

Allergens (Patch Test Studies) from the European Baseline Series

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1. Introduction

The distinction between allergic and irritant contact dermatitis is based on a patient's history and clinical features, in combination with diagnostic patch testing.

- **Irritant contact dermatitis:** An irritant substance is one that would cause inflammation in almost every individual if it was applied in sufficiently high concentration for long enough. An irritant reaction is caused by the direct contact of an irritant substance with the skin and does not involve the immune system.
- **Allergic contact dermatitis:** An allergic reaction is specific to the individual and to a substance (or a group of related substances) called an allergen. Allergy is a hypersensitivity (oversensitivity) to a particular substance, and always involves the immune system. All areas of skin that are in contact with the allergen develop the rash. The rash will disappear if you avoid contact with the substance.

Patch testing is routinely performed by applying a baseline series of the most frequently occurring contact allergens and those contact allergens that may be missed without routine screening. The choice of test concentration is based on patch test experience such that there is a minimum number of irritant reactions and a maximum of clinically explicable allergic positive reactions.

2. Allergens from the European baseline series

Among the major patch test material companies, Hermal, Chemotechnique, and Brial supply with some modifications in the baseline series, as recommended by the European Society of Contact Dermatitis (ESCD). The baseline series can be extended to include allergens of local importance to specific departments (Bruynzeel et al, 1995; Schnuch et al, 1997; Bruynzeel et al, 2005).

In this chapter, we will present some brief guidelines on allergen avoidance measures. Each allergen will be analyzed separately.

	Trolab Hermal ^a	Chemotechnique ^a	TRUE test ^b (µg/cm ²)
Potassium dichromate	0.5% pet.	0.5% pet.	23
Neomycin sulfate	20% pet.	20% pet.	230
Thiuram mix	1% pet.	1% pet.	25
<i>p</i> -phenylenediamine free base	1% pet.	1% pet.	90
Cobalt chloride	1% pet.	1% pet.	20
Benzocaine	5% pet.	5% pet.	
Formaldehyde	1% aq.	1% aq.	180
Colophony (colophonium)	20% pet.	20% pet.	850
Clioquinol	5% pet.	5% pet.	
Balsam of Peru (<i>Myroxylon pereirae</i>)	25% pet.	25% pet.	800
<i>N</i> -isopropyl- <i>N</i> -phenyl- <i>para</i> -phenylenediamine (IPPD)	0.1% pet.	0.1% pet.	
Wool alcohols (lanolin alcohol)	30% pet.	30% pet.	1
Mercapto mix	1% pet.	2% pet.	75
Epoxy resin	1% pet.	1% pet.	50
Paraben mix	16% pet.	16% pet.	1
<i>para</i> -Tertiary-butylphenol-formaldehyde resin (PTBP resin)	1% pet.		40
Fragrance mix	8% pet.	8% pet.	430
Quaternium-15	1% pet.	1% pet.	100
Nickel sulfate	5% pet.	5% pet.	200
Cl+Me-isothiazolinonec	0.01% aq.	0.01% aq.	4
Mercaptobenzothiazole	2% pet.	2% pet.	75
Primin	0.01% pet.	0.01% pet.	
Sesquiterpene lactone mix	0.1% pet.	0.1% pet.	
Budesonide	0.1% pet.	0.01% pet.	1
Tixocortol pivalate	1% pet.	0.1% pet.	3
Methyldibromo glutaronitrile	0.3% pet.	0.5% pet.	
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	5% pet.	5% pet.	
Fragrance mix II		14% pet.	
Caine mix			630
Quinoline mix			190
Black-rubber mix			75
Carba mix			250
Thimerosal			8
Ethylenediamine			50
Hydrocortisone-17-butyrate			20
Diazolidinyl urea			550
Imidazolidinyl urea			600

aq. water; pet. Petrolatum

^a Hermal and Chemotechnique offer more than these allergens

^b TRUE allergens for a Panel 3 are under development

Table 1. The current European baseline patch test series from Trolab Hermal and Chemotechnique, and the contact allergens available from TRUE Test Panel 1-3.

2.1 Nickel sulphate

Nickel sulphate is a white, hard, ductile and malleable metal widely used in alloys. It increases the alloys' resistance to corrosion, wear and abrasion. Nickel is the most common contact allergen in children and adults, particularly in women. Metallic nickel (only after corrosion), as well as nickel salts, gives rise to contact allergy. Sensitisation is not normally occupational, but generally occurs through the use of jewellery (earrings, etc.) and other metal objects in clothing (Shah et al, 1998; Zhai et al, 2003; Garner, 2004; Thyssen et al, 2009).

Stainless steel containing nickel does not normally cause dermatitis because the bonds are very strong and perspiration does not release nickel salts.

- *Synonyms:* Nickel sulphate, Nickel sulphate hexahydrate, and Niccolum sulfuricum.
- *Uses:* a) Batteries; b) Coins, keys, key rings; c) Jewellery (earrings, chains, etc.) (May appear in small quantities associated with other metals: nickel silver, white gold, 14 karat gold, chromium, bronze and brass); d) Metal plating (new silver, China silver, German silver); e) Wire-rimmed glasses; f) Clothing: buttons, zippers, underwire bras, buckles, etc; g) Metal parts of machines; h) Metal parts of furniture: knobs, chairs and tables made from metal tubes, screws, hooks, etc; i) Metal cutting fluids and coolants (metal impurities); j) Orthopaedic plates and material; k) Metal appliances, utensils and instruments; l) Wristwatches; m) Some green dyes: billiard table felt; n) Used occasionally in eye cosmetics.
- *Unusual reactions:* a) Airborne dermatitis; b) Immunologic contact urticaria; and c) Erythema multiforme-like.
- *Avoidance:* a) There is a test on the market: the dimethylglyoxime test for detecting nickel in metal objects or in other components; b) Patients should avoid jewellery and metal objects that contain nickel. As an alternative, they should use objects that contain stainless steel, platinum, titanium, 18 karat gold or sterling silver; c) Patients should avoid perspiration and moisture since they increase the penetration of nickel into the skin; d) Patients should not carry loose change in their pockets; e) They should purchase clothes that do not contain metal; f) Patients should try to isolate commonly used metals using strips of insulating tape or nail polish; g) They should use objects labelled nickel-free; h) If exposure to these products is occupational, patients should alert the company's medical services to this situation. The safety information sheets for the products used will be reviewed to assess exposure to this product; i) Patients should use appropriate gloves (preferably vinyl) when their job requires direct and prolonged contact with nickel metal objects; j) Reactions to dental materials and orthopaedic implants are rare; k) Diets free of foods containing high quantities of this metal have not proven to be useful in improving severe dermatitis lesions.
- *Associations:* People who are allergic to nickel are often allergic to other metals such as cobalt and chromium.

2.2 Wool wax alcohols (Lanolin)

Lanolin (or eucerin) is a complex mixture of esters of fatty acids and alcohols obtained by hydrolysis of the waxy fraction of sheep wool wax. The composition of this wax depends on the place and time of manufacture. Sheep wax constitutes 5% to 25% of the total weight of the shorn wool.

It is used in cosmetics and pharmaceutical preparations due to its emollient, moisturising and emulsifying properties. It is subjected to numerous chemical changes to improve its properties and eliminate its drawbacks. As a complex natural product, its allergens are not well defined, making it very difficult to identify its components. Lanolin sterols (wool alcohols) contain mostly cholesterol and are considered the main causes of allergy to lanolin (Kligman, 1998; Wakelin et al, 2001; Lee & Warshaw, 2008).

In some cases, patients sensitive to lanolin may tolerate preparations containing lanolin. It is a frequent sensitiser in patients with ulcerated legs.

- *Synonyms of Lanolina*: Anhydrous lanolin; Wool fat; Wool wax; Wool grease; Wool alcohol; Clearlin; Glossylan; Golden Dawn; Hychol; Nodorian; Sparklelan; Adeps lanae anhydrous; Aloholes lanae; Eucerin and Cerolan.
- *Synonyms of Modified Lanolina (Lanolin Acid)*: Amerlate; Argo wax; Facilan; Lanolic acids; Ritalafa; and Skliro.
- *Synonyms of Modified Lanolina (Lanolin Alcohol)*: Argo wax; Fancol LA; Hartolan; Lanalol; Nimco; and Rita wax.
- *Synonyms of Modified Lanolina (Lanolin Oil)*: Argonol; Fluilan; Lanalene; Lanogene; Lanoil; Lantrol; Lipolan; Ritalan; and Vigilan.
- *Synonyms of Modified Lanolina (Lanolin Wax)*: Albalan; Lanalene wax; Lanfrac; Lanocerin; and Lanowax.
- *Uses*: a) Cosmetics and personal hygiene products: creams, powders, self-tanners, makeup removers, eye makeup, lipsticks, nail polish removers, barrier creams, hair lotions, shampoos, deodorants, wet wipes, shaving creams, aftershave lotions, etc; b) Baby products: oils, nappy lotions; c) Topical medication: creams, lotions, ointments, haemorrhoid preparations; d) Veterinary products; e) Shoe polish; f) Furniture polish, upholstery cleaners; and g) Others: cutting oils, metal corrosion prevention, carbon paper, coating for rubber boots, dishwashers, printing inks (reducers and thinners), birth control, water-repellent leather, textile and fur finishing, ski wax, insulation for cables, metal finishing, emulsion paints, insect repellent sprays, etc.
- *Avoidance*: a) Patients should tell their doctor that they are allergic to lanolin; b) Their pharmacists can advise them on medicines that contain this substance; c) Patients should check the ingredients on the labels of cosmetics and topical medication (they should not use those that do not list their contents); and d) Wearing wool clothing is not usually a problem for patients sensitive to lanolin.
- *Other substances that may cause a reaction*: Aquaphor.

