the Patch Tester

Contact Dermatitis | Haptens | Patch Testing

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THE LANOLIN ISSUE

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

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PURPOSE

The Patch Tester is an e-mag developed by Chemotechnique to serve as an information resource for all Patch Testers and other Dermatologists around the world; not just in Sweden, or Europe, or America, but wherever the English language can be read and understood. This fifteenth issue comprises forty-four 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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Hapten and Allergens

Dermatology Specialists and relevant other healthcare professionals may well be aware that the two global manufacturers of patch test products Chemotechnique and SmartPractice utilise different terminology to categorise their patch test substances.

Chemotechnique use the term “hapten”, whereas SmartPractice use the term “allergen”.
Which is correct, one or the other, both or neither?

Reviewing the use of the terms “hapten” and “allergen” in the context of patch testing, we must firstly consider the definitions of hapten and allergen.

A brief description can be seen at www.dictionary.com; as follows:

Hapten = a substance having a single antigenic determinant that can react with a previously existing antibody but cannot stimulate more antibody production unless combined with other molecules; a partial antigen.
Allergen = Any substance, often a protein, that induces an allergy: common allergens include pollen, grasses, dust and some medications..

However, these definitions are inadequate, and are simply not "the truth, the whole truth and nothing but the truth".

A far more comprehensive definition of the two terms can be found in Wikipedia. The following text has been taken from Wikipedia on 23/05/2023 but has been modified where necessary for grammar and where appropriate for content relevant to the subject of patch testing and/or skin prick testing.
For full information on the topic of "hapten" please see the original article on Wikipedia at …. https://en.wikipedia.org/wiki/Hapten

The word Hapten is derived from the Greek haptein, meaning "to fasten". They are small molecules that elicit an immune response only when attached to a large carrier such as a protein; the carrier may be one that also does not elicit an immune response by itself.

The mechanisms of absence of immune response may vary and involve complex immunological interactions but can include absent or insufficient co-stimulatory signals from antigen-presenting cells.
Haptens have been used to study allergic contact dermatitis (ACD) and the mechanisms of inflammatory bowel disease (IBD) to induce autoimmune-like responses.
The concept of haptens emerged from the work of Austrian immunologist Karl Landsteiner, who also pioneered the use of synthetic haptens to study immunochemical phenomena.

Immune Reaction on a hapten-adduct Adduct
Haptens applied on skin, when conjugated with a carrier, could induce contact hypersensitivity, which is a type IV delayed hypersensitivity reaction that is mediated by T cells and dendritic cells. It consists of two phases: sensitisation and elicitation.

The sensitisation phase occurs where the hapten is applied to the skin for the first time and is characterised by the activation of innate immune responses, including migration of dendritic cells to the lymph nodes, priming antigen-specific naive T cells, and the generation of antigen-specific effector or memory T cells and B cells, and antibody-secreting plasma cells.

The second elicitation phase happens where the hapten is applied to a different skin area and starts with activation of effector T cells followed by T cell-mediated tissue damage and antibody-mediated immune responses.

Haptens initially activate innate immune responses by complex mechanisms involving inflammatory cytokines, damage-associated molecular patterns (DAMP), or the inflammasome.
Once the body has generated antibodies to a hapten-carrier adduct, the small-molecule hapten may also be able to bind to the antibody, but it will usually not initiate an immune response; usually only the hapten-carrier adduct can do this. Sometimes the small-molecule hapten can even block immune response to the hapten-carrier adduct by preventing the adduct from binding to the antibody, a process called hapten inhibition.

A well-known example of a hapten is urushiol, which is the toxin found in poison ivy. When absorbed through the skin from a poison ivy plant, urushiol undergoes oxidation in the skin cells to generate the actual hapten, a reactive quinone-type molecule, which then reacts with skin proteins to form hapten adducts. After a second exposure, the proliferated T-cells become activated, generating an immune reaction that produces typical blisters of a urushiol-induced contact dermatitis.
Other example of a hapten-mediated contact dermatitis is nickel allergy, which is caused by nickel metal ions penetrating the skin and binding to skin proteins.

Examples of Haptens
A lot of haptens are found in different kinds of drugs, pesticides, hormones, food toxins, etc.
The most important factor is the molecular mass, which is <1000 Da. The first researched haptens were aniline and its carboxyl derivatives (o-, m-, and p-aminobenzoic acid).
Some haptens can induce autoimmune disease. An example is hydralazine, a blood pressure-lowering drug that occasionally can produce drug-induced lupus erythematosus in certain individuals. This also appears to be the mechanism by which the anaesthetic gas halothane can cause a life-threatening hepatitis, as well as the mechanism by which penicillin-class drugs cause autoimmune haemolytic anaemia. Other haptens that are commonly used in molecular biology applications include fluorescein, biotin, digoxigenin, and dinitrophenol.

Antibodies have successfully been raised against endogenous & unreactive small molecules such as some neurotransmitters such as serotonin (5HT), glutamate, dopamine, GABA, tryptamine, glycine, noradrenaline), amino acids (e.g., tryptophan, 5-hydroxytryptophan, 5-metoxytryptophan), by using glutaraldehyde to crosslink these molecules to carrier proteins suitable for immune recognition.
Notably, detection of such small molecules in tissues requires the tissue to be glutaraldehyde-fixed, as the glutaraldehyde covalent-linkage on the molecule of interest often forms a portion of the antibody-recognised epitope.

Hapten Conjugation
Due to their nature and properties, hapten-carrier adducts have been essential in immunology. They have been used to evaluate the properties of specific epitopes and antibodies. They are important in the purification and production of monoclonal antibodies. They are also vital in the development of sensitive quantitative and qualitative immunoassays.

However, to achieve the best and most desirable results, many factors are needed to be taken into the design of hapten conjugates. These include the method of hapten conjugation, the type of carrier used and the hapten density. Variations in these factors could lead to different strengths of immune response toward the newly formed antigenic determinant.

Carriers
In general, carrier proteins should be immunogenic and contain enough amino acid residues in the reactive side chains to conjugate with the haptens. For protein haptenation to occur, hapten must be electron deficient (electrophilic), either by itself, or it can be converted to a protein-reactive species for example by air oxidation or cutaneous metabolism. Haptens become fastened to a carrier molecule by a covalent bond. Depending on the haptens being used, other factors in considering the carrier proteins could include their *in vivo* toxicity, commercial availability, and cost.

The most common carriers include serum globulin, albumins, ovalbumin, and many others. Human serum albumin (HSA) is often the model protein of choice for protein-binding assays. This is a well-characterised protein, and the role of albumin in blood and tissues *in vivo* is often to bind to

xenobiotics via its substrate-binding pockets and remove the invading chemical from the circulation or tissue, thus acting as a detoxification mechanism.

Although proteins are mostly employed for hapten conjugation, synthetic polypeptides such as Poly-L-glutamic acid, polysaccharides and liposomes could also be used.

Mechanisms of Protein Binding
Most common reaction mechanisms forming covalent bonds and predicted to be involved in sensitisation are nucleophilic substitution on a saturated centre, nucleophilic substitution on an unsaturated centre and nucleophilic addition. Other reactions are also possible, such as electrophilic substitution (diazonium salts), radical reactions, and ionic reactions.

Hapten Inhibition
Hapten inhibition or "semi-hapten" is the inhibition of a type III hypersensitivity response. In inhibition, free hapten molecules bind with antibodies toward that molecule without causing the immune response, leaving fewer antibodies left to bind to the immunogenic hapten-protein adduct. An example of a hapten inhibitor is dextran 1, which is a small fraction (1 kDa) of the entire dextran complex, which is enough to bind anti-dextran antibodies, but insufficient to result in the formation of immune complexes and resultant immune responses.

Research
Haptens are widely used in immunology and related fields. Sensitising chemicals can cause different forms of allergy, allergic contact dermatitis, or sensitisation of the respiratory tract. Interestingly, discrete types of chemicals induce divergent immune responses: contact allergens provoke preferential type I hypersensitivity responses, whereas respiratory allergens stimulate selective type II responses, which could be very suitable for modelling how the immune response is polarised towards different types of antigens.

In allergology, *in vitro/in silico* tests for skin sensitisation, hazard identification, and potency evaluation on different drug and cosmetic components are highly preferred in early product development. The ability of a drug to act as a hapten is a clear indication of potential immunogenicity.
Hapten-specific antibodies are used in broad area of different immunoassays, immuno-biosensor technologies and immuno-affinity chromatography purification columns; those antibodies could be used to detect small environmental contaminants, drugs of abuse, vitamins, hormones, metabolites, food toxins and environmental pollutants.

For the definition of an allergen, the following text has been taken from Wikipedia on 29/05/2023 but has been modified where necessary for grammar and where appropriate for content relevant to the subject of patch testing and skin prick testing.

An allergen is something that causes allergies in humans.
Dust, pollen and pet dander are all common allergens. It is possible to be allergic to anything from chlorine to perfume. Food allergies are not as common, but some foods, like peanuts, nuts, seafood and shellfish cause serious allergies in lots of people.

Common Allergens

Some common allergens could be:

Animal products
Fel d 1 (cat allergy)
Fur and dander
Cockroach calyx
Dust mite excretion

Drugs
Penicillin
Sulphonamides
Salicylates
Local anaesthetics

Insect stings
Bee sting venom
Wasp sting venom
Mosquito stings

Mould spores

Plant pollens ("Hay Fever")
Grass
Weeds
Trees

Foods
Celery and celeriac
Corn or maize
Eggs (typically albumen, the white)
Fruit
Pumpkin
Legumes
Beans
Peas
Peanuts
Soybeans
Milk
Seafood
Sesame
Soy
Tree nuts
Pecans
Almonds
Wheat

Other
Latex
Metal (debatable!)

This is unfortunately a particularly poor or at best an incomplete definition of "Allergen" by Wikipedia.

Allergy is one of the most misunderstood, misused, and abused terms in the entire medical field.
A lay person perhaps suffering from Hay Fever or nickel sensitivity will have a very different understanding and comprehension of the term "allergy" compared to a professional medical Allergy Specialist who will have undergone several years of education and training in this speciality field of medicine.

