as atopic eczema, is a long-term type of inflammation of the skin (dermatitis). It results in itchy, red, swollen, and cracked skin. Clear fluid may come from the affected areas, which can thicken over time. AD may also simply be called eczema, a term that generally refers to a larger group of skin conditions.

Atopic dermatitis affects about 20% of people at some point in their lives. It is more common in younger children. Females are slightly more affected than males. Many people outgrow the condition. While the condition may occur at any age, it typically starts in childhood, with changing severity over the years. In children under one year of age, the face and limbs and much of the body may be affected. As children get older, the areas on the insides of the knees and folds of the elbows and around the neck are most commonly affected. In adults, the hands and feet are commonly affected. Scratching the affected areas worsens the eczema and increases the risk of skin infections.
Many people with AD also develop hay fever or asthma.

The cause is unknown but believed to involve genetics, immune system dysfunction, environmental exposures (such as to allergens), and difficulties with the permeability of the skin. Exposure to certain chemicals or frequent hand washing makes symptoms worse. While emotional stress may make the symptoms worse, it is not a cause. A diagnosis is typically based on the signs, symptoms, and family history, but may be supported by the avoidance of causative factors (such as allergens) once they have been reliably identified.

Treatment involves if practically possible avoiding factors that worsen the AD, enhancing the skin barrier through skin care, and treating the underlying skin inflammation. Moisturising creams are

used to make the skin less dry and prevent AD flare-ups. Anti-inflammatory corticosteroid creams are used to control flares-ups. Creams based on calcineurin inhibitors (tacrolimus or pimecrolimus) may also be used to control flares if other measures are not effective. Certain antihistamine pills might help with itchiness. Factors that commonly exacerbate AD include house dust mite, stress and seasonal factors. Phototherapy may be useful in some people. More severe AD cases may need systemic medicines such as cyclosporin, methotrexate, dupilumab or baricitinib. Dietary exclusion does not benefit most people unless food allergies are contributing to the AD. In some cases, AD is caused by sensitisation to foods such as milk, though there is growing consensus that food allergy most likely arises as a result of skin barrier dysfunction resulting from AD, rather than food allergy causing the skin problems. AD sometimes appears associated with coeliac disease and non-coeliac gluten sensitivity. Because a gluten-free diet improves symptoms in these cases, gluten seems to be the cause of AD in these cases. A diet high in fruits seems to have a protective effect against AD, whereas the opposite seems true for highly processed foods.
Exposure to allergens, either from food or the environment, can exacerbate existing AD. Exposure to House Dust Mites, for example, is believed to contribute to the risk of developing AD.

It is very evident from the description of Atopic Dermatitis that the role and importance of allergens is interwoven throughout the causes, signs and symptoms of AD, and so to ignore these allergens in the diagnostic work up and subsequent management of the patient with Atopic Dermatitis would be a serious omission by the Specialist practitioner.

Types of Patch Testing
There are several different types of patch testing, for the Dermatologist and the Allergist.

- **Patients own materials**
  This may be an occupational sensitisation to chemicals or other substances encountered in the work environment, such as Bakers or Dentists, with substances such as perfumed cleansers to complex chemicals; or this may be sensitisation to household or personal-care substances such as glues or cosmetics or hairdressing chemicals. The patch test would be required to identify the patient's own materials, including the use of standardised patch test chambers and reaction evaluation protocols.

- **TRUE Test®**
  Traditionally the first step by an Allergist into the realm of patch testing would be the use of TRUE Test as a comparatively simple ready-to-use screening test. However, there are some significant limitations such as a very limited range of haptens/allergens which includes several haptens that are no longer clinically relevant, and does not include many new clinically-relevant haptens. It is also expensive in material costs per patient. Nevertheless, in some countries a significant proportion of users of TRUE Test are Allergy Specialists, whilst Dermatologists prefer to provide a more comprehensive testing panel and a more definitive hapten identification service. Some Allergy Specialists progress on from TRUE Test, using it as a stepping stone into offering a more comprehensive patch testing capability and an improved clinical service.

- **Open choice Patch Test System**
  This comprises a panel of haptens (in petrolatum in syringes or as a liquid in vials) plus the patch test chambers.

National or International Standard/Baseline Screening Series, e.g., European Baseline Series, etc. Typically, a national or international baseline/standard series will be used to screen for relevant problem haptens in that national environment. The national series will have been developed by the local experts, with experience over many years of the clinically important haptens. The scope of the various national and international series varies from approximately 30 haptens (e.g., Swedish National Series) to 90 haptens (American Core Series).
Such a National/International Screening Series may be used together with a Specialist Series that will focus on the suspected type of hapten, such as Fragrances. Once the most suitable screening series has been selected and the capital purchase of haptens and chambers has been made, then the cost of materials per patient is a fraction of that of TRUE Test. The volume of testing (number of patients per month) as well as shelf life of the products are two crucial interconnected considerations with both TRUE Test and the open choice patch test system.

Specialist Series, e.g., Cosmetics Series, Hairdressing Series, etc. Chemotechnique offer 26 different Specialist Series, varying from several to dozens of different individual haptens.

• **Atopy Patch Test**
Atopy Patch Tests are used to identify Type IV hypersensitivity reactions to biological substances such as milk, wheat, egg, some other foods, and House Dust Mite. These protein-based foods (and HDM) are classically Type I allergens that invoke an immediate IgE-mediated allergic reaction in sensitised persons, yet they can also seemingly invoke a delayed hypersensitive Type IV reaction on occasion to susceptible patients, perhaps even simultaneously to a Type I reaction. Such Atopy Patch Tests have been very controversial and with widely varying clinical results and inconclusive validation. Part of the problem in the reproducibility and subsequent validation of Atopy Patch Tests has been the utter lack of standardisation of the allergen, the volume, the time, and the assessment. However, the commercial availability of standardised dedicated APT patches on adhesive tape has at least potentially taken that one variable out of the equation in the quest to validate the APT and find a role for it in the diagnostic work-up of a suspected allergic patient.

State Health Allergy Specialist, or Private Practitioner
For an Allergy Specialist in a State-run hospital the situations and considerations are very different indeed from the situation for a private practice Allergy Specialist. In a State-funded health service, the hospital will almost certainly have a Dermatology Department or Clinic, though this is not necessarily so for an Allergy Department or Clinic. Assuming both specialities are present in a State-funded hospital then it is all too easy for an Allergist on managing a patient with dermatological symptoms or a suspicion of a chemical sensitisation, to refer the patient to the Dermatology Department and Specialist for their investigation. However, that means yet another appointment, yet another waiting period, and another consultation for a busy Dermatology Specialist, and a requirement for inter-departmental cooperation. Nevertheless, it would be a rare event for a hospital to offer separate patch test services in both the Dermatology Clinic and the Allergy Clinic.

In private practice, where there is at least a degree of competition between Specialist practitioners, an Allergist would be loath to refer away to a separate and independent Dermatologist a patient presenting with dermatological symptoms or a suspicion of a sensitisation to a chemical, when that chemical can be identified by patch tests that can be run by the Allergist. In these circumstances, the Allergist may choose to offer the very limited test panel of TRUE Test or may choose to offer a more comprehensive diagnostic capability with an open-choice patch test system such as

Chemotechnique.

Some Allergy Specialists would take pride in being able to offer such a comprehensive service that covers not only the identification of the biological allergens (pollens, moulds, mites, foods, etc) by Skin Prick Test and various types of s-IgE tests (including the new ALEX test that identifies 300 allergens in one blood test) but also identify the various chemical haptens by the use of patch tests.

The role and the effect of Reimbursement for Patch Testing

In private practice the existence of reimbursement for patch testing is a critical factor in encouraging or discouraging the use of patch tests, by any Specialist. In some countries (such as Singapore) there is simply no reimbursement, not even by comprehensive private medical aids/funds/insurance policies. In such cases the patient will have to pay whatever the Specialists states as the price. This is sometimes a significant mark-up on the cost of the test to the Specialist, thereby earning the Specialist an extra income from the use of the patch test.

In other countries, (such as Australia) patch testing may be reimbursed, sometimes at different levels depending on the number of patch tests performed. There may also be a reimbursement for the clinician's fees for the 3 visits necessary for a patch test procedure. The Specialist may then charge the patient at the rate of reimbursement for the patch test product cost, or may add a significant margin onto the rate of reimbursement, thereby increasing their income from the use of the patch test.