2.3 Neomycin sulphate

Neomycin is a widely used aminoglycoside antibiotic produced from *Streptomyces fradiae* (Kimura & Kawada, 1998; Bjarnason & Flosadóttir, 2000).

- *Synonyms*: Fradiomycin, Framycetin, Myacyne, Neolate, Neodecyllin, Neomas, Neomin, Neomycin sulphate, Neomycin undecylenate, Nivemycin, Pimavecort, Soframycin, and Vonamycin Powder V.
- *Uses*: a) Medications: skin creams, powders, ointments, ear and eye drops, etc; and b) Veterinarians: animal fattening promoter.
- *Unusual reactions*: a) Contact urticaria.

- *Avoidance:* a) Patients should tell their doctor and chemists if they are allergic to this medication. Patients should avoid the use of other antibiotics of the same group (see Cross-Reactivity); b) Neomycin is included in many frequently used medications (with or without prescription) related to corticosteroids and other antiseptics; patients should therefore check the composition of medication; and c) They should use medication containing alternatives to neomycin.
- *Cross reactivity:* Occurs, although not with the same frequency, between different aminoglycosides such as: a) Bacitracyn; b) Butirosin; c) Dihydrostreptomycin; d) Streptomycin; e) Framycetin (Soframycin); f) Gentamicin; g) Kanamycin; h) Paromomycin; i) Spectinomycin; and j) Tobramycin.

2.4 Potassium dichromate

Potassium dichromate is a lustrous bluish-white metal used in the manufacture of various steel and nickel alloys to increase the resistance of other metals. It is one of the most frequent causes of occupational sensitisation in contact dermatitis, particularly in men. When chromium comes in contact with skin, perspiration transforms it into a salt that can cause sensitisation. The most sensitising is hexavalent chromium (Zachariae et al, 1996; Olsavszky et al, 1998; Hansen et al, 2003).

- *Synonyms:* Bichromate of potash, Bicromato potásico, Chromate, Chrome, Chromic acid, Chromite, Chromium, Dicromato potásico, Dichromic acid, Dipotassium dichromate, Dipotassium salt, Hexavalent form of chromium, Iopezite, Potassium bichromate, Potassium dichromate (VI).
- *Uses:* a) Occupational: construction (wet cement), metal industry (cutting oils), production of television sets, galvanised iron, casting (added to sand to make bricks), textiles (printing and dyeing military green, waterproof fabrics), chroming, pyrotechnics, fibreglass, photography (colour developing), photo-etching, dark photo printing, printing, lithography, office supplies (photocopier paper), jewellery, chemical laboratories, automotive industry, wood (preservatives), dry cleaning, leather tanning, artistic and industrial ceramics (clays), biology, fur trade, paint (minium anti-corrosive), welding, milk testing, etc; b) Clothing: Chrome tanned leather clothing (especially footwear, gloves, wrist watches bands, belts); c) Household and personal use objects and materials: detergents and whiteners (bleach), wood ashes, glues, glass, furniture polish, cleaning sprays, shoe polish, inks, certain orange and yellow paints, enamels, adhesives, spray oils, pen ink, safety matches, dry and deteriorated electric batteries, game and billiards tables; d) Cosmetics: shaving cream and lotions, eye shadows and masks (chromium oxide pigment); e) Medical supplies: orthopaedic and dental implants, vitamin supplements, chromium picolinate (weight loss treatments and diets), sutures (chromic catgut); and f) Tattoo minerals.
- *Unusual reactions:* a) Airborne dermatitis.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) If it causes problems related to their job, patients should tell their company's medical department. They should request information sheets on the materials used; c) For foot dermatitis, patients should avoid leather footwear or use alternative with tanned plants without chromium. The use of socks, hydration of the feet and avoidance of perspiration may reduce dermatitis in these patients; d) Patients should avoid cosmetics

that contain potassium dichromate or any of its synonyms; e) They should tell their doctor and dentist that they are allergic to this substance; and f) Patients should protect themselves properly: f1) They should use gloves, avoiding those made of leather (material). There are special cements in which exposure to chromium is reduced by the addition of a chelating agent (ferrous sulphate); and f2) They should use barrier creams containing substances that reduce hexavalent chromium to trivalent: ascorbic acid, EDTA, dithionate, tartaric acid and sodium metabisulfite.

2.5 Caine Mix

Caine Mix is a mixture of local anaesthetics of the group of esters of para-aminobenzoic acid: cinchocaine chloride, amethocaine chloride and benzocaine. It is used to detect sensitisation to these drugs in cutaneous tests (Suhonen & Kanerva, 1997; Sidhu et al, 1999).

- *Uses:* Medicines for veterinary use; b) Adhesives for false palates; c) Cosmetics; and d) Medications: injections, tablets and sprays for sore throats and mouth pain, insect bites, skin rashes; preparations for haemorrhoids and eye drops, suppositories; and antitussives.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) Patients should tell their doctor, dentist and chemists that they are allergic to these drugs; and c) They should use medication with alternatives to these local anaesthetics, such as the amide group (lidocaine, prilocaine, bupivacaine, mepivacaine, etc).
- *Cross-reactivity:* a) Procaine; b) Butethamine; c) Tetracaine; d) Butacaine; e) Merocaine; f) Orthocaine (Orthoform); g) Neo-orthoform; h) Paraphenylenediamine; i) Procainamide; j) Proparacaine; k) Chlorprocaine; l) Risocaine; m) Novocaine; and n) Cinchocaine.

2.6 Fragrance mix I & II

Commercial perfumes are complex mixtures of natural essential oils and synthetic compounds. They are part of the composition of many products including cosmetics (the most frequent cause of allergic contact dermatitis due to cosmetics), topical medication, detergents, air fresheners, food, etc.

Natural essential oils contain scented essences and are obtained from different parts of plants: Lavender oil is extracted from the flowers, eucalyptus from the leaves, cinnamon from the bark and sandalwood from the wood.

There are more than 5000 fragrant substances in current use. Most fragrances contain up to 300-500 different ingredients. The concentration of essential oils varies from 0.5% in cosmetics to 5% in eau de cologne and up to 20% in perfumes. Given the complexity of the product, it is often impossible to determine all the ingredients in the mixture.

Fragrance mix I was developed in the late 1970s, and consists of eight ingredients, each at a concentration of 1%: Amyl cinnamal, Cinnamal, Cinnamyl alcohol, Eugenol, *Evernia prunastri* (oak moss), Geraniol, Hydroxycitronellal, Isoeugenol. Fragrance mix II was officially included in the baseline series in 2008, and consists of six ingredients: hydroxyisohexyl 3-cyclohexene carboxaldehyde 2.5%, citral 1.0%, farnesol 2.5%, coumarin 2.5%, citronellol 0.5%, and a-hexyl cinnamal 5% (White et al, 2008; Bruze et al, 2008).

- *Uses:* a) Perfume; b) Cosmetics: hair ointments, lotions, tonics and glitter, sunscreens, soap and feminine hygiene sprays, cosmetic powders and lipsticks, shaving lotions, natural cosmetics, massage products, etc; c) Household products: air fresheners, waxes, varnishes, insect repellents, detergents, fabric softeners, etc; d) Medications: topical medication such as creams, ointments, salves for wounds, burns and legs ulcers (geraniol); e) Food: chocolate flavouring, sweet cakes, chewing gum, candy, ice cream and cola beverages, vermouth, curacao, liqueurs, spices (cinnamon, cloves, vanilla, curry, etc); and f) Dentistry: dental cements and anaesthetics (eugenol).
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should tell their doctors and dentists that they are allergic to this substance; c) Patients should use gloves when handling products with perfume; and d) They should use cosmetic and medical products marked "unscented" or "without perfume" on the packaging. Products labelled as hypoallergenic contain perfumes that usually do not cause sensitisation. When in doubt, patients should apply a small amount of the product in question to the crook of the elbow twice a day for five consecutive days. If there is no skin reaction, the product is safe to use.

2.7 Colophonium

Colophony (rosin) is a widespread, naturally occurring material that is the residue from the distillation of the volatile oil from the oleoresin obtained from trees of the *Pinaceae* family (*Pinus palustris*, *Pinus caribaea*). It comprises 90% resin acids and 10% neutral material. Resin acids are the major allergens, which include the oxidation products of abietic, pimaric and dehydroabietic acid. They are currently subjected to various chemical modifications depending on later use. Some maleopimaric acid derivatives have high antigenicity (Färm, 1996; Gäfvert et al, 1996; Karlberg et al, 1996; Kanerva et al, 2001).

