EDITED BY
JOHN McFADDEN, PAILIN PUANGPET, KORBKARN PONGPAIROJ,
SUPITCHAYA THAIWAT, LEE SHAN XIAN

COMMON CONTACT ALLERGENS

A PRACTICAL GUIDE TO DETECTING CONTACT DERMATITIS

WILEY Blackwell

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A Practical Guide to Detecting Contact Dermatitis

Edited by

John McFadden

Consultant Dermatologist
Department of Cutaneous Allergy
St John's Institute of Dermatology
King's College, Guy's Hospital
London, UK

Pailin Puangpet

Consultant Dermatologist
Occupational and Contact Dermatitis Clinic, Institute of Dermatology
Bangkok, Thailand

Korbkarn Pongpairoj

Consultant Dermatologist
Division of Dermatology, Department of Medicine, Faculty of Medicine
Chulalongkorn University and King Chulalongkorn Memorial Hospital
Thai Red Cross Society
Bangkok, Thailand

Supitchaya Thaiwat

Consultant Dermatologist
Contact Dermatitis clinic, Division of Dermatology, Department of Internal Medicine
Phramongkutklao Hospital
Bangkok, Thailand

Lee Shan Xian

Consultant Dermatologist
Department of Dermatology
Changi General Hospital
Singapore

WILEY Blackwell

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Dedications

John McFadden: To all my family, friends and colleagues. An especial dedication to Dr. Ian White who has been a teacher, mentor, colleague and friend at St John's for over 25 years.
Pailin Puangpet: For my family, teachers, friends and colleagues.
Korbkarn Pongpairoj: For all my beloved family, teachers, colleagues, and patients.
Supitchaya Thaiwat: I dedicate this book to my father, my other family members, my teachers, and my colleagues.
Lee Shan Xian: I would like to thank my family (especially my husband and son) for their unwavering support, my mentors, my friends/colleagues, and our patients for teaching me so much.

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List of Contributors

Dr. Mahbub M.U. Chowdhury
Consultant Dermatologist
The Welsh Institute of Dermatology
University Hospital Wales
Cardiff, Wales, UK
Setting up a Patch Test Practice

Bo Niklasson
CEO, President
Chemotechnique Diagnostics
Vellinge, Sweden
The Role of Providers of Patch Test Products

Dr. Elin Dafydd Owen
Cutaneous Allergy Fellow
The Welsh Institute of Dermatology
University Hospital Wales
Cardiff, Wales, UK
Setting up a Patch Test Practice

Associate Chapter Editors

Professor Klaus Ejner Andersen
Institute of Clinical Research
University of Southern Denmark
and
Department of Dermatology and Allergy Centre
Odense University Hospital
Odense, Denmark
Nickel

Dr. David Basketter
Toxicologist
DABMEB Consultancy Ltd.
Bedford, UK
Preservatives
para-Phenylenediamine
Immunology of Allergic Contact Dermatitis

Dr. Mike Beck
Emeritus Consultant Dermatologist
Contact Dermatitis Investigation Unit
Salford Royal NHS Foundation Trust
Manchester, UK
Patch Test Technique
History, Microhistory and Allergen Exposure

Dr. Johnny Bourke
Consultant Dermatologist
Department of Dermatology
South Infirmary Victoria University Hospital
Cork City, Ireland
Clioquinol
Neomycin

Professor Magnus Bruze
Professor of Occupational Dermatology
Department of Occupational and Environmental Dermatology
Lund University
Skåne University Hospital
Malmö, Sweden
Gold

Dr. Deirdre Buckley
Consultant Dermatologist
Department of Dermatology
Royal United Hospital
Bath, UK
Fragrances

Dr. John English
Consultant Dermatologist
Nottingham University Hospitals NHS Trust
Nottingham, UK
Colophonium
Epoxy Resin
PTBP Resin
Lanolin
Corticosteroids

Professor Chee Leok Goh
Clinical Professor
National Skin Centre
Singapore
Potassium Dichromate

Dr. Graham Johnston
Honorary Associate Professor
Department of Dermatology
University Hospitals of Leicester NHS Trust
Infirmary Square
Leicester, UK
Cobalt

Dr. Christopher Lovell
Consultant Dermatologist
Royal United Hospital
Combe Park
Bath, UK
Sesquiterpene Lactone and Compositae
Primin

Professor Howard Maibach
Department of Dermatology
University of California
San Francisco, CA, USA
Disperse Blue 106