In some countries, and the USA is a notable example, the high reimbursement of patch tests is such a strong financial incentive for the Specialist that it has significantly distorted the clinical practice, and even affected the price of the patch test from the supplier to the Specialist. This phenomenon is not just seen with patch testing but also for other clinical areas such as Type I allergy tests (SPT and s-IgE) and allergen immunotherapy vaccine treatments.

Summary

In summary, therefore, due to the interweaving of the clinical signs and symptoms of (Type I) Atopic Dermatitis and (Type IV) Allergic Contact Dermatitis, there really should be no artificial barrier due to the specialisation of the managing clinician. Ideally, both Allergists and Dermatologists should be educated, trained and competent to manage both conditions in any patients presenting to them, and one of the first major steps towards that ideal goal is the availability and utilisation of patch tests by Allergy Specialists.

Sulphites

Based on the article….

Sulphites: Allergen of the Year 2024

by Samuel F. Ekstein & Erin M. Warshaw
in DERMATITIS, Jan-Feb 2024, Volume 35, #1, Issue 6, pp 6-12.
https://doi.org/10.1089/derm.2023.0154

Sulphites, or sulfites, has been chosen by ACDS not because it is a really important contact allergen/hapten, but because it might well be important but there is currently insufficient attention, knowledge and testing for it, coupled with a suspicion derived from the few previous investigations, that it is under-reported and under-recognised.

Although this original paper has been written by the ACDS in American English ("sulfite"), the spelling has been converted to International English ("sulphite") in this review article and all other articles in The Patch Tester.

There are numerous points of interest from the paper, which are listed below, plus some editorial data, information and comments (in italics).

• Sodium disulphite, also known sodium metabisulphite or sodium pyrosulphite, belongs to a group of ''sulfiting agents,'' compounds that contain the sulphite ion $SO_3$2-. Importantly, sulphites are completely different from sulphates; these 2 chemical categories do not cross-react.

• Sulphites occur naturally in water, minerals, soil, rocks, plants, and many foods, especially those involving fermentation. Sulphites are commonly added to commercial formulations as preservatives and/or antioxidants. Sulphites are utilised in multiple industries including food, beverages, drug, cosmetic, and occupational settings. They can also be found in personal skin care products and medications, especially topical antifungals, topical steroids, local anaesthetics, and prescription eye drops. Common ingestible sources include wine and dried fruits.

• The recommended patch test vehicle for sulphites is petrolatum, because in aqueous solution, sulphites dissociate into a complex chemical equilibrium, which may lead to false positive or irritant reactions. A 1% solution in petrolatum has been shown to be the optimal concentration for patch test usage. Commercial patch test preparations are available from Chemotechnique Diagnostics (sodium metabisulphite 1% pet) and AllergEAZE (sodium disulphite 1% pet).

• There are numerous other related chemicals that are similar to sodium sulphites, and which may cross-react, potentially leading to co-sensitisation.

- Ammonium bisulphite
- Ammonium sulphite
- MEA sulphite
- Potassium metabisulphite
- Potassium sulphite
- Sodium bisulphite
- Sodium hydrosulphite
- Sodium metabisulphite
- Sodium sulphite

- The prevalence of sensitisation to sulphites has been documented in several previous studies:

A review of 9 European studies averaged 3.1% with a range of 1.4% to 7.0% (n = 37,909)

- Spain 1.9% (n = 1,850)
- Canada 1.9% (n = 2,323)
- Central Europe 3.8% (n= 6,819)
- NACDG 2.7% and 3.3% (n = 4,885 and 4,115)
- Portugal 10.8% of patients with suspected ACD to topical ophthalmic medications.

• The clinical presentation correlates with the sites of exposure, whether lips, or face or hands. A recent study by NACDG found that 28.8% of patch test positive sulphite patients presented with facial dermatitis. The second most common anatomical site of dermatitis in this cohort was hands (20.5%) followed by scattered/generalised distribution (13.6%). These anatomic locations are to be expected, given that frequent sources of sulphites include personal care items, food/ beverages, and occupational materials. Cases of systemic contact dermatitis to sulphites have also been documented as a result of oral, rectal, and parenteral exposure.

• Besides ACD, exposure to sulphites may cause Type I hypersensitivity reactions (anaphylaxis, urticaria, gastrointestinal symptoms, and bronchoconstriction), and non-immunologic adverse reactions. Hundreds of sulphite-related non-dermatological adverse reactions in the United States have been documented, including nausea, abdominal pain, diarrhoea, urticaria, angioedema, asthma, anaphylactic shock, seizures, and even death.
These severe reactions to sulphites prompted the US Food and Drug Administration (FDA) to ban sulphite use on fruits and vegetables served raw or presented as fresh to the public, and implement regulations regarding declaring sulphites on labels. However, these regulations do not apply to food service establishments such as cafes and restaurants, nor to situations where foods are available for immediate consumption such as bakeries, delicatessens, and confectionery shops. Packaged foods are required by the FDA to be labelled if their sulphite content exceeds 10 ppm. Similarly, the FDA mandates that sulphites are listed on prescription drug warning labels.

• Foods high in sulphite content (50 to >100 ppm) include dried fruit, bottled lemon juice, bottled lime juice, wine, molasses, sauerkraut juice, grape juice, pickled cocktail onions, dried potatoes, wine vinegars, gravies, sauces, fruit toppings and maraschino cherries.

• The commercially available sulphites that are used in foods and cosmetics are summarised as follows:

Compound	Formula	E-number	Food	Cosmetics
Sodium sulphite	Na_2SO_3	E221	Yes	Yes
Sodium bisulphite	$NaHSO_3$	E222	Yes	Yes
Sodium metabisulphite	$Na_2S_2O_5$	E223	Yes	Yes
Potassium sulphite	K_2SO_3	E225	Yes	Yes
Potassium bisulphite	$KHSO_3$	E228	Yes	Yes
Potassium metabisulphite	$K_2S_2O_5$	E224	Yes	Yes
Calcium sulphite	$CaSO_3$	E226	Yes	No
Calcium bisulphite	$Ca(HSO_3)_2$	E227	Yes	No
Ammonium bisulphite	NH_4HSO_3	-	No	Yes
Ammonium sulphite	$(NH_4)_2SO_3$	-	No	Yes

• Non-Occupational sources of sulphites etc. include the following:
Personal care products, such as shampoo, hair colour & bleaches, hairspray, skin lighteners, tanning lotions, anti-aging products, facial cleansers, body washes, bath oils & salts, eye creams, make-up, sunscreens, perfumes, and deodorants. Also medications such as topical anti-fungals, topical corticosteroids, local anaesthetics, ophthalmics, and nasal solution. Also swimming pool water.

• Occupational sources of sulphites etc. include the following:
Brewing, wine making, photography, textile industry, leather tanning, mineral extraction, effluent treatment, chemical manufacture, rubber manufacture, health care, wood/pulp/paper industries, glass industry, glove manufacturing, personal care product production, and pharmaceutical manufacturing.

• Sulphites are perhaps most well known for their connection with wine production.
The process of adding sulphite to wine has been known since the time of the ancient Romans to prevent wine from discolouring and to inhibit the growth of bacteria, yeasts, and moulds. Although

small quantities of sulphites may naturally form during the fermentation of wine, most winemakers typically add 30–90 ppm of sulphites during the production process. The purpose is to prevent spoilage and improve its aging properties. In the United States, wines are required to include a warning statement if they contain sulphite levels higher than 10 ppm. Wines labelled as "organic" tend to not have sulphites added during the production process. In some individuals, a side effect of consumption of sulphites, especially in wine, is headaches, however, there seems to be no correlation of that with positive patch test reactions to sulphites.

• The clinical relevance of positive patch test reactions to sulphites has been documented in several studies, but with widely differing results, from 3.9% to 65.2%; though the more recent studies seem to have settled around the 50% mark. Nevertheless, there is still some major disagreement between experts.

• Inclusion of a hapten in a baseline screening series is advocated by some experts when the prevalence of contact allergy to the substance in routinely patch tested populations reaches a threshold of 0.5–1.0%, especially when coupled with ubiquitous use and/or high clinical relevance. Based on these criteria, sulphites surpass this threshold consistently across multiple large studies and in various geographic regions. However, many baseline screening series still do not include sulphites.