- *Synonyms:* Abietic acid, Abietic alcohol, Abietyl alcohol, Abitol, Colophony, Dercolyte ZS, Dertomal 18, Dertophene 18, Disproportionated rosin, Foral 105, Granolite SG, Gum rosin, Hercolyn D, Methyl abietate alcohol, Pine rosin, Resina terebinthinae, Rosin, Rosin gum, Staybelite 10, Tall oil, and W-W wood rosin.
- *Uses:* a) Medications: suppositories, cough medicines, and topical medicines: tulle gras, ointment for wounds, burns, chilblains, haemorrhoids, treatment for scabies, plant and coal tar, tincture of benzoin, myrrh and ratanhia, tiger balm (oriental); b) Cosmetics: hair ointments, lotions, tonics and glitter, sunscreens, soap and feminine hygiene sprays, cosmetic powders and lipsticks, shaving lotions, natural cosmetics; c) Perfumes (including perfume and perfume fixative); d) Food: chocolate flavouring, sweet cakes, chewing gum, sweets, ice cream and cola beverages, vermouth, curacao, liqueurs; spices (cinnamon, cloves, vanilla, curry, etc); Products using citrus peel (jams, cakes, juices) and condiments: ketchup, chilli sauce, pickles; and e) Others: scented products including tobacco, tea, toothpaste, dental cement, orthopaedic materials, porcelain and china paints, floor and shoe polishes, beeswax, milling oil.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should carefully read the ingredients of cosmetics and cleaning products that they use; c) If it causes problems related to their job, patients should tell their company's medical department (they should request information sheets on the materials used and wear sufficient protection; use gloves, glasses, etc); d) Patients should check the

ingredients of medication, especially topical preparations, before using them; e) They should tell their doctor and dentist that they are allergic to this product (they should use hypoallergenic adhesive materials or those that do not contain colophony); and f) Patients should avoid contact with pine sawdust.

- *Cross-reactivity:* Balsam of Peru, Dihydroabietic alcohol, Turpentine oil, Pine resin, Spruce resin (*Pini burgundica*), and Wood tar.

2.8 Epoxy resin

Some 95% of all epoxy resins consist of a glycidyl ether group formed by the reaction of bisphenol A with epichlorohydrin. Epichlorohydrin/bisphenol A epoxy resin can vary in molecular weight from 340 to much larger polymers, the latter having much less sensitising capacity. Along with the resin itself, there are fillers, pigments, plasticisers, reactive diluents, and solvents, and these compounds are then mixed with a hardening/curing agent that polymerises the resin (Bray, 1999; Geraut et al, 2009).

- *Synonyms:* 4,4-isopropylidenediphenol-epichlorohydrin; Diglycidyl ether, Bisphenol A [2,2-bis(4-hydroxyphenyl)propane] (diphenylpropane); Epichlorohydrin; Epoxy resin; (1-chloro-2,3-epoxypropane) (8-chloropropylene oxide).
- *Uses:* a) Adhesives, adhesive tapes and glues for household (model airplanes, models) and industrial use; b) Agents for dental fillings; c) Glues for dental parts; d) Electrical encapsulation; e) Casting moulds; f) Electron microscopy; g) Lens framing; h) Plastic necklaces and handbags; i) Laminate; j) Flooring; k) Repairing cracks in concrete; l) Paints and inks; m) Plasticisers; n) Polyvinylchloride products; and o) Vinyl gloves.
- *Unusual reactions:* a) Contact urticaria; b) Airborne dermatitis; and c) Erythema multiforme-like.
- *Avoidance:* a) Patients should avoid contact with the skin and inhalation of epoxy resin fumes. These are prepared using two compounds (resin and hardener), which must be mixed for later use. They are allergens only when not mixed, as they cause no reaction once they have been combined and have hardened. The drying process may last up to seven days. b) Patients should advise the medical staff at their workplace that they are allergic to this product. Latex gloves do not prevent contact since these substances can penetrate them. They should use synthetic gloves such as those made from nitrile and butyltoluene. If patients are very sensitive, they should avoid working in places where these substances are handled. c) Patients should tell their doctor and dentist that they are allergic to these products. d) If patients have a reaction to the hardener of an epoxy compound, then this is usually an amino compound. Therefore, patients who are sensitised to other amines such as paraphenylenediamine and ethylenediamine may be sensitised to the hardening agent.

2.9 Quinoline mix

The quinoline mix in the European Baseline Series contained a mixture of Clioquinol and Chlorquinaldol.

Quinoline mix is an anti-infective derived from a group of antibiotics called quinolones: antibacterial and anti-amoebic. We found in: poultices, creams and ointments used in the treatment of infected cuts and eczema, fungi, etc (Agner & Menné, 1993).

- *Synonyms*: 3-Hydroxy-5-Chloro-7-iodine-8-quinoline; Amebil; Alchloquin; Amoenol; Bactol; Barquinol; Budoforn; Chinoform; 5-Chloro-7-yodo-8-quinolinol; 5-Chloro-8-hydroxy-7-iodoquinoline; Chloroiodoquin; Clioquinol; Eczecidin; Enteroquinol; Entero-Septol; Entero-Vioform; Enterozol; Entrokin; Esterosan; Hi-Enterol; Entero-Vioform; Iodochlorhydroxyquin; Iodochlorhydroxyquinoline; Iodochloroxyquinoline; Iodoenterol; Nioform; Quinambicide; Rometin; Rometin; Quinaband; Quinambicide; Quinoform; Quinoforma; Vioform; Vioforma; and Yodinacloridequinolina.
- *Uses*: a) Creams, ointments and lotions (e.g. Cuatroderm Crema® - Schering-Plough S.A.; Menaderm Clio Ointment® - Menarini Group Laboratory; Synobel cream® - Yamanouchi Pharma, S.A.); b) Oral medication; and c) Topical medication (e.g. Menaderm otological drops® - Menarini Group Laboratory).
- *Unusual reactions*: a) Brown discolouration of the nails; b) Contact urticaria; and c) Erythaema multiforme-like.
- *Avoidance*: a) Patients should check the ingredients of medication, especially topical preparations before applying them; and b) They should tell their doctor that they are allergic to this product.
- *Cross-reactivity*: Chlorquinaldol and other quinolines: oxyquinoline.

2.10 Balsam of Peru (*Myroxylon pereirae*)

Balsam of Peru (INCI name: *Myroxylon pereirae*) is the natural resinous balsam that exudes from the trunk of the Central American tree *Myroxylon pereirae* or *Toluifera pereirae* after scarification of the bark. Balsam of Peru contains 30-40% resins of unknown composition, while the remaining 60-70% consist of well-known chemicals: benzyl benzoate, benzyl cinnamate, cinnamic acid, benzoic acid, vanillin, farnesol (which is also increasingly being used in deodorants), and nerolidol. It can also come up positive in cutaneous tests as an allergy to spices (cinnamon, cloves, etc.) (Hausen, 2001).

- *Components of Balsam of Peru (and Related compounds)*: Benzoic alcohol, Benzoic acetate, Benzaldehyde, Benzyl salicylate, Cinnamic alcohol, Cinnamic aldehyde, Coniferous alcohols, Vanillin, Benzyl benzoate and other benzoates, Benzoic acid, Cinnamic acid, Cinnamyl cinnamate, Methyl cinnamate, Eugenol, Ioeugenol, and Resinous substances.
- *Synonyms*: Indian balsam, China Oil, Black balsam, Balsamum peruvianum, Honduras balsam, Peruvian balsam, Surinam balsam, Myroxylon pereirae klotzsch resin, Myrospermum pereira balsam, Toluifera pereira balsam, and Myroxylon pereirae klotzsch oil.
- *Uses*: a) Medications: suppositories, cough medicines, and topical medicines: tulle gras, ointment for wounds, burns, chilblains, haemorrhoids, treatment for scabies, plant and coal tar, tincture of benzoin, myrrh and ratanhia, tiger balm (oriental); b) Cosmetics: hair ointments, lotions, tonics and glitter, sunscreens, soap and feminine hygiene sprays, cosmetic powders and lipsticks, shaving lotions, natural cosmetics; c) Perfumes (including perfume and perfume fixative); d) Food: chocolate flavouring, sweet cakes, chewing gum, sweets, ice cream and cola beverages, vermouth, curacao, liqueurs; spices (cinnamon, cloves, vanilla, curry, etc); products using citrus peel (jams, cakes, juices) and condiments: ketchup, chilli sauce, pickles; and e) Others: scented products including tobacco, tea, toothpaste, dental cement, orthopaedic materials, porcelain and china paints, floor and shoe polishes, beeswax, milling oil.

- *Unusual reactions:* a) Erythema multiforme-like.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should alert their doctor and dentist that they are sensitive to this substance; and c) Patients should use cosmetic and medical products marked "unscented" or "without perfume" on the packaging. Products labelled as hypoallergenic contain perfumes that usually do not cause sensitisation. When in doubt, patients should apply a small amount of the product in question to the crook of the elbow twice a day for five consecutive days. If there is no skin reaction, the product is safe to use.
- *Cross-reactivity:* Colophony, balsam of Tolu, cinnamates, benzoates, beeswax, eugenol, isoeugenol, farnesol, propolis, diethylstilbestrol.

2.11 Ethylenediamine

Ethylenediamine dihydrochloride is a solvent for casein, albumin and sulphur. It is a stabiliser for rubber latex and for the pharmaceutical industry, as well as an inhibitor in antifreeze solutions, and an emulsifier (Hogan, 1990).