Allied very closely with the term "allergy" is the term "allergen". This is where the contention arises over the use of the term "allergen" or the use of the term "hapten" when describing the myriad substances known or suspected to cause Allergic Contact Dermatitis, and therefore in the realm of the Dermatology Specialist.

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.

These allergens are the well-known house dust mites, pollens, mould spores, animal danders, stinging insect venoms, and foods. But also included in this definition of the Type I (Gell and Coombs) classification of reactivity are non-biological and non-protein derived substances such as certain drugs (e.g., penicillin), and rarely some other substances. The defining factor is that these substances have invoked in the individual an immunological response that causes the production of IgE (Immunoglobulin E) antibodies and initiated an allergic response cascade of other immune cells (such as cytokines, mast cell tryptase, etc.) that cause an immediate hypersensitivity reaction.

By immediate is meant within 30 minutes. The classical signs and symptoms of this IgE-mediated allergic response are then rhinitis and/or urticaria and/or asthma and/or gastro-intestinal discomfort.

Treatment of Type I hypersensitivity to allergens is manifold:

1. Removal of the stimulus, such as the pollen or the animal dander or the food.
2. Treatment of the symptoms by local topical antihistamines or bronchodilators, or locally applied steroids.
3. Treatment of the symptoms by systemically applied steroids to dampen the immunological response.
4. Allergen-specific Immunotherapy to build up tolerance in the individual against the specific allergens to which the patient is sensitised and that have caused the symptoms. Usually this involves a 3-year course of injections of ever-increasing dose (volume and concentration) of the allergen to which the individual is sensitised. Recent innovations include the use of sprays or drops or tablets to replace the injections.

Recently, immunotherapy against food allergens has become possible, utilising either increasing oral doses of the problem food (usually peanut) or the use of a peanut patch affixed to the arm to provide slow release of the peanut allergen over weeks and months of treatment.

There is also the interesting exception to the rule on biological allergens, with the nickel immunotherapy vaccine that is used to treat hypersensitivity to nickel metal. This is a unique product and remains controversial, though documentation and personal-use anecdotes confirm it can indeed be clinically effective.

Of course, in order to remove the stimulus and even more importantly to plan the 3-year course of allergen-specific immunotherapy, it is absolutely essential to reliably identify the substance or substances that are causing the symptoms of allergy in that individual patient.

There are primarily two main types of diagnostic test used in mainstream medicine to identify these Type I allergens:
1. *In vivo* Skin Prick Tests (SPT)
2. *In vitro* s-IgE tests.

Skin Prick Tests
There is an excellent, though rather USA-centric Wikipedia text on Skin Prick Tests at ..... https://en.wikipedia.org/wiki/Skin_allergy_test

A patient suspected of a sensitivity to one or more classical Type I allergens may be skin prick tested by their Allergy Specialist. This involved the placement of a single drop of an allergen solution of a particular allergen (such as Cat dander, or House Dust Mite, or Bermuda Grass pollen) onto a site on the patients forearm and then a prick is made through that drop by a metal lancet into the superficial dermis of the patient. If there is a resultant wheal and flare reaction within 15 minutes, then the patient is considered to be sensitised to that particular substance. Usually, a testing panel of 10 to 20 allergens could be used in this way, perhaps up to 50 tests on the patients back. The result is measured semi-quantitatively.

Such Skin Prick Tests have always been the default diagnostic test for such allergens, due to their relatively easy, low cost and simple test procedure, though infants and small children may well disagree! However, the use of *in vitro* tests is becoming ever more widespread due to the wide range of allergens, the reliability and the fully quantifiable results.

Intra-dermal tests are rarely used nowadays outside of USA due to the risk of anaphylaxis, and the commercial non-availability of suitable highly diluted allergen solutions.

The "Scratch test" is no longer used outside of USA due to its non-standardised practical procedure and reaction assessment.

Skin Prick Tests and s-IgE blood tests are most usually ordered or performed by an Allergy Specialist, though sometimes some other Specialist may do so; for example Paediatrician, ENT Specialist, or Chemical Pathologist in a laboratory. A trained Nurse may also do the SPT and collect the blood sample for the laboratory-based in vitro s-IgE tests.

The relative advantages and disadvantages, and performance characteristics of Skin Prick Tests and s-IgE blood tests used to identify Type I allergens can be endlessly debated, but one thing is perfectly clear, they are not skin Patch Tests.
But wait, there is of course an exception!

Atopy Patch Tests
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. 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.

s-IgE Tests
Until perhaps a decade or so ago, measurement of a patients Total IgE would be used to assess if the patient was "allergic or not allergic" In theory, the t-IgE value measured in U/ml or kU/L of serum would be a summation of all the different allergen-specific IgE antibodies produced by the patient's immune system against one or more allergens. A Reference Range was established, which for Caucasian-race adults whereby over 100 kU/L indicated allergy, and corresponding values down to age 3 months. However, nowadays, the t-IgE test (or rather assay) is rarely used as there are other much more precise tests for allergen-specific IgE (s-IgE) available and widely used.

The s-IgE test measures allergen specific IgE against a single native allergen, or a component allergen (such as Fel-d-1) or a group of related allergens (such as Mixed European Grasses). The original blood (or serum) test was called RAST (Radio-Allergo-Sorbent Test) developed in the 1980's after the initial discover of IgE by the Ishizaka's in USA and Johannsson & Bennich in Sweden.

In the past 2 decades this test has been further refined so that today there are approximately 500 different allergens that can be reliably identified by this "ImmunoCAP™" lab-based technology. The Allergy Specialist however needs to determine which allergens are most likely and so which should be tested for; with usually one to a dozen tests only. There is therefore a real risk of missing relevant problem allergens even by an experienced Allergy Specialist.

Even more recently is the introduction and commercial availability of a single test that identifies almost 300 different allergens and component allergens in a single small blood sample and laboratory procedure "Allergy Xplorer", thereby providing a definitive comprehensive identification of Type I allergens in approximately 97% of all clinical cases.

IgG-based Tests
These IgE-based tests such as ImmunoCAP and Allergy Xplorer are not to be confused with IgG-based tests that measure allergen-specific IgG against usually foods, for example the Cambridge Test and the FOX/Food Xplorer Test. The clinical rationale and value of such IgG-based tests is still under investigation and needs to be conclusively determined, though they seem to be useful in selected clinical cases such as identification of food intolerance causing IBD.

Patch Tests
Patch tests are used to identify substances that elicit a Gell & Coombs Type IV hypersensitivity reaction in sensitised subjects, to cause Allergic Contact Dermatitis. Note however that sensitisation and symptom induction can be not only by contact but also by inhalation.

With patch tests, the substances are most usually homogenised in an inert carrier such as petrolatum, or in liquid form, and are applied topically to the skin in standard concentrations and for a standardised period of time (usually 3 days and 7 days) and under occlusion to aid penetration of the hapten molecules into the skin layers. The haptens thereby penetrate the skin, where they bind with skin proteins, thereby forming hapten-protein complexes. These complexes are recognised as foreign by antigen-presenting cells, such as Langerhans cells found in the skin. The antigen-presenting cells then process the hapten-protein complexes and present hapten-derived peptides to the T lymphocytes, thus initiating the immune response. This appears as erythema, papules or vesicles at the site of the application of the hapten, which strongly though not conclusively suggests sensitisation to that particular hapten. An irritant reaction to the substance can also cause apparently similar reactions that need to be differentiated from a true Type IV reaction by the expert Dermatologist.

Patch test panels can be a series of substances that are:
1. Related chemicals, such as Preservatives or Metals
2. Found in particular industries, such as Dental or Bakery
3. Considered to be the most important chemicals in a particular country, such as Sweden, or USA or Europe or International.

The great majority of patch test substances are chemicals, and not of biological origin.
Such chemicals are classically as follows:

- Metals
- Dyes
- Plastics
- Glues
- Preservatives
- Fragrances and Perfumes
- Drugs
- Rubber chemicals
- Shoe chemicals
- Dental chemicals
- Chemicals found in Cosmetics, Sunscreens and Hairdressings

However, there are a significant number of patch test substances that are indeed of biological origin, but have been proven to operate through the Type IV pathway to invoke Allergic Contact Dermatitis. Examples are:

- Balsam of Peru / *Myroxylon pereirae*
- *Compositae*
- Many fragrances were originally biologically derived, but may be synthesised.

Summary
A hapten is a low molecular weight substance that by itself is not immunogenic, i.e., capable of eliciting an immune response from a person's immune system when exposed to that hapten. However, when the hapten becomes bound to a larger carrier molecule in the skin, such as a protein, such as human serum albumin, it can generate an immune response in the sensitised host. At that point, the hapten has evolved into an allergen.

Conclusion
Given the definitions above of "hapten" and "allergen" and coupled with the background information on the various types of tests available, whether Skin Prick Tests, s-IgE tests, Atopy Patch Tests and of course Patch Tests, then the reader must determine for themselves when is the correct time to choose the term "allergen" or the term "hapten" in the context of patch testing.
To me, the answer is clear.
What do you think?

Conflict of Interest
The author has originally a scientific background but also decades of experience in the business area of patch testing with haptens and skin prick testing with allergens, and therefore endeavours to give a balanced view of both clinical fields and all tests used to identify haptens and allergens.

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.

12 What's New at Chemotechnique

BasIQ Ultra™

The same IQ experience – with less environmental impact.

The BasIQ Ultra™ shares all features found in the acclaimed IQ Ultra™ Patch Test Units, but without the plastic cover plate.

The BasIQ Ultra™ is a Patch Test Unit especially designed and constructed for:

1. Clinics that are used to open-type Patch Test Units
2. Clinics that do not pre-load haptens yet are still eager to experience the superior IQ features.

By removing the cover plate from over the chambers, the BasIQ Ultra™ has a smaller physical footprint of the unit itself, which results in less materials used for product packaging, which in turn has a smaller environmental impact due to less materials consumed, and less waste produced.

Just because the BasIQ™ Chamber does not have a cover plate and is therefore not intended for pre-loading the chambers, this also obviates the use of the Application Device™ for hapten loading. Instead, a visual guide is included in the BasIQ Ultra™ product package to facilitate the hapten loading of the chambers.

BasIQ Ultra™ is the comfortable and reliable patch test unit choice as it features the acclaimed IQ chambers, mounted on hypoallergenic premium quality carrier tape, but without the plastic cover plate found on the IQ Ultra.