Examples of national or international series or occupational series that do contain sulphites are:

- European Baseline Series
- North American Series
- Hairdressing Series
- Cosmetic Series
- British Standard Series
- Polish Standard Series
- Italian Baseline Series
- Australian Baseline Series

For further information see:
https://www.chemotechnique.se/products/haptens/sodium-metabisulphite/

• The study authors summarise by stating that sulphites are under-recognised and ubiquitous allergens. Historically, clinical relevance of sulphite allergy was debated, but recent studies document >50% current relevance. This, coupled with prevalence frequency of >1% support the inclusion of sulphites in baseline screening series. They advocate for sulphite inclusion in the next revision of the ACDS Core Allergen Series. Contact dermatitis experts should be aware of this important, often missed, allergen.

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

Results of Patch Testing to Botanicals: Review of the Mayo Clinic Experience over 2 Decades (1997-2017)

by Anagha Bangalore-Kumar, et al.
in DERMATITIS, Jan-Feb 2024, Volume 35, #1, pp 43-48.
https://doi.org.10.1089/derm.2023.0109

This study by members of the Mayo Clinic in USA investigated the frequency and identity of sensitisation to various “botanical” products including Essential Oils that are increasingly found in personal household products and are generally considered to be natural and safe.

The US Food and Drug Administration (FDA) defines Botanicals as ‘‘products consisting of vegetable materials, which may include plant materials, algae, macroscopic fungi, or combinations thereof.’’

Over the years, Botanicals have been used for the treatment of various dermatological conditions, including acne, vitiligo, and alopecia. For example:

- Aloe vera is a popular emollient, moisturiser, sunscreen, and wound healing agent.
- Clove oil is used as an antimicrobial agent.
- Jasmine and lavender oil are used in aromatherapy.
- Sandalwood extract has been studied for its anticarcinogenic potential.
- Roman chamomile, fennel, ginger, lemon, lemongrass, mandarin, and peppermint are used in various industries.

Many of these botanicals have been studied for their antioxidant, antimicrobial, wound healing and other medicinal properties. Adverse side effects have been reported, including contact dermatitis, phototoxic reactions, allergic contact dermatitis, and even systemic hypersensitivity adverse reactions.

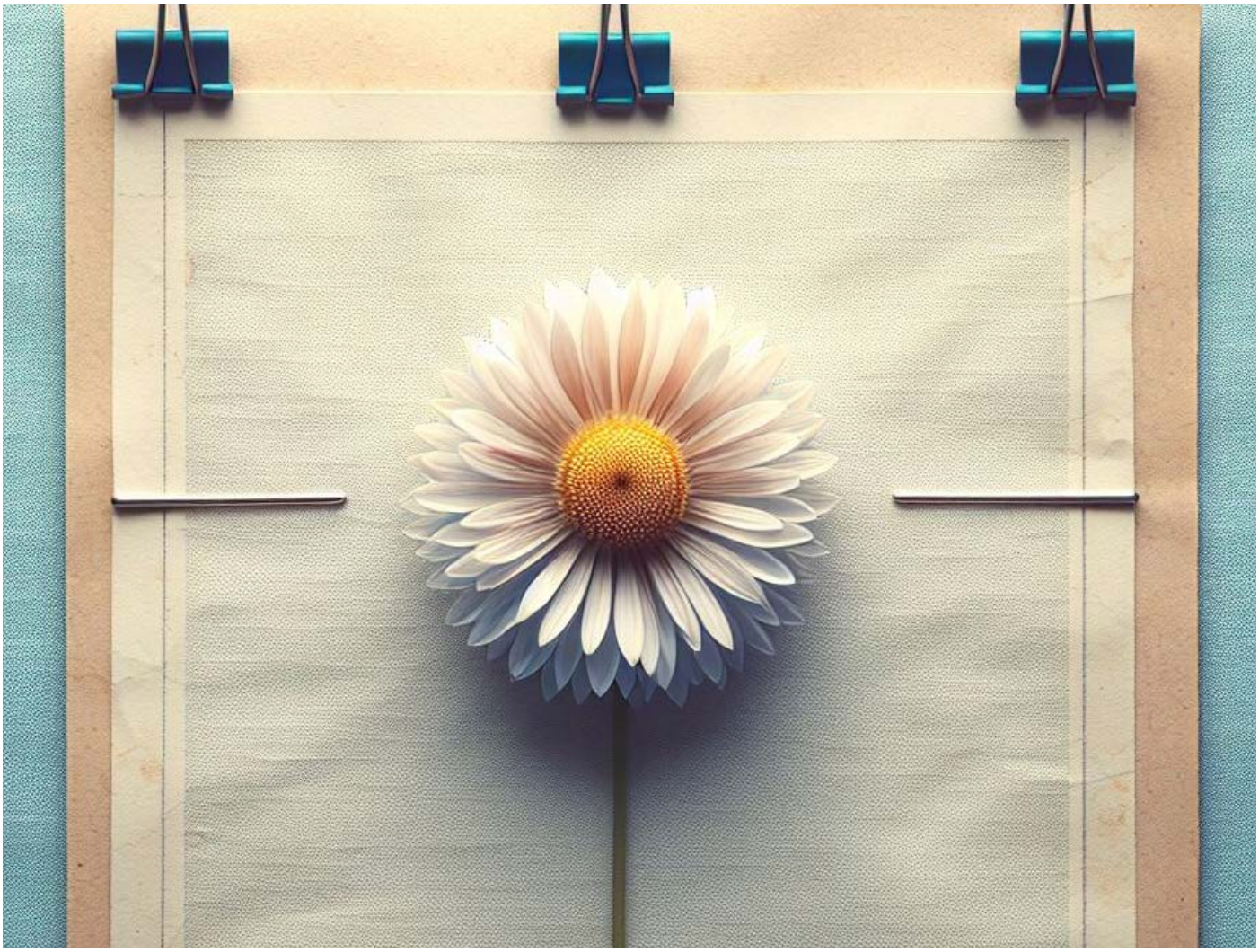
Among the general population, the prevalence for ACD from Botanicals is estimated to be 0.7% and 6.6%.

Despite this significant incidence of adverse reactions to various Botanicals, their use in consumer products continues to be ubiquitous and to expand, including in foods and beverages, personal care, cosmetics, and aromatherapy products. The market for Botanicals is so enormous that it has been estimated to be 131.5 billion US dollars in 2019 and to grow at 7% annually.

A survey of 1,274 botanical product users, reported the following reasons for its use:

- 52% out of curiosity
- 38% out of perceived safety
- 7% out of failure of conventional therapy
- 3% out mistrust in traditional therapy.

Although the phenomenon of sensitivity to Botanicals and Essential Oils is reasonably well described, there is still a dearth of hard data on the incidence and prevalence of contact dermatitis caused



by Botanicals. This study by the Mayo Clinic aims to provide further insights int these Botanicals and their causation of contact dermatitis.

There are numerous points of interest from the paper, which are listed below, plus some editorial data, information and comments (in italics).

• Allergens derived from botanical sources (as defined by the FDA) were included in the study. This comprised 32 allergens from the standard baseline series plus supplemental series at Mayo Clinic. Haptens/allergens were obtained from commercial sources or where necessary compounded by Mayo Clinic Pharmacy.

• A total of 12,169 people were patch tested to Botanicals in the standard, extended standard, fragrance, and plant series, of whom 4,032 (33%) were men and 8,137 (67%) were women. The mean age of the population tested was 54 years.

• Almost 11% (1,320) of the patch-tested population exhibited positive reactions to at least 1 Botanical hapten/allergen. There was a total of 88,624 haptens/allergens tested, of which 1,780 (2.0%) resulted in a positive patch test reaction.