- *Synonyms:* 1,2-Diaminoethane; 1,2-Ethanediamine; Chlorethamine; Ehylenediamine didydrochloride; and Proxel CRL (1,2-Benzisothiazolin-3-one + ethylenediamine).
- *Uses:* a) Medications: aminophylline (is theophylline + ethylenediamine); antihistamines (piperazine derivatives, very similar to ethylenediamine; Including: meclizine, buclizine, chlorcyclizine, cyclizine, promethazine); nystatin creams; thimerosal (merthiolate tincture); veterinary preparations and; b) Others: inhibitor in antifreeze and coolants; colour developers; dyes; galvanised metals and electrophoretic gels; emulsifier; epoxy resins and textile; wall varnish remover; fungicides and insecticides; latex stabiliser; solvent for casein, albumin and sulphur; synthetic waxes; and textile lubricants.
- *Unusual reactions:* a) Contact urticaria; and b) Erythema multiforme-like.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should tell their doctor that they are allergic to this substance; and c) If exposure to these products is occupational, patients should alert the company's medical services to this situation. The safety information sheets for the products used will be reviewed to assess exposure to this product. They should use appropriate gloves for protection.
- *Cross Reactivity:* a) Aminophylline; b) Antazoline; c) Piperazine; d) Promethazine HCl; e) Diethylenetriamine; and f) Triethylenetetramine.

2.12 Cobalt chloride

A greyish, hard, magnetic, ductile and somewhat malleable metal used in the production of cobalt alloys and salts. It is an essential trace mineral that is present in vitamin B12 (cyanocobalamin). Several cobalt salts are coloured and are, on rare occasions, used as pigments for glass, ceramics, makeup and hair dyes. The most frequent cause of sensitisation to this metal is nickel-plated objects, which almost always contain cobalt (Basketter et al, 2003; Garner, 2004)

- *Synonyms:* Cobalt, Cobalt (II) chloride-hexahydrate, Cobalt blue, Cobalt chloride, Cobalt dichloride hexahydrate, and Cobaltous chloride hexahydrate.

- *Uses:* a) Metals: jewellery, coins; b) Occupational: cement, paints, resins, paint driers, galvanized metal, machine parts, manufacturing polyester resins, tools, utensils, metal tools, fertilizer and animal feed additive; c) Home: household detergents, fly paper; c) Pigments: hair dyes and cosmetics, invisible ink, ceramics, glass and marker pens (cobalt blue), blue tattoos; d) Medicine: metal dental prostheses and joints, vitamin B12 (used as a colour marker in hydrogen peroxide-based liquids for contact lenses); e) Clothing: zippers, metal buttons, buckles; and f) Others: foam stabiliser in beer (cobalt acetate).
- *Unusual reactions:* a) Airborne dermatitis; b) Nonimmunologic contact urticaria; c) Erythaema multiforme-like; and d) Photosensitivity.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) Patients should avoid jewellery and metal objects that contain cobalt associated with nickel. (as an alternative, they should use objects that contain stainless steel, platinum, titanium, 18 karat gold or sterling silver); c) Patients should avoid perspiration and moisture since they increase the penetration of metal into the skin; d) They should use tools with contact surfaces made of plastic, rubber or wood; e) Patients should not carry loose change in their pockets; f) They should purchase clothes that do not contain metal; g) Patients should try to isolate commonly used metals using strips of insulating tape or nail polish; h) They should use appropriate gloves (preferably vinyl) when their job requires direct and prolonged contact with metal objects; i) Patients should tell their doctors and dentists that they are sensitive to this substance (reactions to dental materials and orthopaedic implants are rare - there are prostheses that are made from alternative materials); j) Patients should check the ingredients of personal hygiene products and cosmetics; k) If exposure to these products is occupational, patients should alert the company's medical services to this situation (the safety information sheets for the products used will be reviewed to assess exposure to this product; and patients should use appropriate gloves to protect themselves); and l) Patients should avoid direct contact with wet cement.
- *Associations:* People who are allergic to cobalt are often allergic (80%) to other metals such as nickel and chromium.

2.13 Para-Tertiary-Butylphenol-Formaldehyde Resin

Para-Tertiary-Butylphenol-Formaldehyde Resin is used as an adhesive. It is related to allergic sensitisations due to contact with footwear. It is used in footwear for its durability and flexibility. It is used to attach leather, rubber to rubber and rubber to metal surfaces. Formaldehyde is not a primary allergen in this resin (Zimerson & Bruze, 1999; 2002).

- *Synonyms:* 4-(1,1-Dimethylethyl) phenol; 4-tert-Butylphenol formaldehyde resin; Butylphen; p-t-Butylphenol formaldehyde resin; p-tert-Butylphenol formaldehyde resin; Paratertiary Butylphenol formaldehyde resin; and PTBT formaldehyde.
- *Uses:* a) Footwear and leather goods industry (adhesive for footwear, watchstraps, belts, handbags and hats); b) Glues; c) Athletic tape; d) Automotive (sealant); e) Engine oil; f) Parcels office; g) Knee pads; h) Plywood; i) Insulation; j) Fibreglass; k) Inks; l) Paper; m) Film developers; n) Disinfectants; o) Deodorants; p) Nail adhesive; q) Dental amalgams; and r) Waterproofing.
- *Unusual reactions:* a) Depigmentation.

- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should tell their doctors that they are allergic to this substance; c) If exposure to these products is occupational, patients should alert the company's medical services to this situation. The safety information sheets for the products used will be reviewed to assess exposure to this product. Patients should use gloves to protect themselves. They should use gloves when working with glues; d) If their hobbies include working with wood or ceramics, patients should use glues without this substance, such as cyanoacrylates; e) They should avoid waterproof glues for leather. If they have dermatitis from using shoes soaked with water, patients should stop using those shoes. They should avoid shoe repairs with glues and change their socks frequently to avoid getting them damp with perspiration; f) There are special glues for attaching soles to shoes that are free of this substance. However, it is difficult to remove this type of glue from the rest of the shoe; g) It is recommended that patients replace leather watchstraps with metal ones; and h) Patients should avoid direct skin contact with glues for wood, and fibreglass dust and rigid boards.
- *Associations:* People who are allergic to nickel are often allergic to other metals such as cobalt and chromium.

2.14 Parabens Mix

Paraben Mix is a preservative used to prevent the growth of bacteria, fungi and yeast. It is most frequently used in food, medication and cosmetics and is also used as an antioxidant. The mixture includes: methyl, ethyl, propyl, butyl and benzyl parabens, which are often combined due to their synergistic effect.

It has low sensitising power, although greater when applied to wounds (eczema, stasis ulcers, etc). Parabens mixtures are used in the standard battery of contact allergens for cutaneous tests to detect patients who sensitive to these substances (Schorr, 1978; Fisher, 1973; Fisher, 1979; Anonymous, 2008).

- *Synonyms:* Aseptoform; Benzylparaben; Butylparaben; Ethylparaben; Germaben II; Lexgard; Methylparaben; Nipagin; Nipastat; p-Hydroxybenzoate; Parahydroxybenzoate; p-Hydroxybenzoic acid; Parahydroxybenzoic acid; Parabens; Parasept; Liqua par; Perservaben; Phenonip; Propylparaben; Protaben; Undebenzofene-C; Benzyl-4-hydroxybenzoate; Methyl-4-hydroxybenzoate; Ethyl-4-hydroxybenzoate; Propyl-4-hydroxybenzoate; and Butyl-4-hydroxybenzoate.
- *Uses:* a) Cosmetics: all types, especially for eyes. However, patients sensitive to parabens tolerate their use in cosmetics applied to normal eyelids ("paraben paradox"); b) Medications: b1) vaginal, ophthalmic, ear, nasal and oral topical agents, toothpastes and mouthwashes, creams and ointments for the skin, bandages impregnated with medication, injections, tablets and sprays for sore throats and mouth pain, insect bites, skin rashes, preparations for haemorrhoids and eye drops, suppositories and antitussives; b2) parenteral administration: antibiotics, corticosteroids, local anaesthetics, radiopharmaceuticals, vitamins, antihypertensives, diuretics, insulin, heparin, and chemotherapy; c) Food: used in tomato pulp, purees, tomato sauce, pickles, pickled and marinated food, sauces, fruit juices, pureed fruit preserves, dairy preparations, non-alcoholic beverages and packaged fish, meat and poultry; and d)

Others: electrocardiogram gel, boot polish, textiles and glues, starch paste, oils and fat for technical use.

- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should carefully check the composition of cosmetics, personal hygiene products, food and medication (they should use those that do not contain parabens or any of their synonyms); c) Patients should tell their doctors, dentists and chemists that they are allergic to these compounds; d) Given that most patients sensitised to parabens can tolerate their use, a test can be performed before using them or reintroducing them. A small amount of the product in question should be applied to the crook of the elbow twice a day for five consecutive days. If there is no skin reaction, the product is safe to use; and e) Eating food that contains parabens as preservatives does not usually cause problems.
- *Cross Reactivity:* Paraphenylenediamine and other derivatives of the Para-group.

2.15 Carba mix

Carba mix is the combination of three chemicals used as accelerators in the manufacture of rubber and is used to detect sensitisation in skin tests. These accelerators are 1,3-diphenylguanidine, zinc bis(diethylthiocarbamate) and zinc bis(dibutylthiocarbamate) (Logan & White, 1988).