The IQ Chambers are made of soft polyethylene foam chamber with non-sensitising medical grade acrylic adhesive including integrated filter papers, onto non-woven hypoallergenic carrier tape. There are no uncomfortable metal parts that might react chemically with the haptens under test.

Each box of BasIQ Ultra™ contains just 50 Test Units, in contrast to the 100 Test Units of the IQ Ultra™ box.

The unit size is 52 x 125 mm, compared to the 52 x 118 mm of the IQ Ultra™ Units, though both comprise 10 test chambers sites for 10 haptens. The recommended dosage of hapten is the same 25 ul as for the IQ Ultra and IQ Ultimate.

Features & Benefits

The new BasIQ Ultra™ Patch Test Unit has important advances:

1. Each chamber has a filter paper incorporated which eliminates adding loose filter papers to facilitate handling of liquid haptens.
2. The rim of each chamber has an adhesive layer to optimise adhesion to the skin and to eliminate leakage. This makes IQ Ultra™ a closed-cell system enhancing occlusion and confining the test reaction within the chamber parameter.
3. The size of the IQ Ultra™ chamber strip is exceedingly small, to allow the application of multiple test units to patients' backs.
4. The chambers are made of thin and soft polyethylene foam material to maximise patient comfort.
5. The highest quality hypoallergenic surgical tape is used for the BasIQ Ultra™. However, unlike the IQ Ultra™, there is no plastic cover over the 10 chamber sites.

Product Information

- BasIQ Ultra™ is made of additive-free polyethylene plastic foam with a filter paper incorporated.
- BasIQ Ultra™ is supplied in units of 10 chambers (in 2 rows of 5 chambers/row) on a hypoallergenic non-woven adhesive tape.
- The volume of the chamber is 32 µl and the inside area of the chamber is 64 µl.
- The width of the tape is 52 mm, whilst the length is 125 mm.

Packaging & Service

The IQ Ultra™ is supplied in cardboard boxes containing 50 units per box.
(50 chamber strips each of 10 chambers).

Reading Plate for IQ Ultra™ is supplied in each box.

Availability

The BasIQ Ultimate™ is available worldwide through the extensive global network of Chemotechnique Diagnostics distributors. You will need to register and to log in to the Chemotechnique website to see the distributor for your country.

Ordering Information

BasIQ-U

Lanolin is Contact Allergen of the Year 2023

Background
Lanolin has been declared by the American Contact Dermatitis Society as the Contact Allergen of the Year for 2023 at their annual congress in March 2023.

Natural Occurrence
Lanolin is a fat-like substance derived from wool grease or secretions from the sebaceous glands of sheep. Lanolin is composed of esters, di-esters, and hydroxyl esters alcohols and acids of high molecular weight. There are significant differences between the lanolin derived from different sheep breeds, and their habitats, as well as the extraction methods used to obtain the lanolin. Amerchol L101 is the brand name of a commercial product that is based on 10% lanolin in alcohol, with added mineral oils.

Natural Exposure
Lanolin is commonly found in personal care products (PCPs), personal hygiene cleaner products, creams, moisturisers, lotions, lipstick, lip balms, shampoo, soaps, and topical medications and drugs.

It may also be found in more household and industrial-type products such as furniture polish, detergents, ink, leather, textiles, and waxes and products intended to prevent metal corrosion.

Medical Usage
Lanolin is used as a treatment for skin conditions, for example, eczema, xerosis, and nipple soreness in breastfeeding women because of its ability to penetrate deep into the epidermis.

Properties of Lanolin
Lanolin possesses unique properties that make it a valuable ingredient in various skincare products where it acts as an effective emollient, providing moisturisation and water repellence to the skin. However, it is important to note that lanolin contains allergenic components, including lanolin alcohols, lanolin acids, and lanolin esters, which can trigger allergic reactions in susceptible individuals.

Prevalence as an Allergen
The prevalence of lanolin allergy varies among different populations and geographical regions. Patch testing studies have reported a prevalence ranging from 1% to 3% among patients referred for evaluation. However, higher rates have been observed in specific high-risk groups, such as healthcare workers and individuals with pre-existing dermatitis. Patients with atopic dermatitis (eczema) may also have an increased risk of developing a lanolin allergy.

Mechanisms of Sensitisation
The exact mechanisms by which lanolin sensitises individuals are not fully understood. Several theories have been proposed, including the direct allergenic properties of specific lanolin components and cross-reactivity with other allergens. It is believed that repeated or prolonged exposure to

lanolin is required for sensitisation to occur. Factors such as the concentration of lanolin in products, individual susceptibility, and co-existing skin conditions can influence the likelihood of developing a lanolin allergy.

Clinical Presentation
Patients with lanolin allergy may present with a spectrum of cutaneous manifestations, ranging from mild erythema and pruritus to severe vesicular or eczematous reactions of Allergic Contact Dermatitis. The affected areas typically correspond to sites of exposure, such as the face, hands, and areas in direct contact with lanolin-containing products. Importantly, lanolin allergy should be considered in cases of recurrent or chronic dermatitis that are unresponsive to conventional treatments. Atopic Dermatitis may also be involved, which is paradoxically interesting as the lanolin-containing product may have been used to treat or ameliorate an Atopic Dermatitis condition such as eczema, but thereby aggravating the symptoms.

Prevalence
Different studies show differing rates of prevalence, from 0.5% to 1% of the general population, though of course different figures will be obtained if testing specific cohorts such as ACD patients where USA prevalence rates are shown to be around 3%, with approximately 80-85% clinical relevance. Various studies report that there has been a slight increase in prevalence over recent years.

Diagnostic Methods
Accurate diagnosis of lanolin allergy requires a thorough clinical evaluation and appropriate diagnostic testing. Patch testing, the gold standard for detecting contact allergies, involves the application of lanolin to the patient's skin. The patches are then removed after 48 to 72 hours, and the skin is examined for signs of an allergic reaction. A positive reaction to lanolin, characterised by erythema, papules, or vesicles, confirms the diagnosis.

Originally, lanolin alcohol 30% in petrolatum was used as the patch test substance, though in 2011 this was replaced in the NACDG Series by Amerchol L-101 50%, with an immediate increase in the detection rate.

SPIN Factor
The Significance Prevalence Index Number for Lanolin is 140.5, which places it in the top 25% of the 75 haptens/allergens in the NACDG Series. It is also placed 8th in the SPIN Rankings of the Extended European Baseline Series with a Factor of 178, so very similar to Fragrance Mix II.

Management Strategies
Management of lanolin allergy primarily involves avoidance of lanolin-containing products. Patients should be educated on how to identify and avoid products that contain lanolin. Reading product labels for lanolin or its derivatives is essential. Lanolin-free or lanolin-alternative products can provide suitable alternatives for individuals with lanolin sensitivity.

In cases where complete avoidance is challenging, such as in occupational settings, the use of protective measures, such as gloves or barrier creams, should be considered. Additionally, patients should be advised to adopt a comprehensive skincare regimen that includes gentle cleansing, moisturisation, and appropriate use of topical corticosteroids or immunomodulators as needed.

Conclusion
Lanolin is a very significant contact allergen, which is confirmed by the fact that it is present in almost all national and international patch test series of haptens/allergens. Understanding the properties, prevalence, mechanisms of sensitisation, clinical presentation, diagnostic methods, and management strategies associated with lanolin allergies is crucial for Dermatologists. By accurately diagnosing and effectively managing lanolin allergies, healthcare providers can improve patient outcomes, reduce morbidity, and enhance the overall quality of care for individuals affected by this condition. Further research is needed to better elucidate the immunological mechanisms underlying lanolin sensitisation and to develop improved diagnostic tools (such as optimisation of patch test hapten dose and optimisation of hapten used, as well as the development of alternative products for individuals with lanolin allergies.

Patch Test Hapten from Chemotechnique

Art no	Name	Conc.	Veh.
W-001	LANOLIN ALCOHOL	30.0%	pet

Lanolin Allergic Reactions: NACDG Experience, 2001 to 2018

By Jonathan I. Silverberg, et al.
In DERMATITIS, Vol 33, No. 3, May-June 2022, pp 193-199
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This mammoth-scale study of over 43,000 patients, was based on a retrospective analysis of patients who were patch tested with lanolin alcohol 30% or Amerchol L-101 50% in petrolatum by the North American Contact Dermatitis Group between 2001 and 2018.

The NACDG Database is an extremely authoritative indication of the incidence of sensitivity to different haptens/contact allergens in the American population. This is particularly so when using a single standardised test panel (such as the NACDH standard panel) over a long period of time, (such as 18 years).

Lanolin Alcohol vs Amerchol L101: In this case with the investigation of lanolin sensitivity, over the years the NACDG standard panel has evolved somewhat, with the shift from testing using lanolin alcohol 30%, giving way to the use of Amerchol L101 50% in petrolatum from 2011. This was motivated because previous studies had shown more positive patch test reactions to Amerchol L-101 than to lanolin alcohol. This change to Amerchol L101 in the NACDG Screening series immediately showed a higher rate of positivity, thereby affecting the trend data.

Before the changeover from Lanolin Alcohol 30% to Amerchol L101 in 2011, the prevalence of positive reactions to lanolin alcohol 30% was 2.16% (515/23,888). After the changeover to Amerchol L-101 50%, the prevalence significantly increased to 4.63% (916/19,803) between 2011 and 2018. The proportions of currently relevant and allergic reactions remained similar over the changeover period. In this study, Amerchol L-101 had a higher current clinical relevance and increased reaction rates than lanolin alcohol.

However, warn the study authors, a PPTR to Amerchol L-101 must be interpreted carefully because the mineral oil in Amerchol may cause irritation and false-positive results. This may explain the higher proportions of +/− reactions that have been observed in the past decade. Some studies have previously suggested that using both Amerchol L-101 and lanolin alcohol would increase the likelihood of detecting a true lanolin allergy. In summary, Amerchol L-101 leads to the detection of additional cases of lanolin allergy when compared with lanolin alcohol alone, but it may increase the false-positive rate due to irritant reactions. Lastly, the "lanolin paradox" (showing a negative patch test reaction on normal skin, but a positive patch test reaction on dermatitis-afflicted skin) may lead to an underestimation of the prevalence of lanolin allergy.