Botanical hapten	Positive	Tested	Rate	Chemo Art No		
Myroxylon pereirae resin 25%	907	12,096	7.50%	B-001	25%	pet
Geranium 10%	1	17	5.88%	G-002	2%	pet
Hydroperoxides of linalool 1.0%	66	1348	4.90%	H-031A	1%	pet
				H-031B	0.5%	pet
Propolis 10%	139	4280	3.25%	P-022.	10%	pet
Tanacetum vulgare (Tansy) 1%	297	14 477	2.94%	T-033.	1%	pet
Hydroperoxides of limonene 0.3%	26	1300	2.00%	H-032A	0.3%	pet
				H-032B	0.2%	pet
Compositae mix II 5%	61	3256	1.87%	Mx-29A	5%	pet
				Mx-29B	2.5%	pet
Tea tree oil oxidized 5%	83	4461	1.86%	T-035B	5%	pet
Chrysanthemum c. (Pyrethrum) 1%	8	460	1.74%	C-031	1%	pet
Achillea millefolium (Yarrow) 1%	10	630	1.59%	A-025	1%	pet
Natural fragrance mix 2%	76	5071	1.50%	-		
Compositae mix 5%	52	3667	1.42%	Mx-29A	5%	pet
				Mx-29B	2.5%	pet
Oil of lemongrass 2%	35	2507	1.40%	-		
Lavandula angustifolia oil 2%	34	2733	1.24%	L-001	2%	pet
Jasmine absolute, Egyptian 2%	22	2731	0.81%	J-002	2%	pet
Sesquiterpene lactone mix 0.1%	93	11,552	0.81%	Mx-18	0.1%	pet
Taraxacum o. (Dandelion) 2.5%	19	2438	0.78%	T-032	2.5%	pet
Oil of cloves 2%	17	2197	0.77%	-		
Santalum album oil 2%	21	2723	0.77%	S-009	2%	pet
Ylang-Ylang oil 2%	11	1671	0.66%	Y-001	2%	pet
Geranium oil, Bourbon 2%	15	2413	0.62%	G-002	2%	pet
Turpentine oil oxidized 0.4%	2	326	0.61%	T-024B	0.4%	pet
Anthemis nobilis extract 1%	5	994	0.50%	C-029	1%	pet
Rosa damascena extract 2%	12	2542	0.47%	R-003	2%	pet
Menthol 2%	11	2510	0.44%	M-002	2%	pet
Bergamot—natural 2%	9	2148	0.42%	-		
Arnica m. (Mountain tobacco) 0.5%	4	992	0.40%	A-024	0.5%	pet
Narcissus poeticus 2%	9	2782	0.32%	N-006	2%	pet
Neroli oil 2%	6	1976	0.30%	-		
Orange oil 2%	3	1013	0.30%	-		
Oil of Eucalyptus 2%	6	2825	0.21%	-		
Oil of lemon 2%	3	2219	0.14%	-		

• Most patients presented with generalised dermatitis (334, 25.5%), hand dermatitis (284, 21.5%), or face dermatitis (232, 17.6%).

• Sometimes patients were tested to the skin care products they were using; of 8,148 skin care products, 4.7% (385) were positive.

• Positive patch test rates when macular erythema was included as a positive reaction revealed close to 21% of the cohort had a positive reaction to at least 1 Botanical agent [total 2513/12,169 (20.7%), 1719/8137 (21.1%) in women and 794/4032 (19.7%) in men]. This figure is then in accordance with a previous study by NACDG which reported that from 2007 to 2016, 22.7% of patients tested positive to a fragrance or Botanical, which is higher than the 10.8% of patients in this study with positive patch test results but comparable with the 20.7% of positive patch tests to

at least 1 Botanical that was observed when including macular erythema as a positive patch test result.

• 3.4% of the patients reacted to 2 of the allergens and 0.8% of them reacted to at least 3 allergens in the test series.

• There was a considerable increase in overall patch test positivity rates to at least 1 allergen over the period of the study from 1997 to 2017.

• At the time of patch testing, 51.6% positive reactions were thought to be relevant, 45.1% had questionable relevance, 1.3% had past relevance, and 1% were not clinically relevant.

• Clinically, patch testing is useful in determining products that patients may be sensitive to and guides clinicians in advising patients what products they should avoid.

• However, the efficacy of avoidance is confounded by a number of factors, including the concentration of the Botanicals in the patch test materials compared to natural exposure. Also the fact that labelling of fragrances has been hitherto restricted (in USA at least) by industrial secrecy. Soon though this veil is being at least partially lifted by the Modernization of Cosmetics Regulation Act of 2022 (MoCRA) which is expected to go into effect by the end of 2024, which will require Botanicals to have ingredients listed, including fragrance substances. This may facilitate the identification of problem substances by physicians and patients.

• The authors emphasise that with the Botanicals market continuing to grow and the persistence of the narrative of ‘‘natural’’ products as being safe and healthy, the Dermatologist must educate patients about naturally derived Botanicals as potential common causes of ACD, and the products in which their problem haptens/allergens may be found.

• Finally, the authors of the paper encourage extended series patch testing with Botanicals in patients with suspected Botanical-induced ACD.

For further information and insights please read the original article in DERMATITIS.

Piloting Photographic Photonic Patch Testing: Pioneering Equitable Diagnosis of Contact Dermatitis

by Eimear Gilhooley, et al.
in DERMATITIS, Nov-Dec 2023,Volume 34, #6, pp 568-569.
https://doi.org/10.1089/derm.2022.0055

The COVID-19 pandemic precipitated a unique set of circumstances wherein the provision of care through tele-medicine and alternative pathways was rapidly developed and adopted, including in the field of dermatology. One of the areas of the clinical practice of dermatology that utilised tele-medicine was in the evaluation of patch test reactions.

The actual mechanical manipulations of the patch testing procedure, with the dispensing of the haptens/allergens onto the patch test chambers, and the placement securely on the patients back could not of course be achieved through telemedicine, but the evaluation of the subsequent patch test reactions by the Specialist Dermatologist could quite possible be done remotely.

Patch testing is an area of Dermatology where virtual/distant interpretation of results is possible, thereby enabling patients, especially those who are located in more rural areas, better access to high-quality health care.

Virtual photographic assessment of patch testing was introduced in the Dermatology Department of South Infirmary Victoria University Hospital in Cork, Ireland, by the authors of this paper.

The adoption of this technology was also intended to not only improve access to patch testing services through the COVID pandemic, but also to improve patch testing services to patients living in remote areas of the country.

To augment the photographic image quality of our patch test readings, the clinic also employed photographic photonics technology. Photonics is a process that generates, detects, and manipulates physical light (photons) that can then be used to assess blood flow in a clinical photograph, and thereby potentially act as a surrogate marker for cutaneous inflammation, such as occurs in a positive patch test reaction.

Their aim was to assess whether clinical photography plus photonic image analysis could improve the detection of positive reactions in the virtual (distant) interpretation of patch test results.
They also endeavoured to pilot a strategy to reliably promote and improve access to their patch testing service for rural patients who had no easy access to their clinic in central Cork city.

Consecutive patients attending for patch testing were recruited. Photographs of patch test results were taken using a 40-megapixel colour camera on a popular brand of smart phone, on day 4, so contemporaneously to standard patch test assessment by the study investigators.

Literature Review

The photographic images were then analysed including the use of spectral imaging technology software, HyperCube, which employs principal component analysis (PCA), a technique used to reduce the dimensionality of data sets. PCA seeks to represent eye-ball observations.

The photonic images were then examined by 2 blinded observers to determine a combination of variables or colour patterns (red, green, blue [RGB]) that would indicate a positive result. Theoretically, these assessments could act as a surrogate marker for cutaneous inflammation of the patch test reaction sites. The results from the eyeball assessment of the digital photographs and of the photonic pictures were then compared with the patients' clinically recorded outcomes.

Thirty patients provided a total of 101 patch test reactions for evaluation. Two blinded investigators determined whether the results were positive (+), ?positive (+/-) or irritant, or other. Photonic/PCA and photographic clinical images were then compared with the clinical results.

The results from the comparisons were as follows:

- Photographic clinical images captured 63% of patch test results, and Photonic/PCA captured 72%.
- A higher pick-up rate was noted when reactions deemed as ‘‘other’’ were included.
- The concordance between investigators' photonic interpretation was high.
- Eliminating errors due to poor image quality and mislabelling and an error in clinical interpretation, the concordance improved to 90% for both Photonic/PCA and Photographic.

The authors concluded that their current approach in the use of photonics in patch test interpretation relies on visible camera-based interpretation of RGB patterns. The benefits of this approach include its low cost, high resolution, and wide availability. However, there are a number of issues with this approach: it is difficult to automate the analysis process, noise interference (RGB), and image quality. Analysis using a multispectral camera to include specific wavelengths to monitor increased blood flow may have a role and the study authors are currently pursuing this application.