- *Synonyms of 1,3-Diphenylguanidine:* DPG; Nocceler D; Sanceler D; and Soxinol D.
- *Synonyms of Zinc dibutylthiocarbamate:* Butasan; Butazate; Butazin; Butyl Zimate; Nocceler BZ; Soxinol BZ; and ZBC.
- *Synonyms of Zinc diethylthiocarbamate:* Etazin; Ethasan; Ethazate; Ethyl Zimate; Nocceler EZ; Soxinol EZ; ZDC; and ZDEC.
- *Uses:* a) Adhesives; b) Disinfectants, repellents, fungicides and insecticides used in agriculture (e.g. Maneb, Zineb, Benomyl); c) Leather footwear (soles, adhesives, liners); d) Soaps and shampoos; and e) Rubber materials: condoms and diaphragms; gloves (home, work and hospital); medical equipment (rubber bands, syringes with rubber tips, etc.); kidney dialysis machines; rubber pillows; elastic materials in clothing and underwear; makeup sponges and rubber-tipped eyelash curlers; swimming gear (caps, goggles, etc.); toys; strips and tubes; and others: fuel tank coatings, electrical cables, gas masks, rubber supports for binocular eyepieces, conveyor belts, shock absorbers, headphones, aprons, dental dams, balloons, hoses, mattresses, etc.
- *Unusual reactions:* a) Airborne dermatitis; b) Immunologic contact urticaria; and c) Erythaema multiforme-like.
- *Avoidance:* a) It is difficult to know which rubber products contain these substances. Some rubber products are labelled "hypoallergenic". However, patients should be advised to use them for no more than 30 minutes at a time; b) They should be careful with footwear, avoiding those with rubber soles and using those that have synthetic or alternative material in the soles; c) Patients should use rubber-free birth control devices (e.g. Avanti Durex® - SSL International Plc.; and FEMI® - LETI Laboratories), etc.); d) They should use gloves made of synthetic alternatives to rubber: vinyl, nitrile, neoprene, etc; e) Patients should wear clothes without elastic in them; f) They should avoid other rubber materials: makeup sponges, balloons, etc; and g) Patients should avoid occupational exposure and tell their company's medical department about their condition.

2.16 Para-phenylenediamine mix (black rubber mix)

PPD mix or black rubber mix is the combination of three substances: N-isopropyl-N-phenyl paraphenylenediamine, N-cyclohexyl-N-phenyl paraphenylenediamine and N,N-diphenyl paraphenylenediamine. They are used as additives in the manufacture of natural and synthetic rubber (nitrile-butadiene, styrene-butadiene, isoprene, butadiene and chloroprene). N,N-diphenyl paraphenylenediamine is also used as a polymerization inhibitor (Menné et al, 1992; Geier & Gefeller, 1995; Holness & Nethercott, 1997). The mixture is used to detect sensitisation in cutaneous tests.

- *Synonyms of N-Phenyl-N'-cyclohexyl-p-phenylenediamine (CPPD):* Phenylcyclohexyl PPD; Flexizone GH; and N-Cyclohexyl-N-phenyl-N'-4-phenylenediamine.
- *Synonyms of N-Isopropyl-N'-phenyl-p-phenylenediamine (IPPD):* Isopropyl 0 PPD; Akrochem antioxidant PD1; Permanex IPPD; Flexizone 3-C; and Santoflex IP.
- *Synonyms of N,N'-Diphenyl-p-phenylenediamine (IPPD):* Diphenyl PPD; 1,4-Dianilinobenzene; N,N'-Diphenyl-4-phenylenediamine; and N,N'-Diphenyl-1,4-phenylenediamine.
- *Uses:* a) Food antioxidant (N,N-diphenyl paraphenylenediamine); and b) Rubber materials: condoms and diaphragms, gloves (home, work and hospital), rubber boots, medical equipment (rubber bands, syringes with rubber tips, etc.), kidney dialysis machines, rubber pillows, elastic materials in clothing and underwear, makeup sponges and rubber-tipped eyelash curlers, sports equipment (diving masks, suits and fins, squash balls, windsurfing boards, rubber swimming boots, caps and goggles, racquet coatings, etc), toys, strips and tubes, and others: hoses, fuel tank coatings, electrical cables, gas masks, rubber supports for binocular eyepieces, conveyor belts, shock absorbers, headphones, aprons, dental dams, balloons, radiator hoses, mattresses, bumpers, head gaskets, calculator and remote control keypads, etc.
- *Avoidance:* a) Patients should be careful with materials made of black or dark grey rubber; b) It is difficult to know which rubber products contain these substances (Some rubber products are labelled "hypoallergenic". Still, it is best that patients use them for no more than 30 minutes at a time); c) Patients should be careful with footwear (They should avoid those with rubber soles and use those that have synthetic or alternative material in the soles); d) Patients should use gloves made of synthetic alternatives to rubber (vinyl); e) Patients should wear clothes without elastic in them; f) They should avoid occupational exposure. They should tell their company's medical department about their condition and use alternative materials; and g) Patients should use appropriate gloves when doing car repairs (changing tyres, etc).
- *Cross-reactivity:* Paraphenylenediamine (PPD), para-aminodiphenylamine (hair dyes).

2.17 Methylchloro- and Methylisothiazolinone (MCI/MI) (Kathon CG)

Isothiazolinones (5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one, 3:1 ratio by weight) are the active ingredients in Kathon CG (Rohm and Haas, Philadelphia), a cosmetic preservative. Isothiazolinones are used extensively as effective biocides to preserve the water content of cosmetics, toiletries, household, and industrial products, such as metalworking fluids, latex emulsions, cooling tower water, water-based paints and for slime control in paper mills (de Groot et al, 1988; Frosch et al, 1995; Zachariae C et al, 2006).

- *Synonyms:* 2-methyl-4-isothiazolin-3-one, Acticide, Euxyl K100, 5-Chloro-2-methyl-4-isothiazolin-3-one, Algucid CH50, Amerstat 250, Cl+Me-isothiazolinone, Fennosan IT 21, Grotan K, Grotan TK2, GR 856 Izolin, Kathon 886 MW, Kathon CG, Kathon DP, Kathon LX, Kathon UT, Kathon WT, MCI/MI, Mergal K7, Metat GT, Metatin GT, Methylchlorisothiazolinone/Methylisothiazolinone, Mitco CC 32 L, Paretol, Paermetol DF 35, Paermetol DF 12, Paermetol A23, Paermetol K50, Paermetol K40, Paermetol DF 18, P3 Multan D, Piror P109, and Special Mx 323.
- *Uses:* a) Cosmetics: shampoos, soaps, conditioners, gels (hair and body), creams and lotions for the skin, face packs, etc; b) Household products: detergents, bubble baths, adhesives, glues, wet wipes, fabric softeners, cleaning products, toilet paper, etc; c) Occupational: jet engine fuel, latex emulsions, cutting oils, air conditioning, milk samples, oils and coolants, paints, pesticides, pigments, varnishes, preservatives, printing inks, X-rays, etc; and d) Others: biocides for swimming pool water.
- *Unusual reactions:* a) Airborne dermatitis.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should tell their doctor that they are allergic to this substance; c) Patients should check the ingredients of personal hygiene products and cosmetics; and d) If exposure to these products is occupational, they should alert the company's medical services to this situation. The safety information sheets for the products used will be reviewed to assess exposure to this product. Patients should use gloves to protect themselves.
- *Cross-reactivity:* With other isothiazolinones.

2.18 Quaternium-15

Quaternium-15 is one of the formaldehyde-releasing preservatives. Although it releases small quantities of this substance, not all patients that are allergic to quaternium are allergic to formaldehyde, and viceversa (Dickel et al, 2003).

- *Synonyms:* Azoniaadamantane chloride; Azonium-adamantane chloride; Chloroallyl methanamine chloride; Cis-1-3-(3-chloroallyl)3,5,7-triaza-1-azoniaadamantane chloride; Dowicil 75; Dowicil 100; Dowicil 200; 1-(3-Chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride; Methanamine-3-chloroallylochloride; N-(3-chloroallyl) hexaminium chloride; and Preventol D1.
- *Uses:* a) Adhesives; b) Construction materials; c) Cosmetics: creams, lotions, shampoos, soaps, sunscreens, powders, suntan lotions, makeup removers, masks, eye makeup, eye pencils, moisturisers, etc; d) Inks; e) Joint cement; f) Latex paints; g) Textile finishing solutions; h) Metalworking fluids; i) Topical medication; j) Paper (pulp) and wallpaper; k) Floor wax, varnishes; and l) Shoe polish.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should carefully check the composition of cosmetics, personal hygiene products, etc. They should use products that do not contain quaternium-15; c) Patients should tell their doctor that they are allergic to this substance; and d) If it causes problems related to their job, patients should tell their company's medical department. They should request information sheets on the materials used. They should wear sufficient protection (use gloves, glasses, etc.)
- *Cross-reactivity:* Formaldehyde and other formaldehyde releasers.

2.19 Mercaptobenzothiazole

Mercaptobenzothiazole (MBT) in contact with your skin may result in dermatitis. Brief or occasional contact may not pose a problem (Geier et al, 2002; Diepgen et al 2006).

MBT is an additive used as an accelerator in the manufacture of both natural and synthetic rubber.