SPIN Factor: Of particular interest in this study was the use of the SPIN Factor to determine the relative clinical importance of any individual hapten in comparison to all other haptens.

The Significance-Prevalence Index Number (SPIN) was calculated, according to the following formula, to assess the relative importance of lanolin compared to other haptens/contact allergens.
SPIN = (number of patients allergic to lanolin / total number of patients patch tested) × ([1 × percentage with definite relevance] + [0.66 × percentage with probable relevance] + [0.33 × percentage with possible relevance]) × 100.

In this study, the mean SPIN for lanolin was 140.5 overall, 137.8 in adults and 193.8 in children, thereby placing it in the top 25% of the 70 allergens on the NACDG screening series. Between 2001 and 2010, the SPIN for lanolin alcohol 30%, increased steadily during the period of 10 years. After 2011, and the changeover to the use of Amerchol L101 as the test substance, there was a sharp spike in SPIN until 2014, after which the trend returned to the previous gradual increase over time.

Other Interesting points and snippets from the results of the investigation were as follows:

- Of the 43,691 subjects included in the study, 3.3% had a positive reaction to and 2.8% were considered to be clinically relevant.
- The strength of the positive reactions was + for 52%, ++ for 18% and +++ for just 6% of subjects.
- Clinically, the most common primary anatomic sites of dermatitis were the hands, at 20.7% Scattered/ generalised distribution was 19.6%, and face was 17.0%.
- Allergic reactions to lanolin were more common in children (4.5%) than in adults (3.2%).
- Compared with non-allergic patients, lanolin-allergic patients were more likely to have history of allergic eczema or allergic rhinitis, male sex, older than 40 years, or Black race.
- Common lanolin sources were personal care products and drugs/medications.
- Among the adults and children with an allergic reaction to lanolin, the most common source of lanolin was Personal Care Products, particularly moisturisers/lotions/creams (23%), as well as lipsticks and lip balms (4%).
- Only 2.24% of positive patch test reactions were linked to occupation, mostly in women (69%), those older than 40 years (66%), and Whites (84%). Rarely, industrial materials, for example, metalworking fluids (0.3%), were sources of lanolin in adults with an allergic reaction to lanolin.
- Individuals with occupationally related lanolin allergy most commonly had any involvement of the hands (78%), and the most common source was from moisturisers/lotions/creams (22%).
- Most lanolin-allergic patients had a primary (76%) or any (65%) final diagnosis of ACD, compared to 11% and 15% respectively with a primary or any final diagnosis of atopic dermatitis (AD).
- When comparing lanolin-allergic adults with non-allergic adults, lanolin-allergic adults were more likely to have a final diagnosis of ACD or AD and less likely to have a diagnosis of other dermatitis, irritant contact dermatitis, psoriasis, seborrheic dermatitis, and nummular eczema.
- When comparing lanolin-allergic children with non-allergic children, lanolin-allergic children were more likely to have a final diagnosis of ACD and less likely to have a final diagnosis of other dermatitis and irritant contact dermatitis.
- Adults with lanolin allergy were less likely to have a final diagnosis of AD than children.
- Of all lanolin-allergic patients with dermatitis affecting the legs and no history of eczema, the most common final diagnoses were ACD (70%) and stasis dermatitis (SD, 11%); the most common non-primary diagnosis was SD (62%).

For details of the study design and results please consult the original article in DERMATITIS journal.

Systematic Review of Allergic and Irritant Contact Dermatitis of the Vulva

By Sander Vanderweegs et al,
In CONTACT DERMATITIS, April 2023, Volume 88, Issue 4, pp 249-262.
https://doi.org/10.1111/cod.14258

This systematic review of Vulvar Allergic Dermatitis is believed to be the first ever undertaken and published and so should provide valuable insights into both the condition and the use of the patch test to identify potential problem haptens.

The study authors whittled down 580 records in the literature to just 17 studies that were assessed as being within the inclusion criteria. These 17 studies comprised 1,363 patients, from USA, Europe, and Australia/NZ, during the period 1992 to 2020.

Patch testing was done in the various studies utilising one or more of the following standard series:

- European Standard Series
- Corticosteroids
- Preservatives
- Medicaments
- Cosmetics
- Patient's Own Products

Although Patch testing was used as the diagnostic test for assessment, its accuracy could not be determined against any other standard method, though positive patch test results were considered relevant when clinical improvement occurred after removal and avoidance of the indicated allergen/hapten.

Focus is given by the authors to the identity of the haptens/allergens as indicated by the positive patch test results.

- Nickel allergy was common in most studies, which is perhaps unexpected but dietary nickel intake could well be the cause, as avoidance has anecdotally been reported to resolve anogenital symptoms, presumably through a reduction in the urinary excretion of the nickel.

- Cobalt was also frequently a positive patch test reaction. Again, this may well be due to urinary excretion of cobalt, as an oral challenge with cobalt has previously been shown to cause a flare of the dermatitis.

- Positive reactions to multiple classes of topical drugs were also common and included reactions to antibiotics, neomycin, framycetin, clioquinol and quinoline mix. However, the relevance of these specific antibiotics has been decreasing over the years since usage of these products is diminishing.

- Contact allergy to corticosteroids was also frequent and obviously particularly relevant, considering the common use of topical corticosteroids to treat vulvar disease.

- Contact allergy to local anaesthetics was another frequent occurrence, and of defined interest here, as local anaesthetics and topical haemorrhoid preparations are typical OTC products frequently and repeatedly used to relieve vulvar symptoms.

- Other topical drugs causing positive reactions included antiseptics, antimycotics, non-steroidal anti-inflammatory drugs, immuno-suppressants and topical hormones.

- The common finding of positive reactions to Fragrance mix I and *Myroxylon pereirae* (Balsam of Peru) was not unexpected, and exposure to fragrances may relate to use of cosmetics, perfumes, fabric, scented toilet tissue, haemorrhoid creams, topical drugs, female hygiene products, etc.

- Preservatives are still of concern, despite evolving regulatory restrictions. Formaldehyde releasing preservatives can be found in up to 25% of the cosmetic products in the United States and Europe. The non-formaldehyde releasing preservative methyldibromoglutaroni trile has been banned by the European Commission from leave-on products in 2003 and later, in 2007, from rinse-off products. Sensitisation remains high in Europe however, since it is still used in other, non-regulated sources like industrial materials, while in the United States it is still used in skin care products.

- Other cosmetic constituents such as para-phenylenediamine (PPD) may cause cross-reac tions with para-aminobenzoic acid (found in sunscreen preparations), sulphonamides/sulp honylureas (medication), azo dyes (clothes), benzocaine/tetracaine (local anaesthetics), etc. Patients with sensitisation to PPD have a higher risk of simultaneous reaction to other chemically related dyes.

- Disperse dyes, including Disperse Orange 3, Disperse Blue 106 and Disperse Blue 124, were another recurrent allergen class in this study. Possible exposure to these dyes came from underwear and patients with allergic reactions to these agents should therefore be advised to avoid dark, synthetic clothes and wear clothing made out of non-synthetic fibres such as cotton.

- Dermatitis of the ano-genital area has previously been shown to be associated with contact allergy to lanolin that is found in cosmetics, shampoo, shaving creams, and topical medica ments.

- Of interest are also rubber additives and sulphur containing vulcanising chemicals such as Thiuram mix, carba mix and Mercapto mix in particular. Vulvar exposure to these allergens may occur through condoms or other contraceptives. These additives typically cause a type IV allergy, in contrast to natural rubber (latex) itself, which causes a type I (IgE-mediated) allergy.

- Some studies identified botanical allergens such as chamomile, tea tree oil, *Arnica montana,* calendula, Primin and the *Compositae* mix as sensitisers.

- Tea tree oil was shown to be the most common sensitiser among essential oils and is espe-cially potent when oxidised. Reactions to the *Compositae* family of plants (chamomile, ca lendula, *Arnica montana*) are comparatively rare.

- Spices were a common culprit, giving multiple relevant positive reactions. Spices involved were cayenne pepper powder, coriander powder, curry mix (“Djawa”) powder, nutmeg powder, onion powder, pepper (white) powder and peppermint oil. A previous study has shown that patients who reacted to colophonium, Balsam of Peru or Fragrance mix had significantly more reactions to nutmeg, paprika and cloves compared to patients who did not react to colophonium, Balsam of Peru or Fragrance mix. Fragrance mix was the most important indicator allergen for these three spices.

The study authors came with two specific recommendations; on the panel of patch test haptens/ allergens to be used, and on the benefit of late patch test readings.

1. The Patch Test panel of haptens/allergens: As one of the studies included in the review stated, using only the EECDRG Series would have missed 31.1% of positive results. This illustrates the importance of broadening the test spectrum with othe test substances, such as personal care products, extended and specialised series, common over-the-counter pro-ducts, etc. Recommendations for the addition of allergens to the European Baseline Series have been made that include sodium metabisulphite, 2-bromo-2-nitropropane-1,3-diol, diazolidinyl urea, imidazolidinyl urea and Compositae mix II.

2. Testing on Day 7 for late reactions: Some studies in this review performed an additional reading at day 6 or 7 to identify late corticosteroid reactions. This is in line with the findings of other prominent researchers who found that 13.5% of contact allergies would have been missed when no reading was performed on day 7. Topical drugs (corticosteroids not included) and corticosteroids were the two groups that gave the most late positive reactions, with 33.3% and 28.4%, respectively. The individual allergen with the highest proportion of new positive reactions was neomycin sulphate (81.5% of total). These findings suggest a need for readings at day 7 to identify late reactions that could otherwise go undetected.

For details of the study design and results please consult the original article in CONTACT DERMA-TITIS journal.

Epoxy allergy: Investigation of a modern industry

By Tina Lejding et al,
In CONTACT DERMATITIS, May 2023, Volume 88, Issue 5, pp 383-388
See https://doi.org/10.1111/cod.14293

The occurrence of 5 cases of epoxy resin allergy at a manufacturing plant of carbon-fibre-reinforced epoxy plastics prompted a review of all the workers in that factory to assess occupational dermatoses and contact allergies at that manufacturing plant in Sweden.