Patterns of simultaneous contact allergies in patients with contact sensitisation to oxidised Linalool and oxidised Limonene

by Thanisorn Sukakul et al.
in CONTACT DERMATITIS, February 2024, Issue 2, pp 134-142.
https://doi.org/10.1111/cod.14445

This article is yet another high-powered study of the increasingly recognised importance of the hydroperoxides of linalool and limonene as contact allergens.

The authors studied 5-year's worth of 4,192 consecutive dermatitis patients in Malmö Sweden, and investigated the prevalence of multiple contact allergies (MCA) associated with limonene and/or linalool sensitivity.

4,192 consecutive patients with dermatitis presenting at the Department of Occupational and Environmental Medicine at Lund University Hospital, Malmö, were tested with the Swedish Baseline Series (of currently just 29 haptens) + hydroperoxides of linalool and limonene + individual ingredients of fragrance mixes.

There are numerous points of interest from the paper, which are listed below, plus some editorial data, information and comments (in italics).

- Of all 4,192 dermatitis patients, 1,851 (44.2%) had at least one positive PT reaction.

- This leaves a remarkable 55.8% of dermatitis patients with no positive patch test reactions when tested with the Swedish Baseline Series (of currently just 29 haptens) + hydroperoxides of linalool and limonene + 15 individual ingredients of the two fragrance mixes.

  For a list of the 29 haptens of the Swedish Baseline series see chemotechnique.se

The non-oxidised linalool and limonene are among the most commonly used fragrances in cosmetics and other products (such as healthcare and household products), but these fragrance materials are not considered to be contact sensitisers *per se*. It is virtually impossible to know whether products containing linalool and/or limonene also contain their hydroperoxides without advanced chemical analyses. It therefore may be difficult to establish clinical relevance in positive patch-tested patients in daily clinical practice. Consequently, the hydroperoxides of linalool and limonene have not been introduced to many commercially available national or international baseline series.
See the table below for information on which national and international series do indeed include the hydroperoxides of linalool and/or limonene.

Patients were described as "dermatitis", but it is also stated that "a history of atopic dermatitis was

reported in 26.8% of patients". *Of the 1,851 dermatitis patients with at least one positive PT reaction, 410 (22.2%) had MCAs. Therefore, logically, 77.8% showed sensitivity to only a single hapten of those tested. However, MCAs were defined as having 3 or more positive PT results; so there would appear to be a group of patients who had 2 positive PT results that were neither grouped in the MCA group nor counted as single-sensitised.*

MCAs were associated with increasing age of the patients, which may be a function of longer cumulative lifetime exposure to the haptens/allergens.

Having just 29 haptens in a national series is a comparatively low number; for example:

Country	n	Linalool HP	Limonene HP
- European Baseline	= 32	-	-
- European Extended	= 42	1.0% + 0.5%	0.3% + 0.2%
- International Standard	= 30	-	-
- International Comprehensive	= 80	0.5%	0.2%
- Australia	= 60	1.0%	0.3%
- Belgium	= 38	1.0%	0.3%
- China	= 60	1.0%	0.3%
- Finland	= 30	-	-
- Britain	= 40	1.0% + 0.5%	0.3% + 0.2%
- LATAM	= 40	-	-
- North American	= 60	0.5%	0.2%
- New Zealand	= 30	1.0%	0.3%
- ACDS	= 90	0.5%	0.2%
- Polish Standard 1	= 30	1.0%	0.3%
- Spanish	= 29	-	-
- Portuguese	= 32	-	-
- Italian	= 33	-	-
- Sweden	= 29	-	-

Information taken from chemotechnique.se

The mean age of the 4,192 patients included for analysis was 44.4 years, of which 117 patients (2.8%) were aged under 18. The majority was female (2 858, 68.2%).

- The prevalence of sensitisation to hydroperoxides of linalool and/or limonene was 10.2% (n = 428).
- The prevalence of sensitisation to hydroperoxides of linalool alone was 4.4% (n = 185).
- The prevalence of sensitisation to hydroperoxides of limonene alone was 2.7% (n = 114).
- The prevalence of sensitisation to hydroperoxides of linalool and limonene was 3.1% (n = 129).

Patients with a positive reaction to linalool HPs only had a significant overrepresentation of simultaneous positive reactions to all fragrances in the Swedish Baseline Series and many of the individual ingredients of the fragrance mixes.

Patients with a positive reaction to limonene HPs only had a lower total number of haptens/allergens with a significant simultaneous positive reaction compared with linalool HPs.

Patients with reactions to both linalool HPs and limonene HPs were shown to have multiple significant simultaneous positive reactions to fragrances and cosmetic-related haptens/allergens such as preservatives.

Patients with a positive PT reaction to only linalool HPs had a significantly higher likelihood of having MCAs, but not patients positive only to limonene HPs.

The prevalence of MCAs in this study (9.78%) was comparable with a multicentre study reported in 2009–2014 (7.02%), even though linalool HPs and limonene HPs were included in this Swedish

study.

More additional positive reactions to other haptens/allergens were observed in the group of patients with simultaneous reactions to both linalool HPs and limonene HPs. This indicated that the patients with contact allergy to these HPs might be more susceptible to contact sensitisation in general, and/or having larger concurrent exposure to other haptens/allergens.

Patients with sensitisation to linalool HPs seemed to have concomitant sensitisation to cosmetic allergens such as preservatives and other fragrances. Conversely, the patients with an exclusively positive reaction to limonene HPs seemed to have primarily concomitant positive reactions to haptens/allergens related to fragrances. This association has been previously noted in other studies.

The mechanisms underlying contact allergy to the linalool and limonene hydroperoxides are complicated and still partially elusive. Linalool and limonene are known as pre-haptens, which can be activated by air oxidation. The main sensitising mechanism of the oxidised products, mainly the hydroperoxides, could be via radical pathways. Although the HPs are reactive oxygen species themselves since they contain a peroxide group (-O- O-), they can also undergo further reactions after penetration of the dermis. Linalool hydroperoxides appear to be a stronger activator of the pathway than limonene hydroperoxides since they can produce a greater extent of reactive species via the transcription factor Nrf2 pathway.

Sensitisation to both linalool HPs and limonene HPs is significantly overrepresented in patients with photo-contact allergy to ketoprofen, for which the underlying mechanism remains unknown. Therefore, there might be other unidentified explanations for why patients with contact allergy to linalool HPs exhibit concurrent sensitisation to many chemically unrelated haptens/allergens. Genetic factors might also play a role.

For further information and insights please read the original article in CONTACT DERMATITIS.

Patch Test Hapten from Chemotechnique

Art no	Name	Conc. Veh.
H-031A/B	Hydroperoxides of Linalool	1,0 / 0,5% pet
H-032A/B	Hydroperoxides of Limonene	0,3 / 0,2% pet

The Contribution of Metal Allergy to the Failure of Metal Alloy Implants, with special reference to Titanium: Current knowledge and controversies

by Chenghao Huang et al.
in CONTACT DERMATITIS, March 2024, Volume 90, Issue 3, pp 201-210.
https://doi.org/10.1111/cod.14481

After several decades of debate about the role of clinical sensitisation to the metals most commonly used in joint prostheses (for primarily hip and knee joints), the only conclusion is that there is indeed an association regarding nickel, cobalt and chromium, but it is still not confirmed whether allergy develops as a consequent of mechanical failure and subsequently exacerbates the clinical problem, or whether sensitisation starts first and induces failure of the joint as a consequence. Currently, opinion favours the former hypothesis.

The scale of the clinical situation is considerable, as in the UK alone, over 200,000 such hip or knee prosthesis operations are performed annually.

The implants are usually made of alloys such as stainless steel, vitallium (cobalt 65%, chromium 30%, molybdenum 5%) and cobalt-chromium. However other metals such as aluminium, nickel, vanadium, titanium, zirconium, and iron are also used.

The first-generation metal-on-metal (MoM) prostheses of the 1960 and 1970s were often cobalt–chromium alloys, and were associated with complications such as dislocation and sciatic nerve damage in the short term, and mechanical failures in the longer term. Some studies showed a high incidence of metal sensitivity (13% up to 38%), amongst patients with such first-generation MoM prostheses. Second-generation MoM prostheses were introduced in the 1980s.