- *Synonyms:* 2-Benzathiazalethiol; 2-Benzisothiazoline; 2-Mercaptobenzothiazole; Captax; Dermacid; MBT; Mercaptobenzothiazole; Mertax; Nocceler M; Rotax; and Thiotax.
- *Uses:* See 2.22 Mercapto Mix.
- *Avoidance:* See 2.22 Mercapto Mix.

2.20 Para-phenylenediamine (PPD)

Para-phenylenediamine is a chemical dye used as an intermediary in permanent dyes for hair and leather (Thyssen & White, 2008; Thyssen et al, 2009).

- *Synonyms:* 1,4-Benzenediamine; 1,4-Phenylenediamine; 4-Benzenediamine; 4-Phenylenediamine; Orsin; PPD; PPDA; p-Aminoaniline; p-Diaminobenzene; p-Phenylenediamine; Para-aminoaniline; Para-diaminobenzene; Paraphenylenediamine; Phenylenediamine base; Rodol D; and Ursol D.
- *Uses:* a) Cosmetics (permanent hair dyes, some cosmetic dyes); b) Lithography (printing ink); c) Photocopy, typographic plates; d) Photography (used as a developer for black and white photographs. Hydramine is another photographic developer that contains hydroquinone and paraphenylenediamine); e) Diesel, grease and fuel oils; f) Photographic developers; g) Primary intermediary in the production of azo dyes; h) Occasionally used in leather or animal hide colouring; and i) Rubber and plastics industry: antioxidants and accelerators.
- *Unusual reactions:* a) Airborne dermatitis; b) Contact urticaria; c) Erythema multiforme-like; and d) Photosensitisation.
- *Avoidance:* a) If patients need to dye their hair, they should use products that do not contain this substance; b) Patients should read the labels for dyes and cosmetics to avoid using those that have paraphenylenediamine or related chemicals; c) They should take care when using semi-permanent dyes (check the ingredients). Some 10% of patients who are allergic to PPD also react to these types of dyes; d) For hairdressers, the use of synthetic gloves is recommended when applying hair dyes; e) Patients should avoid work or hobbies that require the handling of products containing PPD, such as China ink (printing, photography, etc.), and black rubber and textile and leather dyes, unless the materials being used are known to be free of the substance; f) Patients should beware of clothes with dark dyes (blue, black and brown); g) They should avoid sunscreens and sun lotions that contain PABA; and h) Avoid products that contain local "caine" anaesthetics (benzocaine, procaine, etc).
- *Cross-reactivity:* a) Para-aminobenzoic acid (PABA) (sunscreens and sun creams); b) *p*-aminoazobenzene (75%); Disperse Orange 3 (66%); Disperse Yellow 3 (36%); Disperse Red 1 (27%); and Disperse Blue 124 (16%); c) Semi-permanent hair dyes; d) Diaminodiphenylmethane (epoxy hardener); e) Dyes derived from PPD: Ortho-aminophenol (*o*-aminophenol), Ortho-nitro-para-phenylenediamine (ONPPD), Para-toluenediamine (*p*-toluenediamine, PTDA), Para-aminodiphenylamine (*p*-

aminodiphenylamine, PADA); f) Para-aminosalicylic acid (p-aminosalicylic acid); g) 2,4-diaminoanisole; h) Parabens; and i) Medications: sulphonamides, sulphates, local "caine" anaesthetics (e.g. benzocaine or procaine). On rare occasions, patients sensitive to para-amino-phenylenediamine may react to these drugs, but tolerate them in most cases.

2.21 Formaldehyde

Formaldehyde is a ubiquitous product due to its multiple uses and its incorporation into numerous products and reagents in chemical processes (formaldehyde releasers, plastic polymers, metalworking fluids, drugs, cosmetics and detergents) (Agner et al, 1999; de Groot et al, 2009).

- *Synonyms*: BFV; Fannoform; Formaldehyde; Formalin; Formalith; FYDE; Formol; Formic aldehyde; HCHO; HOCH; Karsan; Lysoform; Melamine-formaldehyde resin; Methan 21; Methanal; Methylene glycol; Methylene oxide; Methyl aldehyde; Morbicid; Oxomethane; Oxymethylene; Superlysoform; and Veracur.
- *Formaldehyde-releasing preservatives*: Quaternium-15; Germall 115; Germall II; Tris Nitro; Bronopol; Glydant; Dociwill 75; Grotan BK; Onyxide 500; Myacide BT; and Vancide TH.
- *Uses*: a) Occupational: embalming solutions; dry cleaning materials; fertilisers; insulation in urea formaldehyde foam; metalworking fluids; automobile in distributor, fuse box, brake linings and clutch pedals; glues, adhesives, paints, varnishes; paper industry in high quality paper; explosives; laboratory fixatives in anatomopathology; photography; plastics and resins: urea, phenolic resin; rubber industry: preservatives, antioxidants and production of synthetic rubber; and wood composites (plywood, chipboard); b) Cosmetics; creams, shampoos, makeup, nail polish, antiperspirants; c) Clothing; starches, textile resins, footwear; and d) Others; astringents, dental plastics, disinfectants, sandpaper, anti-wart solutions.
- *Unusual reactions*: a) Airborne dermatitis; b) Contact urticaria; c) Erythema multiforme-like; d) Photosensitivity; and e) Phototoxic reactions.
- *Avoidance*: a) Patients should avoid contact with sources of exposure described above; b) They should carefully check the composition of cosmetics, personal hygiene products, etc; c) They should use products that do not contain formaldehyde or any of its synonyms; d) Patients should tell their doctors that they are allergic to this substance; e) If it causes problems related to their job, patients should tell their companies' medical department. They should request information sheets on the materials used. They should wear sufficient protection (use gloves, glasses, etc.); and f) Patients should wash new clothes in hot water before use and avoid starched clothing.
- *Cross Reactivity*: a) Arylsulfonamide resins; b) Chloroallyl-hexamine chloride; and c) DMDM hydantoin.

2.22 Mercapto mix

The mercapto mix contains the following four compounds, each at a concentration of 0.5% pet.: 2-mercaptobenzothiazole (MBT), *N*-cyclohexyl-2-benzothiazyl sulfenamide (CBS), 2,2-dibenzothiazyl disulphide (MBTS), and Morpholinyl mercaptobenzothiazole (MMBT). These chemicals are present in many rubbers, to which they are added as accelerators before vulcanisation takes place, and like thiurams, they are ubiquitous in rubber products (Geier et al, 2002; Diepgen et al 2006).

- *Synonyms of Dibenzothiazyl disulphide:* 2,2'-Benzothiazyl disulphide; Altax; Naugex MBT; and Thiofide.
- *Synonyms of N-cyclohexyl-2-benzothiazole sulfenamide:* CBTS; CBS; Cyclohexylbenzothiazyl sulphonamide; Durax; Santocure; and Vulkacit DM.
- *Synonyms of Morpholinyl mercaptobenzothiazole:* MOR; MMBT; and 4-Morpholinyl-2-benzothiazyl disulphide.
- *Uses:* a) Rubber materials: condoms and diaphragms ; gloves (home, work and hospital); rubber boots; medical equipment (rubber bands, syringes with rubber tips, etc.); kidney dialysis machines; rubber pillows; elastic materials in clothing and underwear; makeup sponges and rubber-tipped eyelash curlers; sports equipment: diving masks, suits and fins, squash balls, windsurfing boards, rubber swimming boots, caps and goggles, racquet coatings, etc.; toys; strips and tubes; and others: hoses, fuel tank coatings, electrical cables, gas masks, rubber supports for binocular eyepieces, conveyor belts, shock absorbers, headphones, aprons, dental dams, balloons, radiator hoses, mattresses, bumpers, head gaskets, calculator and remote control keypads, etc; b) Anti-corrosive agent; c) Anticoagulants; d) Fats; e) Cements and adhesives (glue for leather and plastic); f) Cutting oils; g) Detergents; h) Disinfectants, repellents, fungicides and insecticides used in agriculture; i) Emulsion for photographic film; and j) Veterinary products: flea and tick sprays and powders.
- *Avoidance:* a) Patients should be careful with materials made of black or dark grey rubber; b) It is difficult to know which rubber products have these substances. Some rubber products are labelled "hypoallergenic". Still, it is best if patients use them for no more than 30 minutes at a time; c) Patients should be careful with footwear, avoid those with rubber soles and use those that have synthetic or alternative material in the soles; d) Patients should use gloves made of synthetic alternatives to rubber: vinyl, neoprene, nitrile, etc; e) They should use rubber-free birth control devices (e.g. AVANTI® (Durex), FEMI® (Leti Laboratories), etc.); f) Patients should wear clothes without elastic in them; g) They should avoid occupational exposure and tell their company's medical department about their condition. They should use alternative materials; and h) Patients should avoid animals treated with products that contain these products.
- *Cross Reactivity:* Mercaptobenzothiazole.

2.23 Thiomersal

Thiomersal is used as an antiseptic and preservative in topical medications, cosmetics and vaccines. It is composed of two distinct components: a compound of organic mercury and thiosalicylate. Allergic reactions may be due to either of these two parts (van't Veen & van Joost, 1996; Hammonds et al, 2009). Patients sensitive to thiomersal may be classified into three groups:

- a. Group I) Positive to thimerosal but negative to other mercury compounds and thiosalicylic acid.
- b. Group II) Positive to thiomersal and other mercury compounds but negative to thiosalicylic acid.
- c. Group III) Positive to thiomersal and thiosalicylic acid but negative to other mercury compounds.