As background information, epoxy resin systems include epoxy resins, curing agents, and modifiers. ERSs, are a frequent cause of occupational allergic contact dermatitis (OACD). Resins based on diglycidyl ether of bisphenol A (DGEBA®) are the most commonly used, and the majority of the epoxy resins used worldwide are derived from DGEBA®. In contrast, whereas fewer epoxy resins are based on diglycidyl ether of bisphenol F (DGEBF®). Some products contain both bisphenol A and bisphenol F epoxy resins.

In this particular investigation, the chemicals of interest, according to their SDS, were as follows:

1. NM Infusion 664 resin: comprising: DGEBF® (60%–80%) + DGEBA® (10%–30%) + BDDGE (10%–30%); trimetylolpropantriglycidylether (5%–10%).

2. NM 675N hardener: Bis(aminometyl)norbornan (60%–100%).

3. NM 650B hardener: Isophorone diamine (30%–60%); poly(oxypropylen)triamin (30%–60%).

Other Interesting points and snippets from the results of the investigation were as follows:

- ERSs are the most important allergens in construction workers in Finland. However, exposure to ERS substances can also be non-occupational, but the sensitisation through private use is largely unknown.

- Another study from Finland of patients with occupational allergy to ERSs during a 25-year period (1991–2014) showed that 82% reacted to DGEBA®. Therefore, the inclusion of DGEBA® in the Baseline Series would detect the vast majority of contact allergy to ERSs.

- ERA sensitivity is known to be acquired within a short time of exposure.

- In this particular investigation, 28% (7/25) of the workers showed reactions to ERSs when patch tested, using the Swedish Baseline Series, with four out of the seven patients (57%) testing positive to DGEBA® that is included in the Swedish Baseline Series.

- In the Swedish Baseline Series as well as in ICDRG Baseline Series and the ESCD Baseline series, an epoxy resin based on DGEBA® is included.

- The Swedish Baseline Series comprised at the time of testing (2019-2020) a total of 30 haptens. The current Swedish Baseline Series comprises 29 haptens.

- In this particular investigation, additional contact allergies to ERS components were found in three patients by testing with the Epoxy Series.

- The *ad hoc* Epoxy Series used by these investigators at the time of testing (2019-2020) comprised 19 haptens. The current Epoxy Series comprises 11 haptens. For full details of the *ad hoc* Epoxy Series used in this investigation, please see below, and consult the original article in CONTACT DERMATITIS journal.

- As usual, if possible, testing with the patients' own material from the workplace may reveal additional sensitivities and so should be used to find all relevant occupational contact allergies.

- Education of susceptible workplace staff, not only on induction, but repeatedly throughout their engagement, has been shown in many studies including this one, to be a necessary step to reduce the incidence of OACD. Updated Safety Plans should be made as necessary.

- Preventive measures include education, safe working places, routines, and personal protection equipment (PPE) will all contribute to a reduction in the OACD.

- In a German study reporting an increasing trend for contact allergy to ERSs among construction workers, effective measures to prevent sensitisation was pointed out to be needed urgently. In a Danish study it was concluded that despite efforts to lower the incidence of sensitisation to ERSs by a compulsory educational program before commencing work with ERSs, the

incidence of sensitisation to ERSs was increasing. Another Danish study showed that only one third of patients with contact dermatitis caused by ERSs used protective gloves, and that only half of the patients had participated in a compulsory educational program.

If a worker presents with apparent OACD, then a medical investigation including patch testing is necessary to find any relevant contact allergens. As a first step, a national baseline series needs to be included in the investigation, and such patch testing will most likely find the majority of contact allergies to ERSs since DGEBA® is included in such a standard screening series. However, it is important also to test additional contact allergens to which the worker is exposed, such as by using an Epoxy Series. Patients own products from the workplace should be evaluated and if possible tested. Only after such an investigation and the validation of its findings for relevance, it is possible to correctly recommend proper actions and further preventive measures for the individual worker, and for the workplace as a whole.

The *ad hoc* Epoxy Series used in this investigation comprised the following haptens:

	Name	Conc.
1.	Methenamine	2% pet
2.	Triethylenetetramine	0.5% pet
3.	Diethylenetriamine	1% pet
4.	Isophorone diamine	0.1% pet
5.	Epoxide 8	0.5% alc
6.	Butyl glycidyl ether	0.1% pet
7.	o-Phenylenediamine	1% pet
8.	Bisphenol A	1% pet
9.	Dibuthyl phthalate	5% pet
10.	m-Xylylenediamine	0.1% pet
11.	Epoxy resin, cycloaliphatic	0.5% pet
12.	2-Phenyl glycidyl ether	0.25% pet
13.	2,4,6-Tris(dimethylaminomethylene)phenol	0.5% pet
14.	3-(Dimethylamino)-1-propylamine	1% aq
15.	Epoxy resin, bisphenol F	0.25% pet
16.	1,6-Hexanediol diglycidylether	0.25% pet
17.	1,4-Butanediol diglycidyl ether	0.25% pet
18.	Trimethylolpropane triglycidyl ether	0.25% pet
19.	Ethylenediamine dihydrochloride	1% pet

Shedding a light on the importance of Photopatch testing: a 12-year experience in a Dermatology unit

By Carlos Codeço et al,
In CONTACT DERMATITIS, June 2023, Volume 88, Issue 6, pp 438-445
https://doi.org/10.1111/cod.14297

Photoallergic contact dermatitis (PACD) is a delayed-type IV hypersensitivity reaction that occurs when an exogenous agent (photo-allergen) is applied to the skin and subsequently exposed to ultraviolet (UV) and/or visible radiation. These exogenous agents are believed to be mostly organic UV filters and topical non-steroidal anti-inflammatory drugs.

Although PACD is currently considered to be uncommon, it is probably not be as rare as previously thought, particularly in areas with high sun exposure and common use of topical drugs and medicaments. However, it may still be under-diagnosed due to the under-use of the photo-patch test (PPT). In 2002, a task force from the European Society of Contact Dermatitis (ESCD) and the European Photo-Dermatology Society (EPDS) was established, with the purpose to recommend a consensus methodology for photopatch testing and compile a series of photo-allergens, in order to perform a European Multicentre Photopatch test study (EMCPPTS).

Based mostly on the results of this two-decade old study, there now exists a recommended European Baseline Photo-Patch Series with 20 chemical haptens, and an extended PPT series with 15 additional chemical haptens. Despite the existence of the PPT Series and the Extended PPS, the patients' own products should also be used for testing in selected cases.

In this study by the authors, based in Portugal, 3,788 consecutive patients were tested during the 12-year period, of which 223 were photo-patch tested.

Interesting points and snippets from the results of the investigation were as follows:

- 33.6% of photo-patch tested patients (75/223) gave positive reactions, but of these only 58.1% (72/124) were considered to be clinically relevant. This is in line with previous studies.
- Most relevant positive PPT reactions were caused by topical drugs, which significantly contrasts with ACD, where allergens in cosmetics are more frequently encountered than topical drugs
- Most of the clinically relevant positive reactions were to haptens within the PPT Series.
- Topical drugs were the most common cause (45.8%) of relevant positive PPT reactions, with the main culprits being NSAIDs (especially ketoprofen, benzydamine and etofenamate).
- Systemic drugs induced 9.8% of the PPT positive reactions, with fenofibrate, piroxicam, and hydrochlorothiazide tested as pure chemicals, and other three cases with preparations from the patients' tablets (amiodarone, fluvastatin, and hydroxychloroquine).

- UV absorbers/sunscreens were the second most frequent relevant photoallergens: 19.4% with benzophenone-4, and benzophenone-3, butyl methoxydibenzoylmethane, ethylhexyl salicylate, isoamyl-p-methoxycinnamate, ethylhexyl triazone (Uvinul T 150®), Diethylamino hydroxybenzoyl hexyl benzoic acid (Uvinul A Plus®) and Methylene bis-benzotriazolyl tetramethylbutylphenol (Tinosorb®M).
- No positive PPT reactions occurred with the other 'newer' UV filters tested.
- Five patients reacted to their own sunscreen with no reaction to the UV absorbers in the photo-allergen series, representing 13.9% of all relevant PPT reactions.
- The remaining relevant positive PPT reactions were caused by plants and cosmetics, including fig tree leaf extract (*Ficus carica*) and 8-methoxy-psoralen at 0.01% and 0.001% in pet. Other plants included *Angelica archangelica, Ruta graveolans,* and *Pelargonium graveolans*.
- Among the 223 photopatch tested patients, 44 patients had contact allergy, with 73 positive PT reactions, mostly to UV filters/sunscreen products (30) and topical drugs (23) . Eight patients had positive PT reactions to Tinosorb® M (six with reactivity to glucosides), one to Tinosorb® S, and six PT reactions to 'classical' UV filters, whereas the remaining 15 PTs occurred with the patient's own sunscreens tested 'as is'.
- As observed in most European studies and contrasting to South American or Asian cohorts, NSAIDs were the most frequent topical drugs eliciting relevant positive PPT reac tions. 5,11,16 Ketoprofen was the main culprit, due to its benzophenone moiety, which also explains its well-known cross-reactivity with piketoprofen, benzophenone-3 fenofibrate, and octocrylene.
- Topical benzydamine was the second commonest NSAID causing PACD, in accordance with previous results. Diclofenac, now frequently used in a gel for the treatment of actinic keratosis, was responsible for three relevant PPT reactions in the current cohort.
- Phenothiazines were recommended to be included in the photo-patch series of specific geographical regions. For example, Promethazine has been banned in other European countries, but is still widely used as an antipruritic cream in Portugal and other Southern European countries.
- Newer UV filters elicited fewer positive PPT reactions than the 'classical' UV filters (three positive PPT compared to six to the 'classical' filters), despite their wide use in European sunscreens. Classical UV filters are less photostable and have a low molecular weight (137.1–361.5 kDa) compared with the 'newer' UV filters, which have higher photostability and higher molecular weight (397.5–823.2 kDa). These characteristics act to reduce both epidermal penetration and chemical modification upon UV exposure, which may explain their lower reactivity in the PPT.
- No positive PPT was observed with six out of the nine 'newer' UV filters tested and seven of them did not cause any positive PPT reaction, reinforcing the likelihood of safety for most of these newer chemicals.
- The study showed a high number of potentially relevant PACD to plants using low concen trations of their extracts and highly diluted 8-methoxypsoralen from Oxoralen® capsules.
- Photopatch testing is not usually indicated in the investigation of phyto-photodermatitis or in dermatitis after exposure to a known phototoxic chemical, as a phototoxic test reaction will develop in most individuals. However, when the patient refers to low sun exposure or short contact with the possible culprit, photopatch testing performed with low concentrations of the chemical and low UV doses may indeed reveal photo-allergy. Furthermore, damage caused by phototoxicity may facilitate sensitisation, leading to overlapping conditions.