Metal Allergy Prevalence
The estimated prevalence of cutaneous allergies to nickel, cobalt, and chromium in the general population (unrelated to arthroplasty) is, according to patch testing and blood analysis, approximately:

Nickel	10% to 13%
Cobalt	2%
Chromium	1%.

Titanium
One of the more recently introduced metals for joint prostheses is titanium. Unfortunately, the original high hopes for this biocompatible and corrosion-resistant metal have not been fulfilled. Titanium has been introduced for use in human replacement joints based on its biocompatibility and corrosion resistance, in part due to the bioinert layer of TiO2 that forms on the surface of a prosthesis using a

titanium-containing alloy. Despite this, *in vitro* and *in vivo* studies have proven that this oxide layer can be compromised, for example by local mechanical trauma, with release of titanium particles and ions. Proteins such as albumin, α-globulin, transferrin, fibrinogen, and amino acids have a strong affinity for metal ions, and since these elements are capable of forming metallo-organic complexes, they significantly increase the corrosion rate of titanium alloys. So although titanium was once considered to be bio-inert compared to cobalt and chromium, it is now recognised that titanium ions released from implants can trigger hypersensitivity reactions.

There is also a second major issue with titanium – patch testing to detect sensitisation. There is still great debate and uncertainty about which titanium salt and at which concentration, or multiples thereof, should be the best hapten for patch test investigations of titanium sensitisation.

Surgical Glues

The role of surgical glue, principally methyl methacrylate, should also not be forgotten, though there is a trend away from the use of such glues in principle. Methyl methacrylate is $CH_2=C(CH_3)COOCH_3$. This is used is as cement in total hip replacements as well as total knee replacements. This is used as the ”grout” by orthopaedic surgeons to make the bone inserts fix into bone. It greatly reduces post-operative pain from the insertions, but has a finite lifespan. Typically, the lifespan of methyl-methacrylate as bone cement is 20 years before revision surgery is required. Cemented implants are usually only done in elderly populations that require more immediate short-term replacements. In younger populations, cementless implants are used because their lifespan is considerably longer. This has been made possible by the ever-improving precision of the surgical cutting of the femur and tibia bones, and the consequent better fit of the metal prostheses into the bones. Methyl methacrylate is a mild skin irritant in humans and has the potential to induce skin sensitisation in susceptible individuals.

Plastic Joint Components

Similarly, the existence of the polyethylene spacers as a potential source of sensitisation must not be overlooked. If, or perhaps when, over a decade or more of daily use, a plastic polypropylene spacer between the metal heads of the two bones becomes worn, with the shedding of particles or it then that may invoke local toxic effects causing inflammation and osteolysis. Over recent years the development of ever more resilient spacers acts to minimise this risk and incidence. Polyethylene is $(C_3H_6)n$.

Clinical Complications

Ever since such implant operations were first performed, clinical complications have been documented, which may be mild local reactions such as localised dermatitis, urticaria, bullous reactions and vasculitis eruptions and, uncommonly, systemic allergic dermatitis reactions. Pseudo-tumour formation and implant loosening are important non-cutaneous complications.

Tests for Sensitisation

The testing of sensitisation to the metals used in joint prostheses is also not a straight-forward situation. Epicutaneous patch testing is generally considered the gold standard to diagnose cell-mediated (type IV) hypersensitivity to metals. Patch testing is widely available, and to a wide range of metals and plastics and glues, though it requires expert interpretation. It has a general sensitivity of 77% and a specificity of 71%. However, there is concern that the epicutaneous route utilises a different

immunological pathway, utilising epidermal Langerhans cells, than that which may be relevant in joints, where macrophages and tissue dendritic cells might mediate the antigen presentation. Hence some researchers have sought *in vitro* tests utilising peripheral blood lymphocytes, as alternatives in an attempt to overcome such concerns. Of these, the best known is the lymphocyte transformation test (LTT), and its commercial incarnation, the MELISA test system (www.melisa.org). The LTT is based on measuring the proliferation of lymphocytes in response to the addition of a metal salt in the presence of appropriate antigen-presenting cells. LTT may have a higher sensitivity, estimated at between 55% and 95%, than patch testing, and can also deliver objective fully quantitative results, though it is a technically complex assay procedure that is not widely available. The commercial variant is also not widely available, covers only a limited number of metals, and is comparatively expensive.

Metal Particles

In the earliest generation of metal-on-metal (MoM) joints, there was a real possibility of metal particles being produced and having a negative physical effect on the joint functionality. Some studies showed a high incidence of metal sensitivity (13%–38%), amongst patients with first generation MoM prostheses. This was thought to have been due to the MoM articulations shedding wear particles of metal, producing high concentrations in the local tissue and blood, that would in some cases lead to the development of cell-mediated allergy.

Metal Ions

Metal ions *per se* that are released from arthroplasties undoubtedly can cause toxic effects, including local inflammation and osteolysis—quite apart from the induction of allergy—that contribute to joint failure. Electrochemical corrosion of metal alloys whilst in contact with bodily fluids causes release of metal ions. The resultant inflammatory response is proportional to the particulate load. Metal particles are pro-inflammatory, and generation of wear particles can cause osteoclast activation via macrophage ingestion. Pro-inflammatory cells trigger an immune response that could cause soft-tissue inflammation with subsequent periprosthetic tissue damage.

New Bio-degradable Metal Implants

A new class of biodegradable metals has emerged as an alternative to traditional fixation implants. These biodegradable materials are expected to degrade completely *in vivo*, being replaced by newly formed bone. The three main types of biodegradable alloys are based on magnesium, iron, and zinc. The magnesium-based alloys have been most extensively studied *in vitro* and *in vivo*. Iron-based alloys still need more long-term clinical trials. One drawback of iron-based alloys is the slow degradation in the physiological environment of the joint. Zinc-based alloys, which are still in the initial stage of development, have a degradation rate mid-way between. Some alloys based on non-toxic or low toxicity elements including zinc, zirconium, calcium, strontium, and tin are being considered for orthopaedic use, including in various combinations. Allergic problems with these biodegradable metal alloys are anticipated to be uncommon.

Non-metal Implants

Two classes of orthopaedic ceramic implants, the bio-inert and the bio-active, are actively under development. Bioinert ceramic materials possess excellent wear resistance, high compressive strength, inherent chemical inertness, are biocompatible, and therefore elicit no or minimal immunological response from the living tissues because they undergo little physical or chemical alteration inside the human body. Bioinert ceramic materials are commonly used as articular components in

total joint replacements but generally have not been applied to fracture fixation applications mainly due to their poor ductility. Amongst the various types of bioinert ceramics, Al_2O_3 (alumina), ZrO_2 (zirconia) and silicon nitride (Si_3N_4) have been investigated.

The second class of non-metal implants are the bioactive ceramic materials which can bond directly with surrounding living bone tissues. These ceramic materials are applied as coatings on metal bone implants rather than load-bearing components, due to the low mechanical strength. As an example, hydroxyapatite has a porous structure which allows bone tissues to infiltrate and grow inside the pores, leading to a better integration between the implant and the adjacent tissues. Allergic problems are not anticipated with such elemental salts. Hopefully, these new non-metal implants, and especially the bioactive materials coated onto metal, will resolve the questions still persisting and tainting the use of full-metal implants.

Pre-Implant Testing
Routine pre-operational 'predictive' patch testing or LTT is not generally recommended, the exceptions being the stipulation by maxillo-facial surgeons for this prior to the insertion of replacement temporo-mandibular joints and, according to guidelines of the American Contact Dermatitis Society, prior to the Nuss procedure for correction of *pectus excavatum* using either a stainless steel or a titanium alloy bar.

However, it would not be surprising if more institutions and individual surgeons were to recommend or request predictive patch testing, particularly in societies where trigger-happy lawyers are hovering. Such predictive testing would be a good defence against any subsequent potential litigation due to a joint failure.

Of course, neither patch testing for metal sensitivity, nor plastics nor glues, nor the use of LTT assays is any guarantee, considering the false negatives and false positives, and cost, and difficult interpretation, and all the other limitations, but it is nevertheless the best defence for the surgeon.