- *Synonyms:* Mertiolate; Tiomersal; Ethyl [2-mercaptobenzoato(2<)-O,S]-mercurate(1<) sodium; Ethyl (2-mercaptobenzoato-S) mercury, sodium salt; Mercurothiolate; Merfam; Merthiolate; Mertorgan; Merzonin; [(o-carboxyphenyl)thio]ethylmercury sodium salt; Sodium ethyl mercurithiosalicylate; Thiomersal; Thiomersalate; Thiomersalan; and Thimerosal.
- *Uses:* a) Antiseptics (sprays); b) Antitoxins (diphtheria, tetanus); c) Cosmetics (makeup removers, masks, moisturising creams, eye shadows, etc); d) Personal hygiene products (soap-free cleaners, etc); e) Eye preparations (eye drops, contact lens cleaning solutions, ointments); f) Antigenic extracts for skin tests; g) Topical and systemic medication (nasal and ear drops, tincture of merthiolate); h) Vaccines, immunotherapy; and i) Tuberculin test.
- *Unusual reactions:* a) Airborne dermatitis; and b) Photosensitivity.
- *Avoidance:* a) Patients should check the composition of cosmetics, medication (eye drops, other drops, topical preparations, etc.) They should use only labelled products that do not contain thimerosal or any of its synonyms; b) Patients should tell their doctor that they are allergic to thimerosal; c) Live virus vaccines, such as the influenza vaccine, may contain thimerosal. It can also be found in some recombinant and heat denatured vaccines. Usually, patients allergic to thimerosal do not have reactions when the vaccine is administered intramuscularly. However, some patients may suffer dermatitis at the site of administration. It is recommended that one needle be used for injection and another for extracting the contents of the vial. Possible reactions are not life threatening. If there are no alternative thimerosal-free vaccines, patients should assess the risks and benefits of its administration with their doctors.
- *Cross Reactivity:* a) Other organic mercury derivatives (mercurochrome, etc.); and b) analgesic Piroxicam (due to its thiosalicylic component).

2.24 Thiuram Mix

Thiuram Mix is used in skin tests for detecting contact allergies to four closely related chemical substances, which are added as accelerators in rubber production. These substances are: dipentamethylenethiuram disulphide (PTD), tetraethylthiuram disulphide (TETD), tetramethylthiuram disulphide (TMTD) and tetramethylthiuram monosulphide (TMTM). Rubber objects are frequently found in both home and workplace environment. Prolonged exposure to these materials may cause dermatitis, unlike occasional exposure (Conde-Salazar et al, 1993; Uter et al, 2010).

- *Synonyms of Tetramethylthiuram disulfide (TMTD):* Thiram; Thirad; Thiosan; Thiramyl; Puralin; Pomarsal; Tuads; Arasan; Nomersan; Rezifilm; Thylate; Tiuramyl; Fernasan; Tersan; and Tulisan.
- *Synonyms of Tetramethylthiuram disulfide (TETD):* Disulfiram (Antabuse); Bis (diethylthiocarbonyl) disulphide; Cronetal; Abstenisil; Stopetyl; Contralin; Robac TET; Antadix; Ethyl thiurad; Antiethanol; Etabus; Ro-Sulfiram; Abstynil; Thiranide; Tetratine; and Noxal.
- *Synonyms of Dipentamethylenethiuram disulfide (PTD):* Robac PTD.
- *Uses:* a) Adhesives (neoprene); b) Disinfectants, repellents, fungicides and insecticides used in agriculture; c) Food preservatives; d) Wood preservatives; e) Scabies medication; f) Antabuse (disulfiram) (used as a fungicide in agricultural and

commercial products); g) Leather footwear (soles, adhesives, liners); h) Rubber shoes (tennis, canvas, etc.); i) Surgical spray (Nobecutan®) for creating an isolating layer over surgical wounds; j) Elastic surgical bandages; k) Sunscreen creams; l) Soaps (Lifebuoy®) and shampoos; m) Peat for golf courses; and n) Rubber materials: condoms and diaphragms, gloves (household, work and hospital), medical supplies (elastic bands, stethoscopes, syringes with rubber-tipped plungers, etc.), kidney dialysis machines, rubber pillows, elastic materials in clothing and underwear, makeup sponges and rubber-tipped eyelash curlers, swimming gear (caps, goggles, etc.), toys, strips and tubes. Others: Fuel tank coatings, electrical cables, gas masks, rubber supports for binocular eyepieces, conveyor belts, shock absorbers, headphones, aprons, dental dams, balloons, hoses, mattresses, etc.

- *Avoidance:* a) It is difficult to know which rubber products contain these substances. Some rubber products are labelled "hypoallergenic". Still, it is best for patients to use them for no more than 30 minutes at a time; b) Patients should be careful with footwear, avoid those with rubber soles and use those that have synthetic or alternative material in the soles; c) Patients should tell their doctor that they are allergic to these products. They should avoid taking and handling Antabuse; d) Patients should use rubber-free birth control devices (e.g. AVANTI® (Durex), FEMI® (Leti Laboratories), etc.); e) They should use gloves made of synthetic alternatives to rubber: vinyl, nitrile, neoprene, etc; f) Patients should wear clothes without elastic in them; g) They should avoid other rubber materials: makeup sponges, balloons, etc; and h) Patients should avoid occupational exposure. They should tell their company's medical department about their condition and use alternative materials.

2.25 Sesquiterpene Lactone mix (SL mix)

Oleoresins that are present in plants of the *Compositae* family (chrysanthemum, ragweed, chamomile, dandelion, yarrow, dahlia, lettuce, escarole, chicory, endive, parthenium, etc). The allergens that make up the mixture are: Alantolactone, Dehydrocostus lactone and Costunolide (Orion et al, 1998; Paulsen et al, 1999).

- *Synonyms:* Sesquiterpene lactone; Gamma-lactone; Helenin; Alant camphor; Elecampane camphor; Inula camphor; Eupatal; [3aR-(3aa,5b,8ad,9aa)]-3a,5,6,7,8,8a,9,9a-Octahydro-5,8a-dimethyl-3-methylenenaphthol-[2,3-b]furan-2(3H)-one 8b-hydroxy-4aH-eudesm-5-en-12-oic acid.
- *Uses:* a) Occupational: florists, gardeners, agricultural workers, cooks, domestic workers, and homemakers; b) Others: cosmetics, perfume, natural remedies, alternative medicine.
- *Unusual reactions:* a) Airborne dermatitis; and b) Photosensitivity.
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) If it causes problems related to their job, patients should tell their company's medical department; and c) Patients should avoid direct and indirect contact with the plants mentioned above.

2.26 Euxyl K 400 (phenoxyethanol and methylidibromoglutaronitrile)

Euxyl K400 (Schülke & Mayr, Hamburg, Germany) is a combination of methylidibromoglutaronitrile (1,2-dibromo-dicyanobutane) (MDBGN) and phenoxyethanol

(1:4). It is used in body lotions, cosmetics, creams, shampoos, sunscreens and wet wipes. (Corazza et al, 1993; Basketter, 2010).

- *Synonyms of Phenoxyethanol*: 1-Hydroxy-2-phenoxyethane; 2-Hydroxyethyl phenyl ether; 2-Phenoxyethanol; b-Hydroxyethyl phenyl ether; Aerosol; Beta-phenoxyethyl alcohol; Dowanol ep; Dowanol eph; Emeressence 1160; Emery 6705; Ethanol-2-phenoxy; Ethylene glycol mono phenyl ether; Ethylene glycol phenyl ether; Euxyl K 400; Glycol monophenyl ether; Phenyl cellosolve; Phenylmonoglycol ether; Phenoxethol; Phenoxetol; Phenoxytol; Phenoxyethyl alcohol; Phenoxy ethanol; and Rose ether.
- *Uses*: a) Topical antiseptic; b) Bactericidal (attached to 1,2-dibromo-2,4-dicyanobutane in Euxyl K 400); c) Insect repellent; d) Perfume fixer; e) Solvent for cellulose acetate, dyes, inks and resins; f) In the organic synthesis of plasticisers, germicides, drugs, cosmetics and preservatives; and g) Toilet paper.
- *Synonyms of Methyldibromoglutaronitrile*: Euxyl K-400, Merck 48051; Metacide 38, 1-Bromo-1-(bromomethyl)-1,3-propanedicarbonitrile; 1,2-Dibromo-2,4-dicyanobutane; 2-Bromo-2-(bromomethyl) pentanedinitrile; 2-Bromo-2-(bromomethyl)-glutaronitrile; Bromo-1-(bromomethyl)-1,3-propanedicarbonitrile; Bromo-2-(bromomethyl)glutaronitrile; Bromo-2-(bromomethyl)pentanedinitrile; Dibromo-2,4-dicyanobutane; and Tektamer 38.
- *Uses*: a) Active ingredient in Euxyl K 400 and Tektamer 38 (methyldibromo glutaronitrile); b) Adhesives; c) Cosmetics, shampoos, sunscreens; d) Toilet paper; e) Preservative for fluids in the metalworking industry; f) Emulsions and latex paints; and g) Disperse dyes and detergents.
- *Avoidance*: a) Patients should avoid contact with sources of exposure described above; b) If it causes problems related to their job, they should tell their companies' medical department. Patients should request information sheets on the materials used; and c) Patients should avoid cosmetics and products that list Euxyl K 400 (or one of its components) in its ingredients.