The study also emphasised the need to continuously improve the European Photo-Patch Baseline Series, adapting it to geographical differences and modifications in allergen exposure.
Further research is necessary to on the implementation of additional photopatch testing procedures, with different exposure times to the chemical haptens, different doses, and UV wavelengths for irradiation, which may increase the diagnostic performance of photopatch testing.

For details of the study design and results please consult the original article.

Chemotechnique manufacture a Photo-Patch Series PP-1000, comprising 30 chemical haptens.
The Photopatch Series contains chemicals and substances which one might find in skincare products which protect against the sun. The series contains chemicals that are UV-blockers, additives and pharmaceutical compounds that may become allergenic after UV activation.
Note that a special test method is required for this series (including a broad-spectrum UVA source).

	Art.No	Name	Conc.
1.	H-014C	BENZOPHENONE-3	10.0% pet
2.	H-023C	BENZOPHENONE-4	2.0% pet
3.	M-024B	4-METHYLBENZYLIDENE CAMPHOR	10.0% pet
4.	E-019C	ETHYLHEXYL METHOXYCINNAMATE	10.0% pet
5.	O-009	OCTOCRYLENE	10.0% pet
6.	I-009	ISOAMYL p-METHOXYCINNAMATE	10.0% pet
7.	A-006C	PABA	10.0% pet
8.	B-029C	BUTYL METHOXYDIBENZOYLMETHANE	10.0% pet
9.	B-037	BIS-ETHYLHEXYLPHENOL METHOXYPHENOL TRIAZINE	10.0% pet
10.	D-055	DROMETRIZOLE TRISILOXANE	10.0% pet
11.	K-002B	Ketoprofen	1.0% pet
12.	D-062	2-(4-Diethylamino-2-hydroxybenzoyl)-benzoic acid hexylester	10.0% pet
13.	O-010	ETHYLHEXYL TRIAZONE	10.0% pet
14.	M-037	Methylene bis-benzotriazolyl tetramethylbutylphenol	10.0% pet
15.	E-025	Etofenamate	2.0% pet
16.	D-063	DIETHYLHEXYL BUTAMIDO TRIAZONE	10.0% pet
17.	P-033	Piroxicam	1.0% pet
18.	D-065	DECYL GLUCOSIDE	5.0% pet
19.	H-020B	BENZOPHENONE-10	10.0% pet
20.	P-024B	PHENYLBENZIMIDAZOLE SULFONIC ACID	10.0% pet
21.	H-024B	HOMOSALATE	10.0% pet
22.	O-007B	ETHYLHEXYL SALICYLATE	10.0% pet
23.	P-035	Polysilicone-15	10.0% pet
24.	D-064	Disodium phenyl dibenzimidazole tetrasulfonate	10.0% pet
25.	T-014	TRICLOSAN	2.0% pet
26.	D-061B	Diclofenac sodium salt	5.0% pet
27.	T-026	Thiourea	0.1% pet
28.	H-001	Hexachlorophene	1.0% pet
29.	M-028	METHYL ANTHRANILATE	5.0% pet
30.	T-013	TRICLOCARBAN	1.0% pet

Contact Sensitisation to benzoisothiazolinone: IVDK Data for the years 2002 to 2021

By Johannes Geier et al,
In CONTACT DERMATITIS, June 2023, Volume 88, Issue 6, pp 446-455
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Benzisothiazolinone (1,2-benzisothiazolin-3-one; 1,2-benzisothiazol-3 (2H)-one; BIT; is a biocide and preservative due to its microbicidal and fungicidal properties. It is often used in combination with methylisothiazolinone (MI).

Almost every person in Western society and elsewhere comes into contact with BIT in one or another household products. BIT is also found in a wide variety of occupational substances and products. Classic examples of such household and occupational products are:

- Water-based Paints
- Varnishes
- Metal working fluids
- Printing inks
- Tattoo inks
- Polishes
- Cleaning fluids
- Fillers
- Floor coatings
- Adhesives
- Detergents
- Fabric softeners
- Fuels
- Wood preservatives
- Antifouling paints
- Vinyl/PVC gloves

The most important sources of sensitisation appear to be paints and varnishes.

Amongst the documented cases of sensitisation to BIT, there are several cases or small series of occupational sensitisation that was mostly acquired by handling concentrated solutions, in the manufacture of paints and varnishes, polyacrylate emulsions, paper, rubber, perfumes and air fresheners, carpets, and water softeners, as well as in laboratory activities. Other patients acquired occupational sensitisation to BIT from handling paints, metal working fluids, putty, wallpaper paste, shoe glue, a release oil in the ceramics industry, a rubber roller in lithographic printing, from wearing PVC gloves and by contact to a continuous positive airway pressure mask liquid soap. Allergic reactions to BIT were also observed in handicraft instructors, presumably by exposure to

glue, and in screen printers, without any obvious evidence of exposure.

BIT is a skin irritant in humans at concentrations above 0.05%. The optimal test concentration for clinical diagnostic patch testing with BIT was controversial in the 1990s. BIT 0.05% in petrolatum (pet.) often triggered questionable and/or irritative reactions. Nowadays, BIT is mostly patch tested at 0.1% pet.; in Germany, the BIT sodium salt at 0.1% in petrolatum is used for patch testing.

Reproducibility of positive reactions to BIT is not good, and is possibly influenced by the irritant nature of BIT at tested concentrations.

There has been an unsteadily upward trend of increasing sensitisation amongst many tested populations, with the current figure of approximately 5% in this European study to 7% in a USA study. The higher incidence in USA may be due to the fact that BIT is allowed in cosmetic products in USA but not in Europe.

Concomitant sensitisation to other substances is often reported, most usually to MI. Concomitant sensitization to BIT and other isothiazolinones may be acquired by co-exposure, in particular to BIT and MI, which are often used in combination. As they share common chemical structures, immunological cross reactions between different isothiazolinones also seem possible.

The authors of this investigation conclude that considering the current frequency of sensitisation, that BIT should be included in the European Baseline Series, as was previously proposed in 2019 by the EBS working group. In Germany, the DKG decided to include BIT in the German Baseline Series already from January 2022.

In fact, BIT is now included in the latest 2023 update of the European Baseline Series, as hapten #30 of the 32.

Sunscreens: A review of UV Filters and their allergic potential

By Samuel F. Ekstein, et al
In DERMATITIS, May 2023, Volume 34, Issue 3, pp 176-190
See https://doi.org/10.1097/DER.0000000000000963

The authors of this review article referenced no fewer than 133 other published articles and condensed it into this 14-page review.

The article opens with a history of the use of sunscreens, followed by an explanation of the effects of UVA and UVB light; but the focus of the article is on the various chemical UV filters found in the many sunscreen products available currently in USA.

Sunscreen products contain 2 categories of UV filters: organic (chemical) and inorganic (physical). Both categories are approved by the US Food and Drug Administration (FDA), though with different levels of approval.

The inorganic UV filters include zinc oxide (ZnO) and titanium dioxide (TiO2). The inorganic filters titanium dioxide and Zinc oxide derive most of their photoprotective properties through partial absorption, reflection, and refraction of UV rays, and thereby provide UVA and UVB protection.

The organic UV filters include oxybenzone and octinoxate, among others, and these function due to their ability to absorb specific wavelengths of UV radiation and convert that light energy into heat, and are degraded in the process.

In a document issued by the FDA in 2019, 16 different UV filters were recognised in sunscreen products but only 2 were classified as GRASE Category I (Generally Safe and Effective and not misbranded): that is the 2 inorganic UV filters, titanium dioxide and zinc oxide. The FDA classified 2 UV filters as non-GRASE (category II): aminobenzoic acid along with its related structures (para-aminobenzoic acid [PABA], glyceryl-PABA, ethyl dihydroxypropyl–PABA) and trolamine salicylate.

The FDA determined that the following UV filters required further study regarding their safety and are classified as category III: oxybenzone, avobenzone, octinoxate, octocrylene, octisalate, homosalate, cinoxate, padimate O, sulisobenzone, dioxybenzone, ensulizole, and meradimate. It should be noted that the FDA did not intend to communicate that the category III UV filters were unsafe. However, there have been recent studies showing systemic absorption of oxybenzone with oxybenzone being found in human blood plasma, urine, amniotic fluid, and breast milk after cutaneous application.

This phenomenon of absorption, partnered with the increased use of sunscreens by the public, led the FDA to determine whether they are in need of additional information and thus the category III designation for many of these commonly marketed organic UV filters.

As far as potential ACD is concerned, it must be remembered that sunscreen products also contain a myriad of other substances, such as emollients, fragrances, preservatives, antimicrobial agents, and multiple stabilising agents that could themselves cause an ACD reaction.

There have been multiple reports on ACD to UV filters and photoallergic contact dermatitis (PACD) to UV filters, with the latter being apparently more common. ACD occurs when an allergen induces a type IV cell-mediated hypersensitivity reaction. Photoallergic contact dermatitis occurs when UV radiation induces a transformation in the initial chemical that leads to allergen formation. Only organic UV filters have been implicated thus far, however. There are no reports of ACD or PACD to the inorganic UV filters. In addition, as organic UV filters are becoming more widely used, reports of allergic and photoallergic reactions to these filters are becoming more common. Oxybenzone (benzophenone-3) is the most frequently reported contact and photo-contact allergen, compared with all other UV filters.

In 2009, 201 sunscreen products sold in the United States were evaluated. The most prevalent ACD-causing substances included in the ACDS Core Series that were found in these sunscreen

products include the following substances:

- Oxybenzone (68%)
- Fragrance (63%)
- Vitamin E (53%).