Post-Implant Testing
For patients who are experiencing dermatological symptoms, or signs of failing metal articulated prostheses, especially if blood levels of metal ions are elevated, then patch testing or LTT are indicated to inform clinicians of how to best to manage the individual patient. This may well include the removal of a failing or failed joint and its subsequent replacement by another joint constructed of other metals or non-metals to which the patient appears (after testing) to be not sensitised.

Monitoring of metal ion values in blood is now recommended in certain situations after joint replacement, when increasing levels may be an indication that allergy with joint failure may in due course develop. In such cases then patch testing is indicated, and suggested patch test series are available.

Readers are highly recommended to read the original article in CONTACT DERMATITIS to obtain maximum information and benefit from this excellent article.

Contact Allergy in African Countries: A review of published Patch Test Studies

by Nikolaj Menné Bonefelf et al.
in CONTACT DERMATITIS, February 2024, Volume 90, Issue 2, pp 103-109.
https://doi.org/10.1111/cod.14471

Only a few studies on contact allergy in African countries have been published. The aim of this study was to provide an overview of the most common contact allergens identified by the use of patch tests in African countries based on a review of the existing literature. A total of twenty-four publications from eight African countries were initially identified by search in PubMed. The abstracts and method sections were screened, and 15 studies in which patch tests were actually used to identify the allergen causing the allergic contact dermatitis (ACD) were finally selected.

The results showed that nickel, cobalt, chromium, fragrance mix, and p-tert-butylphenol-formaldehyde resin were the dominating contact allergens, responsible for 40% to 90% of the positive patch test reactions.

This study indicates that a targeted effort should be directed towards prevention, and avoidance and regulation of reliably identified contact allergens, as this should reduce the disease burden of ACD considerably in some African countries.

The high burden of eczematous skin diseases in African countries suggests that prevention of ACD should be prioritised. However, due to the limited volume and quality of relevant data and the scarcity of medical doctors trained in dermatology in almost all African countries, many cases of ACD are probably not diagnosed and the contact allergen is therefore not identified.

A PubMed search was made on ACD and Patch Test for each of the 54 countries of the continent.

For a list of the 54 countries see https://www.worldometers.info. This includes various offshore islands such as Cape Verde, Mauritius, Seychelles, Madagascar, Comoros, and Sao Tome. Remarkably, whilst South Africa is of course included in the definition of Africa, there were no such published papers on studies in that country, despite the fact that patch testing is readily available in the country.

Nickel
Nickel allergy is common in the African countries, but is actually within the same range as occurs in the European general population, despite the fact that the African countries are not subject to the EU regulations on nickel content and exposure. It would be interesting to explore this phenomenon more closely as it is unexpected, considering the documented reduction in nickel sensitisation in EU countries due to the introduction of the EU regulations.

Chromium
From the published data, there was seen a significant rise in the prevalence of chromate allergy in Nigeria since 1985. This coincides with a boom in building activity, so that contact with concrete that contains chromates has also increased correspondingly. According to EU regulations from 2005, the total content of Cr(VI) in cement should not exceed 2 mg/kg. This regulation was developed and applied because chromate allergy in cement workers increased from 1960 to 1970 in European countries. However, since the implementation of the new limit, then chromate sensitisation has decreased, most probably due to the addition of ferrous sulphate to the cement mix. In addition, it has been speculated that the addition of ferrous sulphate, and thereby a reduction of Cr(VI), might also have led to a decrease in sensitisation to the cobalt in the cement. However, it has also been suggested that the decrease in cobalt sensitisation is a result of overall more hygienic and protective work environments, rather than a result of the addition of ferrous sulphate.

In addition to cement, leather shoes are a source of chromium. Chromium is used for tanning the leather. It has been reported that leather shoes are the most frequent cause of chromium allergy in the general population in southern EU. Due to the warmer climate in southern Europe, it is common to wear leather shoes/sandals without socks for better ventilation. This could very well be the case in African countries too. The EU regulation on chromate is effective in regulating contact allergy from cement and leather, as there has been a decrease in the prevalence of chromate allergy observed in Europe.

Cobalt
Cobalt exposure is possible in many ways, but it is still difficult for the experienced dermatologist to explain the majority of positive patch tests to cobalt. The reason for the rise in cobalt allergy worldwide is not completely understood. Studies covering more than one continent might be helpful in the expansion of our understanding of exposure to common contact allergens such as cobalt.

Fragrances
Fragrance allergy and allergy to PTBP were common in African countries. The prevalence of fragrance allergy is probably underestimated, not just in Africa but globally, as the diagnosis is dependent on the availability of newly developed patch test mixes containing newly developed or newly utilised fragrances. Furthermore, it is likely that locally produced fragrance products that might have a sensitising potential are not included in the patch test mixes in African countries.

PTPB
p-tert-butylphenol-formaldehyde resin is used in the production of leather shoes and sandals. The problem with PTBP allergy is reduced in scale in the EU and USA, though not entirely resolved. This reduction is probably due to the increased automation of the production process, leading to reduced occupational exposure.

In conclusion, this review indicates that a targeted effort directed towards improved prevention, avoidance and regulation of the contact allergens nickel, cobalt, potassium dichromate, fragrances and PTBP could reduce the disease burden of ACD in African countries.

Frequency and Relevance of Contact Allergy in Dental Patients

by Malak Al-Gawahiri et al.
in CONTACT DERMATITIS, January 2024, Volume 90 Issue 1, pp 66-73.
https://doi.org/10.1111/cod.14440

There are numerous reports and publications on the occupational allergy by dental staff to their materials and substances, but considerably fewer reports on the sensitisation by dental patients to these materials and substances. This research study carried out in Netherlands aimed to provide a better insight into such sensitisations by dental patients.

A total of 360 patients with intra-oral and perioral conditions suspected of having a contact allergy were patch-tested with the Dental Allergen Series of 26 haptens/allergens, as well as the European Baseline Series, and the Extended Amsterdam Baseline Series of 29 haptens/allergens, at Amsterdam University Medical Centres, between January 2015 and November 2021.
The Chemotechnique haptens/allergens were predominantly used.

A total of 285 patients (79.2%) gave a positive patch test reaction for either one (18.6%) or multiple allergens (60.6%).

There were 1,158 positive patch test reactions amongst the 360 patients. Most reactions were caused by allergens in the EBS and Extended Amsterdam Baseline Series, which yielded 688 (59.4%) positive reactions, whilst the Dental Series elicited 470 (40.6%) positive reactions.

Of the haptens/allergens tested, the following showed the greatest clinical incidence.

Sodium tetrachloropalladate	(Palladium)	= 27.2%
Nickel sulphate	(Nickel)	= 23.3%
Methylisothiazolinone		= 15.6%
Fragrance mix I		= 14.2%
Palladium chloride	(Palladium)	= 13.9%
Stannous chloride	(Tin)	= 13.1%
Cobalt chloride	(Cobalt)	= 10.0%
Potassium dicyanoaurate	(Potassium)	= 9.2%
Balsam of Peru		= 8.3%
Fragrance Mix II		= 7.5%
Methacrylates		= 7.2%
Cocamidopropyl betaine		= 4.9%
Caine Mix III		= 1.8%.

Metals
The heavy preponderance of metals amongst the sensitisers is not unexpected. Metals are commonly used in dental amalgam, which comprises mercury, tin, silver, zinc, and copper, used as permanent fillings. Even though adverse reactions to metals are rare and measures have been taken to reduce the use of common metal sensitisers in dental material, ideally, they should be entirely replaced by the use of non-metal or low-metal materials, at least for dental patients known or suspected to be sensitised to various metals.

Clinical relevance was found in 68 of 208 patients (32.7%), with patients having one (15.4%) or multiple (17.3%) patch test reactions clinically relevant to their (peri)oral complaints.

Palladium
The fact that Sodium tetrachloropalladate was the most frequent sensitiser at 27.2% of the 360 patients is remarkable. The few previous studies (in Japan, Finland, and Israel) investigating sensitisation to dental materials have not tested for this palladium metal. However, one previous study of 906 patients suspected of having contact allergy with or without eczema showed that 10.7% reacted positively to palladium chloride and 24.3% reacted to sodium tetra-chloropalladate, which is in line with this Netherlands study with positive reactions to palladium chloride at 13.9% and sodium tetrachloropalladate at 27.2%. The use of sodium tetrachloropalladate has only recently proved to be a more reliable test material for diagnosing a palladium allergy. Palladium is commonly used as a component of dental casting alloy and dental plates with other metals such as dental gold, silver, zinc, and copper. However, due to the low dissolution rate of palladium ions in these dental castings, it is often well-tolerated by patients.