2.27 Glucocorticoids

Glucocorticoid *budesonide* is an epimeric mixture of the α - and β -propyl forms of 16 α , 17 α -butylidenedioxy-11- β ,21-dihydroxypregna-1,4-diene-3,20-dione. It has been used topically (0.025% in a cream or ointment) for the treatment of various skin disorders, but is more often used by inhalation in the management of asthma, and as a nasal spray for the prophylaxis and treatment of allergic rhinitis. Budesonide belongs to group B corticosteroids (e.g., triamcinolone acetonide and derivatives) (Lepoittevine et al, 1995; Goossens et al, 200; Isaksson et al, 2000).

Glucocorticoid *tixocortol pivalate* is 11 β , 17 α -dihydroxy-21-mercaptopregn-4-ene-3,20-dione 21-pivalate. Used in buccal, nasal, throat, and rectal preparations, but not for the treatment of skin diseases. Tixocortol pivalate belongs to group A corticosteroids (e.g., hydrocortisone and derivatives).

It is used in the standard battery of contact allergens to detect those people who are sensitive to corticosteroids.

- *Synonyms of Budesonide*: 16,17-Butylidenebis(oxy)-11,21-dihydroxy-pregna-1,4-diene-3,20-dione; Budesonide; and Budeson.

- *Synonyms of Tixocortol pivalate:* Pivalone, Procolon, Rectovalone, Tivalon-NT, Tiprederm, (11b)-21-[(2,2-dimethyl-1-oxo-propyl)thi-o]-11,17-didihydroypereg-4-ene-3,20-dione, Tixocortol-21-pivalate.
- *Unusual reactions:* a) Airborne dermatitis; and b) Erythaema multiforme-like (budesonide).
- *Uses:* a) Medication: creams, ointments, nasal and bronchial sprays, etc.
- *Avoidance:* a) Patients should check the ingredients of medicines carefully, especially topical drugs such as sprays, creams, ointments, etc; b) They should tell their doctor that they are allergic to this product; and c) Their allergy specialist will advise them as to which topical and/or systemic corticosteroids they should avoid and what others may be used as alternatives.
- *Cross Reactivity:* other corticosteroids of its corticosteroid group or from other structurally related groups.

Group A: type hydrocortisone:

- *Topical:* Cloprednol; Dichlorisone acetate; Fludrocortisone acetate; Fluorometholone; Fluprednisolone acetate; Hydrocortisone; Hydrocortisone-21-sodium; Hemisuccinate medrysone; Meprednisone; 6- α -Methylprednisolone acetate; Methylprednisolone; Prednisone sodium phosphate; and Tixocortol pivalate.
- *Systemic:* Cortisone acetate; Hydrocortisone-21-acetate; Methylprednisolone acetate; Prednisolone acetate; and Prednisone.

Group B: type triamcinolone:

- *Topical:* Amcinonide; Budesonide; Desonide; Fluocinolone acetonide; Fluocinonide; Flumoxonide; Flunisolide; Flurandrenolide; and Halcinonide.
- *Systemic:* Triamcinolone acetonide; Triamcinolone; Triamcinolone benetonide; Triamcinolone diacetate; and Triamcinolone hexacetonide.

Group C: type betamethasone:

- *Topical:* Betamethasone-21-disodium phosphate; Desoximetasone; Dexamethasone-disodium phosphate; Diflucortolone pivalate; Diflucortolone valerate; Flumethasone; Fluocortin butyl; Fluocortolone hexanoate; Fluocortolone pivalate; Fluocortolone caproate; Fluprednidene acetate; and Halometasone.
- *Systemic:* Betamethasone (non valerate); Dexamethasone acetate; and Paramethasone acetate.

Group D: type hydrocortisone 17-butyrate:

- *Topical:* Alcometasone dipropionate; Betamethasone valerate; Betamethasone dipropionate; Clobetasol propionate; Clobetasone butyrate; Diflorasone diacetate; Fluticasone propionate; Halobetasol; Mometasone furoate; Hydrocortisone aceponate (17-butyrate); Hydrocortisone valerate; Prednicarbate; and Methylprednisolone aceponate.
- *Systemic:* Beclometasone dipropionate; and Betamethasone dipropionate

Table 2. The original classification proposed (Coopman et al, 1989) has been distinguished corticosteroids into four groups according to their molecular structure.

3. Other allergens of interest

The baseline series can be extended to include allergens of local importance to specific departments.

3.1 Mercury

It is a metal that has had many uses over time. It is toxic to humans. There are organic and inorganic compounds derived from mercury that may also cause sensitisation (Babich & Burakoff, 1997; Boyd et al, 2000; Bains et al, 2008).

- *Synonyms:* Mercury; Hydrargyrum; Liquid silver; Quicksilver; Rathje; and Marcero.
- *Uses:* a) Agriculture (chemical products); b) Dirt repellent paints; c) Antiparasitic powders; d) Electrolysis (cathode); e) Dental amalgams; f) Lamps (mercury arc); g) Non-electronic thermostats; h) Some electrical switches; i) Batteries; j) Drugs (mercury derivatives e.g. mercurochrome, thimerosal, etc.); k) Thermometers, barometers, hygrometers, pyrometers; l) Oesophageal dilators (bougie tubes); m) Cantor and Miller Abbott tubes (used in intestinal obstructions); n) Feeding tubes; and o) Laboratories (fixatives, tinctures, reagents and preservatives).
- *Unusual reactions:* Airborne dermatitis (Baboon syndrome) (Häusermann et al, 2004).
- *Avoidance:* a) Patients should avoid contact with sources of exposure described above; b) They should avoid using instruments containing mercury (they should use digital thermometers. If a mercury thermometer is broken, they should avoid contact with the mercury or inhalation of its fumes); c) Patients should tell their doctor and dentist that they are allergic to this substance; d) Dental fillings (amalgams) that contain mercury should be avoided; e) If the use of antiseptics is required, patients should avoid those with mercury derivatives (mercurochrome, thimerosal) and use alternatives: e1) Iodine compounds (Povidone-iodine, tincture of iodine), e2) Phenolic compounds (Germisidin, Germix), e3) Oxidants (hydrogen peroxide, potassium permanganate) and e4) Chlorhexidine.

3.2 Diallyl disulfide (Garlic)

Garlic (*Allium sativum*) is a plant belonging to the lily family (Liliaceae). It has a bulb (head) consisting of bulblets (cloves) arranged around the stem. It has been used since ancient times as a spice in food and as a natural remedy due to its numerous therapeutic properties, both with the dried extract and the distilled oil (detoxifier, antibacterial, antiviral, antimycotic, antihypertensive, hypoglycaemic, anticoagulant, antioxidant, lipid lowering, anticancer, immunomodulator, etc.)

Diallyl disulphide is a compound with low molecular weight and is the main allergen in garlic. Other allergens are Garlicin and Allyl dipropyl disulphide, which contribute to the taste and pungent odour of this plant. People sensitive to garlic have characteristic dermatitis affecting the pads of the fingers (index, middle and ring fingers of the non-dominant hand), producing pulpitis. Sensitisation can sometimes go unnoticed when it occurs with other concomitant sensitisations (rubber, metals, etc.) or with irritant dermatitis ("housewife's dermatitis"). The most affected professions are cooks and kitchen staff, as well as domestic service employees and homemakers (Jappe et al, 1999; Cabanillas et al, 2006; Bordel-Gómez & Miranda-Romero, 2008).

- *Synonyms:* Allium; Allium sativum; Disulfide; Di-2-propenyl; Allyl disulfide; Allyl disulphide; DADS; Dialil disulfuro; Dialilo disulfuro; Diallyl disulfide; Diallyl disulphide; Disulfuro de alilo; Dithia-1,7-octadiene; Garlic; and Garlicin.

- *Uses:* a) Food (handling garlic, onion, etc.); b) Aromatherapy; and c) Medications: Garlic extract preparations (capsules, essential oil, juice, dry extract, tincture, syrup).
- *Unusual reactions:* a) Photosensitivity; b) Systemic contact dermatitis; and c) Anaphylaxis.
- *Avoidance:* a) Patients should tell their doctor that they are sensitive to this substance; b) They should avoid handling garlic and other lilies, such as onion; c) People with contact dermatitis due to garlic and its components rarely have problems consuming it; d) Pharmacists can advise patients on medicines that contain this substance; e) Patients should check the ingredients on the labels of drugs sold in pharmacies and natural medicine centres; and f) The use of rubber gloves does not prevent dermatitis due to the handling of garlic.

4. Conclusion

The baseline series is dynamic and subject to regular changes depending on population exposures and prevalence of contact allergy. Among the major patch test material companies, Hermal, Chemotechnique, and Brial supply with some modifications in the baseline series, as recommended by the European Society of Contact Dermatitis (ESCD), and Mekos supplies TRUE Test Panel 1-3, which, in the collection and preparation of the allergens, differ from the ESCD baseline series on several positions. The frequency of allergic contact sensitization to the allergens of the standard series varies from study to study, depending on the composition of the study population.

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