Several other potential inactive ingredients found in many of these sunscreens include the following substances:

- Cetylstearyl alcohol derivatives (27%),
- Triethanolamine (27%),
- Sorbitan sesquioleate derivatives (18%),
- Butylhydroxytoluene (16%),
- Propolis (13%).

The most common preservatives seen in these products were:

- Parabens (30%),
- Benzoic acid (13%),
- Phenoxyethanol (13%),
- Methylisothiazolinone/methylchloroisothiazolinone (9%),
- Diazolidinyl urea (7%),
- DMDM hydantoin (2%),
- Iodopropynyl butylcarbamate (2%),
- Imidazolidinyl urea (1%).

A decade later, in a 2019 review of 52 sunscreens sold in the United States, the most common high-prevalence haptens were:

- Fragrance (found in 30 products)
- Propylene glycol
- Methylisothiazolinone.

The authors of the review paper then proceeded to write a paragraph on each of the more important UV filters, as follows:

Organic UV Filters

Avobenzone (Butyl Methoxydibenzoylmethane)
Butyl methoxydibenzoylmethane is a frequent contact and photo-contact allergen, although ACD is less commonly reported than PACD. This UV filter is commonly found in sunscreens. In a recent ingredient analysis of sunscreens sold in the New Zealand market, 70% of the products contained avobenzone. Avobenzone is one of the most frequent UV filters found in a survey of cosmetic products sold in Germany. A 2019 survey of 52 sunscreens in the United States found avobenzone in 41 of the products. It provides absorption of wavelengths in the UVA range and is thus frequently combined with other UV filters, such as octocrylene, to provide broad photoprotection coverage.

Cinoxate
Cinoxate is a cinnamic acid derivative similar to octocrylene found in many cosmetic products. It is able to absorb UVB wavelengths. Cinoxate's allergenic potential is low. There are no reports of ACD in the literature but 8 reports of PACD.

Dioxybenzone (Benzophenone-8)
Benzophenone-8 is neither a frequent contact nor a photo-contact allergen. It is not commonly used in sunscreens. There are 4 reports of ACD to benzophenone-8 and no reports of PACD. However, there is a reported case of anaphylactoid reactions to benzophenone-3, benzophenone-8, and benzophenone-10. Cross-reactivity between benzophenones is not widely reported.

Ensulizole (Phenylbenzimidazole Sulphonic Acid)
Ensulizole absorbs UVB and UVA2 wavelengths of light. It is used in many moisturisers and sunscreens. There is a low number of allergic and photoallergic reactions to ensulizole in the literature. The majority of these reactions are photoallergic, with 19 reactions documented compared with 7 allergic contact reactions.

Homosalate (Homomethyl Salicylate)
Salicylates are able to solubilise highly insoluble UV filters, such as benzophenones. Homomethylsalicylate absorbs UVB and UVA2 light. There are few reports of homosalate-related contact dermatitis in the literature. There are 9 ACD reactions and 6 PACD reactions documented. It remains uncertain as to why reactions to homomethyl salicylate are not as common compared with other salicylates, such as octyl salicylate and benzyl salicylate. Cross-reactions between homomethyl salicylate and the other salicylates are uncommon.

Meradimate (Menthyl Anthranilate)
Menthyl anthranilate provides UVA coverage. There are few reports of menthyl anthrilate allergic and PACD in the literature: the 3 ACD and 2 PACD reactions documented were found in a 10-year retrospective chart review study in Canada.

Octinoxate (Ethylhexyl Methoxycinnamate)
Octinoxate is a type of cinnamate with cross-reactivity involving cinnamic acid and cinnamaldehyde. It functions by absorbing the UVB and UVA2 wavelengths. Cinnamic acid derivatives, such as octinoxate, are commonly used in cosmetics for UV protection and perfuming function. In an ingredient review of 283 cosmetic products in Italy, octinoxate was found in 13.6% of products. There are few reports of octinoxate-related ACD and PACD in the literature compared with other UV filters with 32 ACD reactions and 39 PACD reactions reported.

Octisalate (Ethylhexyl Salicylate)
Ethylhexyl salicylate is a UVB and UVA2 absorber. There are a limited number of allergic and photoallergic reports in the literature. It seems that ethylhexyl salicylate more commonly induces ACD reactions with 15 reported compared with 5 PACD reactions.

Octocrylene
There are a large number of ACD and PACD reactions to octocrylene in the literature. In a European multicentre photopatch study of 1031 patients, octocrylene was the most frequent

photo- allergen. There is cross-reactivity with ketoprofen and benzophenone-3, which may be related to their structural similarity. Octocrylene is a frequent contact allergen in children and more commonly causes PACD in adults, especially in those with a history of exposure to ketoprofen. This UV filter absorbs UVB and short UVA wavelengths and is included in a variety of cosmetics, including face creams and lip balm products.

Oxybenzone (Benzophenone-3)
Oxybenzone is one of the most common UV filters used in sunscreens. In a 2011 survey of 201 sunscreens in the United States, oxybenzone was found in 68% and avobenzone in 53% of the sunscreens, but it's use seems to be waning. A survey by the Environmental Working Group released in May 2022 showed that it is in only 30% of non-mineral sunscreens in the United States, which is 50% less than in 2019. Furthermore, as a result of public and environmental concerns, most products sold in European Union do not have oxybenzone. Interestingly, there is a documented case of PACD to oxybenzone after the use of a sports t-shirt containing this UV filter. Oxybenzone is also responsible for the most ACD and PACD reactions in the literature compared with any other UV filter and thus is considered the most common sunscreen contact and photo-contact allergen in North America. It is also the most common allergen in a photopatch study of 355 patients in Sweden and the most common photo-allergen in children. Review of the literature found more reported cases of PACD than ACD with oxybenzone (360 vs 118, respectively). Oxybenzone demonstrates cross-reactivity with the UV filter octocrylene and a topical nonsteroidal anti-inflammatory drug, ketoprofen. In addition to many sunscreens, oxybenzone can be found in styling products, conditioners, hand sanitisers, and shampoos.

Padimate O (Ethylhexyl Dimethyl PABA)
Para-aminobenzoic acid was a commonly used class of UV filters that mainly absorbed UVB and was responsible for most sunscreen PACD cases historically. At the 1964 Annual Meeting of the Dermatological Association of Australia, PABA was identified as such a common allergen that there was a consensus to have it removed from sunscreens. Para-aminobenzoic acid began to be replaced by new classes of UV filters and by its ester derivatives, such as octyl di-methyl PABA (Padimate O), dimethyl PABA (Padimate A), and glyceryl PABA. Ethylhexyl dimethyl PABA is an ester derivative of PABA and absorbs UVB light. There are 80 reports of ACD and 49 reports of PACD to Padimate O in the literature.

Sulisobenzone (Benzophenone-4)
Sulisobenzone absorbs UVB and UVA2 wavelengths. It does not display the same high allergic potential as benzophenone-3. There were 57 reports of ACD and 29 reports of PACD in the literature. Interestingly, there is a case of allergic contact dermatitis caused by benzophenone-4 in printing ink.

Inorganic UV Filters

Titanium Dioxide and Zinc Oxide
There are no reports of ACD or PACD to titanium dioxide or zinc oxide. They are photostable, and there are no reports of sensitisation reactions. These filters are the only FDA category I filters considered GRASE because there is adequate effectiveness and safety data to make this determination.

Although there are no reports of ACD or PACD to titanium dioxide in the literature, it is proposed that this inorganic UV filter may liberate gold particles from jewellery, resulting in dermatitis at a site other than the location of primary contact. Frequently, inorganic UV filters are combined with organic UV filters in products.

The reader is encouraged to read the original article in DERMATITIS journal for full information on the brands of products and the incidence reported in the literature.

Chemotechnique offer the Sunscreen Series SU-1000 comprising 21 test substances, as follows:

	Art.No	Name	Conc
1.	B-029C	BUTYL METHOXYDIBENZOYLMETHANE	10.0% pet
2.	A-006C	PABA	10.0% pet
3.	H-024A	HOMOSALATE	5.0% pet
4.	M-024B	4-METHYLBENZYLIDENE CAMPHOR	10.0% pet
5.	E-018D	ETHYLHEXYL DIMETHYL PABA	10.0% pet
6.	H-014C	BENZOPHENONE-3	10.0% pet
7.	E-019C	ETHYLHEXYL METHOXYCINNAMATE	10.0% pet
8.	H-020B	BENZOPHENONE-10	10.0% pet
9.	P-024B	PHENYLBENZIMIDAZOLE SULFONIC ACID	10.0% pet
10.	H-023C	BENZOPHENONE-4	2.0% pet
11.	D-055	DROMETRIZOLE TRISILOXANE	10.0% pet
12.	O-009	OCTOCRYLENE	10.0% pet
13.	O-007A	ETHYLHEXYL SALICYLATE	5.0% pet
14.	O-010	ETHYLHEXYL TRIAZONE	10.0% pet
15.	I-009	ISOAMYL p-METHOXYCINNAMATE	10.0% pet
16.	B-037	BIS-ETHYLHEXYLPHENOL METHOXYPHENOL TRIAZINE	10.0% pet
17.	M-037	Methylene bis-benzotriazolyl tetramethylbutylphenol	10.0% pet
18.	D-062	2-(4-Diethylamino-2-hydroxybenzoyl)-benzoic acid hexylester	10.0% pet
19.	D-063	DIETHYLHEXYL BUTAMIDO TRIAZONE	10.0% pet
20.	D-064	Disodium phenyl dibenzimidazole tetrasulfonate	10.0% pet
21.	D-065	DECYL GLUCOSIDE	5.0% pet

Contact Dermatitis in the Surgical Patient: A Focus on Wound Closure Materials

By William J. Nahm, et al
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See https://doi.org/10.1097/DER.0000000000000860

This article provides the latest overview of the three most frequently used forms of wound closure materials that have been associated with contact dermatitis. Sutures, staples, and adhesives.

The article also provides guidelines for diagnosis and treatment.
The focus of this review is ACD to the materials used in surgical wound closure procedures.

Although occurring only rarely, irritant dermatitis (ID) and allergic contact dermatitis (ACD) are known to occur with all three types of wound closure materials, and can compromise the efficacy and visual appearance of wound repair, and create discomfort and even considerable anxiety for patients.