Cross-reactivity is said to exist between palladium and nickel, which makes it difficult to detect the clinical relevance of a positive patch test to palladium, as nickel is itself a most common sensitiser amongst dental materials for dental patients.

Dental Series
The Dental Series was evaluated for its relevance and suitability for screening purposes. Sensitisation to haptens/allergens in the Dental Series was demonstrated in 57.8% of the 360 subjects. In total, 26 of 30 allergens (86.7%) with positive patch test reactions in the Dental Series proved clinically relevant. This resulted in 68 patients (32.7%) having one (15.4%), or multiple (17.3%), patch test reactions clinically relevant to their (peri) oral complaints. Some haptens/allergens were clinically relevant for all positive patch tests; namely 1,4-butanediol dimethacrylate, urethane dimethacrylate, TEGDMA, and Bisphenol A dimethacrylate. In contrast certain haptens/allergens only gave clinically irrelevant positive patch test reactions; namely eugenol, camphoroquinone, ammonium molybdate, and gallium(III)oxide.

N-Ethyl-p-toluenesulfonamide was the only hapten/allergen in the Dental Series that did not cause at least one reaction.

Methacrylates
A previous Swedish study and a previous Israel study investigated sensitisation to methacrylates amongst dental staff and patients.

	Sweden	Netherlands	Israel
Dental Patients	2.3%	7.2%	-
Dental Staff	5.8%	-	-
2-HEMA	2.2%	4.2%	5.8%
EGDMA	1.1%	3.1%	-
TEGDMA	0.5%	2.5%	-
MMA	0.3%	2.8%	- .

Fragrances
In previous studies, dental patients were most often only tested with a Dental Series. Therefore, common allergens such as fragrances may be missed. In this Netherlands study, fragrances yielded many positive reactions: FMI (14.2%), balsam of Peru (8.3%), and FMII (7.5%), though previous research has reported lower rates of allergies to FMI (9.8% and 6.7%) and balsam of Peru (7.2%). This difference might be caused by selection and referral bias. Fragrance mixes I and II are composed of eight and six different fragrances, respectively, including eugenol and Lyral. Both eugenol and Lyral were tested separately which resulted in an allergy in 0.3% and 2.2% of patients, respectively. Previous literature has shown that fragrances are one of the most frequent causes of contact allergy. Although the study authors did not address the question of the possible source of the fragrance sensitisation, this would probably have occurred prior to the dental work or may have been due to the use of fragrances in some dental materials, or dental clinic items.

Whatever the source, it seems advisable to also patch test fragrances in patients suspected of having oral complaints possibly caused by contact allergy to dental materials.

The study authors concluded that it is important to test dental patients presenting with intra- and peri-oral conditions for suspected contact allergy with a Dental Series in addition to the EBS.

Although this study provided some information on contact allergy in dental patients, further studies are needed. These studies should investigate patch test reactions and clinical relevance in both Dental Series and Extended EBS, including allergens such as dental amalgam and sodium tetrachloropalladate, and should also include an analysis on cross-reactivity with comparison to other populations.

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 Dermatolologic 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

Website Review

In this eighteenth issue of “The Patch Tester” we are taking a look at the website of the European Academy of Allergy and Clinical Immunology (EAACI), and in particular their Dermatology Section.

The European Academy of Allergy and Clinical Immunology (EAACI) is a non-profit association of clinicians, researchers and allied health professionals, dedicated to improving the health of people affected by allergic diseases.

EAACI is an association of clinicians, researchers and allied health professionals, dedicated to improving the health of people affected by allergic diseases with more than 15,000 members from 124 countries and over 50 National Allergy Societies.

EAACI Sections

The academy has established the following five EAACI Sections:

- Basic & Clinical Immunology
- Asthma
- Pediatric
- Dermatology
- ENT

The sections are represented in the EAACI Executive Committee by their chairs and have the opportunity to propose task forces as well as joint sessions with appropriate specialised societies. Every 2 years, new board members, chair and secretary and ExCom members are elected.

EAACI Interest Groups

The EAACI Interest Groups represent an area of more specific interest within allergology. Additionally, Interest Groups provide a focus for scientists and clinicians interested in particular aspects of allergic diseases. The Interest Group forms a focus for discussion at EAACI scientific meetings, provides input to the scientific programme, and can make proposals for the task forces. Every 2 years, new board members, chair and secretary and ExCom members will be elected.

- Food Allergy
- Drug Allergy
- Allergen Immunotherapy
- Environmental & Occupational Allergy
- Allergy Diagnosis & Systems Medicine

EAACI Working Groups

The EAACI Working Groups are established as part of the Interest Groups or Sections. Each chair of the Working Group sits automatically as an additional board member in their respective Interest Group or Section board. The EAACI Working Groups represent relevant and growing scientific areas for the academy and have a clear link or common interest to their Interest Group or Sections.

- Eosinophilic Esophagitis
- Comparative Veterinary Allergology
- Aerobiology and Pollution
- Insect Venom Hypersensitivity

EAACI Task Forces

Task forces are projects that deal with specific topics that are relevant, controversial or new in the field. All EAACI members can apply for a specific task forces in alignment with the chair and secretary of a specific section or interest group. All task forces are supported by EAACI and have been approved by the Executive Committee.

78 Taskforces existed in 2023, including 9 with a particular interest in dermatology:

- Skin Allergy Club
- Human Skin Microbiota
- Severe Atopic Dermatitis associated with hypogammaglobulinemia
- Systematic Review on the Dietary Interventions in Children after acute respiratory or skin infections
- ENIGMA Exploring non-IgE Mediated Allergy
- Urticarial Vasculitis
- Diagnosis of Fluoroquinolone hypersensitivity
- Urticaria and Anaphylaxis in Athletes
- Food allergy in Atopic Dermatitis: An Algorithm for Diagnosis and Risk Evaluation

EAACI Focussed Meetings

EAACI runs focussed meetings on average once or twice a year, including a Dermatology meeting approximately every two years. These are the Skin Allergy Meetings, SAM, organised in coordination with ESCD, with the most recent being in 2021.

The SAM meeting of 12th – 13th March 2021 in coordination between EAACI and ESCD was the 6th SAM meeting and that year was the leading European meeting in 2021 devoted to skin allergy. The sixth edition of this biannual event was a digital event (due to COVID pandemic). So we would seem to be overdue the next SAM meeting for 2024. Click here for the eight presentations at that 2021 SAM focussed meeting.

EAACI Master Classes and Winter Schools

Covering both clinical and transitional topics of a specific field, EAACI Master Classes aim to dive deeper and therefore target professionals and specialists with a higher level of experience. Conducted in exclusive workshop formats of up to 60 international participants, they offer an excellent interactive platform for the exchange of knowledge over a two-day period.

So, in total, although EAACI is primarily an organisation for Allergy Specialists, and it manages an enormous program for the education and training and development of Allergy Specialists, there is a very significant degree of overlap into Dermatology and therefore to be of great interest for Dermatology Specialists.

Dermatologists are therefore encouraged to support EAACI in general, but in particular to get involved in developing the content of Dermatology within the various EAACI operations.

Contact Dermatitis / Patch Testing

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

Dermatology - International

16th – 18th May 2024
EADV Symposium
Malta
https://eadv.org/symposium/

25th – 28th September 2024
EADV Congress 2024
Amsterdam, Netherlands
https://eadv.org/events/calendar/

31st May - 3rd June 2024
EAACI Congress 2024
Valencia, Spain
https://eaaci.org/events_congress/eaaci-congress-2024/

National

2nd – 4th July 2024
British Association of Dermatologists 2024
Manchester, UK
https://badannualmeeting.co.uk/

11th – 13th May 2024
Australasian College of Dermatologists 2024
Perth, WA, Australia
https://www.dermcoll.edu.au/event/2024-australasian-college-of-dermatologists-annual-scientific-meeting/

The webpage at www.waset.org/dermatology-conferences-in-2024 is one potentially very useful source of information of Dermatology congresses in 2024.

WASWT is the World Academy of Science, Engineering and Technology. Their webpage states numerous dermatology-related congresses and conferences for 2024.

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