Postoperative contact dermatitis related to wound closure materials can be either irritant in nature (by direct cytotoxic effect) or allergic (by a delayed type IV hypersensitivity reaction). Symptoms can range from a mild non-specific pruritus and erythema to severe cases exhibiting a strong papulo-vesicular weeping eruption.

Inflammation incurred from such contact dermatitis can mimic surgical site infections, and can compromise wound healing, and may result in wound dehiscence. Therefore, a rapid identification of the condition, and of the problem contact allergen, should lead to optimal management of the patient and their ACD. This management should include relief of symptoms, the unnecessary use of antibiotics and imaging procedures, and even surgical interventions.

The diagnosis of the contact dermatitis to any of the three wound closure types of materials relies on examination of the surgical site for relevant clues:

The geometric borders of the erythema
- Weeping
- Absence of warmth
- Tenderness,
- Purulence

Review of the symptoms
- Pruritus typically more predominant than pain
- Timing of the symptom onset of symptoms compared to the potential exposure
- Comprehensive audit of potential perioperative exposures
- High index of suspicion.

Even when ACD is suspected, there are several different potential culprit materials or procedures that can be responsible:

- Pre-operative (i.e., antiseptics, anaesthetics)
- Intra-operative (wound closure materials, sterile and protective equipment, and surgical implants),
- Post-operative (dressings, wound care supplies) exposures.

Sutures
Both absorbable and non-absorbable sutures can cause either ID and/or ACD, though the usual culprits include non-absorbable sutures and sutures derived from natural products that have been coated in dyes (such as D&C Violet #2), or exposed to sterilising agents (such as ethylene oxide) or are impregnated with antibiotics (such as chlorhexidine or triclosan). Synthetic sutures are generally less allergenic but have nevertheless been documented to cause post-operative ACD.

A good example quoted in the article is about the use of catgut as a suture. Catgut is a natural absorbable suture with good knot security, good tensile strength, and easy handling, and little or no documented cases of ACD. However, the same could not be said for Chromic catgut which has been treated with chromic salts to increase tensile strength. Reports in the literature of ACD to chromic gut sutures usually indicate chromate as the cause of the ACD, although purified collagen components are also implicated. Therefore, a history of ACD to chromate can be a contraindication to the use of chromic-coated sutures. Sensitisation to chromic salts can occur from previous exposure to numerous nonsurgical contacts where chromates are to be found, such as paints, dyes, cement, dental implants, cosmetics, leather tanning materials, etc.

Suspected ACD to suture can be evaluated by patch testing. Coiled suture material can be placed in a patch test chamber and applied to the skin, in a similar manner to other test substances. However, the placement of a single interrupted suture through the cutaneous surface is the preferred method of patch testing suture materials.

Neither the ACDS Core Series, nor the NACDG Standard Series contain components of suture materials for testing, though they both include chlorhexidine digluconate and chromate (potassium dichromate).

Adhesives
In this group are dedicated tissue adhesives based on longer-chain cyanoacrylates, but also more familiar household-name shorter-chain cyanoacrylates such as Loctite and Superglue. The use of tissue adhesives or glues has become more frequent in operating rooms, outpatient surgery centres, and emergency departments for the closure of surgical incisions and lacerations, because adhesives offer greater efficiency compared to sutures and have been shown to enhance wound edge approximation and stability of the wound environment and therefore also the final appearance of the healed wound.

Most wound closure tissue adhesives contain cyanoacrylate, a substance that polymerises after exposure to moisture. Longer-chain derivatives of the original cyanoacrylate were found to have increased tensile strength, reduced rates of polymer degradation, decreased inflammation, and lower levels of toxic by-products compared to the shorter-chained cyanoacrylate derivatives such as methyl cyanoacrylate and ethyl cyanoacrylate. On normal intact skin, liquid cyanoacrylate molecules quickly polymerise on the keratin of the stratum corneum, thereby acting to seal the wound and so reducing the available time for skin invasion and also sensitisation However, on broken skin, cyanoacrylate monomers may interact with antigen-presenting cells before the polymerisation process is complete, which may result in a hypersensitivity reaction, such as ACD.

Ethyl cyanoacrylate, a short-chain cyanoacrylate, can be found in widely available and utilised commercial glues (e.g., Loctite, Super Glue), false eyelashes, industrial glues, sealants, and household adhesives. Although not intended for medical use, it is sometimes used in the treatment of superficial cutaneous fissures, dental procedures, and even for larger postoperative wound closures in areas where commercial surgical glue would be prohibitively expensive.

However, ethyl cyanoacrylate is a known contact allergen: There are several reports of ACD to ethyl cyanoacrylate related to cosmetic glues applied to the nails, face, and ears. Medical devices that use adhesive backings, such as continuous glucose monitors, have also been implicated in ACD to ethyl cyanoacrylate.

Current patch testing methods for cyanoacrylate include dilutions in petrolatum at 10% and not acetone or alcohol. It is recommended that plastic chambers be used for cyanoacrylate testing regardless of the vehicle. The TRUE Test® (Thin-layer Rapid Use Epicutaneous test) does not include any acrylates for patch testing. The NACDG-80 series includes ethyl acrylate, methyl methacrylate, and 2-hydroxyethyl methacrylate, but not any cyanoacrylates. Patch testing to the adhesive glue “as is” can confirm sensitisation when suspected and tested; however, this does identify the exact problem substance which may be the acrylate itself or some additive in its proprietary formulation. If a test provides an unexpected negative result, then it may be repeated on abraded skin, that may be a more sensitive test.

ACD to cyanoacrylates should be treated by removal of the material (which may be dissolved by acetone) and transient use of a topical steroid to suppress the inflammation.

Staples

ACD to staples results from the hypersensitisation to the staples’ metal ingredients, which are usually nickel, chromium, molybdenum, and titanium. Nickel is unsurprisingly the most common culprit. Nowadays, surgical-grade stainless steel is more widely used and consists of mainly iron and chromium. Steel alloys vary greatly and may contain other metals such as molybdenum for improved rust prevention or even nickel within the inner-most layers. Hypersensitivity reactions may occur when iron or chromium ions are released from intact steel, or if there is nickel exposure after compromise of the external steel layer. Titanium staples are an alternative, as they show little risk of corrosion and a high degree of biocompatibility.

In summary, patients with a reported history of metal ACD or positive patch tests for metal allergies should avoid common surgical staples. The routinely used standard patch test series and even supplementary patch testing series do not incorporate all the relevant allergens for wound closure materials. Although techniques for *ad hoc* testing of wound closure material have been described in the literature, approaches are highly variable and not standardised. Patch testing before surgery may be indicated in select patients with a history supportive of ACD to wound closure materials as potential reactions may impact surgical management decisions. In general, however, patch testing is otherwise not routinely recommended as the overall risk of postoperative ACD in the average surgical patient is low.

For full information on the types and brands of wound closure materials, please read the original article in DERMATITIS journal. Be aware though that the brand names of the products are for the American market and may not be available or the same name in other countries.

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

In this fifteenth issue of “The Patch Tester” we are taking a look at the websites of two of the national distributors for Chemotechnique;

1. The company Canute Pharma, of UK
2. The company Sugelabor, S.A. of Spain.

Canute Pharma is a dedicated Dermatology distributor company for the market of United Kingdom. They distribute Chemotechnique and also SilDerm® and Zindaclin®.

See www.canutepharma.com

Canute Pharma was formed in 2020 after the previous company Crawford Healthcare was acquired by a large USA-based mega-corporate in 2018, retaining the key staff who had worked successfully with Chemotechnique products for many years and had built up the reputation for excellence in both products and service amongst UK Dermatologists. That same team now owns and runs Canute Pharma, and so extends their partnership with the UK Dermatologists.

Their graphics-rich website includes an online shop, allowing the viewer to purchase the Chemotechnique Spot Tests and SilDerm scar treatment products.

The section of the Canute Pharma website on Chemotechnique products, at https://canutepharma.com/our-products/chemotechnique-diagnostics/ provides a highly detailed presentation of the products, not just a link through to the Chemotechnique corporate website – though that link is included as well for convenience.

Whilst the IQ Ultra chambers and the IQ Ultimate chambers are both presented in some detail, the latest addition to the Chemotechnique product range of the BasIQ Ultra chambers is not yet shown on the Canute Pharma website, but will doubtless appear very shortly! There is also a Downloads section, where the viewer can download for local printing various order forms and Information brochure for patients.

Wouldn’t it be great if all the websites of all the Chemotechnique distributors globally were this good !

Sugelabor SA is a Madrid-based distributor company with a wide range of products besides Chemotechnique, with laboratory equipment and instrumentation and products from nineteen international manufacturers, as well as used laboratory equipment and technical support services for laboratories.

See http://www.sugelabor.es/

The website is primarily in Spanish language, but of course readable in English with the right browser (such as Google Chrome).

The company was founded in 1982 and is now active also in Portugal and in Latin American countries. With more than 20 staff, Sugelabor offers more than 50,000 “products”.

That could mean that Chemotechnique and their ~600 products might get lost in the background noise, but being the only pharma-style product in Sugelabor’s enormous portfolio, Chemotechnique occupies a dedicated speciality niche within the company.

The website section on Chemotechnique at http://www.sugelabor.es/alergenos/ is colourfully illustrated with information on the 34 different national and international series and hapten series as well as on the IQ Ultra and IQ Ultimate chambers, the Accessories, and the two Spot Tests. The addition of the BasIQ Chambers and the 2023 Chemotechnique catalogue will bring the website up-to-date.

Contact Dermatitis / Patch Testing

27th – 29th June 2023
BAD 2023
Liverpool, UK
https://badannualmeeting.co.uk/

4th – 7th September 2024
16th ESCD
Dresden, Germany
https://escd.org/meetings-courses/

Dermatology - International

11st – 14th October 2023
EADV 2023
Berlin, Germany
https://eadvcongress2023.org/

27th – 28th July 2023
23rd European Dermatology Congress
Paris, France
eurodermatology@europeanmeets.com

3rd - 8th July 2023
ILDS WCD-2023
World Congress of Dermatology
Singapore
https://www.wcd2023singapore.org/

The webpage at www.waset.org/dermatology-conferences-in-2022 is one potentially very useful source of information of Dermatology congresses in 2023.

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

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