Associate Professor Rosemary Nixon
Director, Occupational Dermatology Research and Education Centre
Skin and Cancer Foundation Inc.
Melbourne, VIC, Australia
Tosylamide Formaldehyde Resin

Dr. David Orton
Consultant Dermatologist
152 Harley Street Ltd
London, UK
Rubber Chemicals
Cetearyl Alcohol

Dr. Jason Williams
Consultant Dermatologist
Contact Dermatitis Investigation Unit
Salford Royal NHS Foundation Trust
Manchester, UK
Benzocaine

Preface

In many ways practising contact dermatitis resembles the work of a detective. They both require searching for clues in a systematic, detailed manner. They also both require a thorough grasp of relevant subject information and skills learnt from previous purposeful experience. This book aims to assist the physician in acquiring the skills necessary for optimal clinical practice in contact dermatitis.

The first section addresses methodology. Concepts such as microhistory and microexamination are introduced. We illustrate a detailed, systematic approach to contact dermatitis.

The second section gives a grounding in common non-allergic dermatitis/dermatoses. Approximately half of the patients seen in patch test clinics do not have allergic contact dermatitis, so recognising these other dermatitis/dermatoses is essential.

The third section involves common contact allergens that physicians are likely to encounter. Allergens are reported within their individual chapters. Key points followed by a synopsis of clinical disease are presented in a coherent, systematic way. Where appropriate, allergen profiling (potential sources of allergen exposure, routes of allergen exposure and clinical manifestations of contact allergy) is demonstrated. Bullet points have been color coded according to exposure sources. Throughout this section the emphasis is on helping the physician decide on the clinical relevance of the contact allergy identified by patch testing.

Electronic supplements for the allergen chapters give extra clinical, epidemiological, immunological and chemical material for an inquiring mind.

All but two of the chapters have been drafted by the five co-editors. This was a deliberate decision to keep the style and presentation consistent throughout the book. We have been fortunate to have, as associate chapter editors, some of the leading international experts in the chapters they have 'refereed', invariably improving the content.

We hope this book provides the methodology and background knowledge to assist the reader to practise contact dermatitis purposefully. Practising contact dermatitis can be fully rewarding and of great benefit to the physician's patient. We wish you every success.

John McFadden
Pailin Puangpet
Korbkarn Pongpairoj
Supitchaya Thaiwat
and
Lee Shan Xian

About the Companion Website

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SECTION 1

Methodology

CHAPTER 1

Immunology of Allergic Contact Dermatitis

Allergic contact dermatitis is a T cell immune mediated inflammatory skin condition. It is characterized by the following immunological properties:

- *Immunological memory*: induction of sensitization. When a contact allergen penetrates and reacts covalently with protein in the skin, it is transported to the local lymph node by antigen presenting cells. There, it is presented to naive T cells through interactions between the haptenized antigen-peptide complex, Major Histocompatibility Complex (MHC) groove, and T cell receptor. On recognition of the antigen and in the presence of danger signals, a naive T cell will undergo clonal proliferation to produce memory and effector T cells.
- *Elicitation*: repeated exposure to the antigen will cause further clonal proliferation until a threshold is surpassed when the pool of cloned T cells recognizing the antigen is sufficiently large that when the antigen is encountered within the skin, the T cells will activate and initiate local dermal inflammation.
- The *Th1* and *Th17* immune pathways are predominantly involved with the production of pro-inflammatory cytokines such as IL-1, IL-2, tumor necrosis factor-α (TNF-α), α-interferon, IL-6, IL-8, IL-12, IL-17, and IL-23 [1].
- *Friedmann's principle*: the single most important factor in sensitization is allergen dose per unit area of skin (except for areas of skin less than 1 cm^2 when the aggregate dose is paramount). Therefore, someone who sprays perfume for 2 seconds on just a small area of the neck is more likely to become sensitized to the fragrance allergen(s) than someone who sprays the perfume for 2 seconds all over the torso [2].
- Contact allergens are *haptens*, which are protein reactive and bind chemically to proteins/peptides within the skin. Contact allergens/haptens are usually electrophilic and form covalent bonds with nucleophilic amino acids such as lysine, cysteine, and/or histidine [3]. Sometimes the contact allergen needs to be first oxidized (pre-hapten) or metabolized (pro-hapten) before becoming sufficiently electrophilic. The altered peptide/protein is then recognized by the immune system.
- *Danger signals* (Figure 1.1). Contact allergens/haptens also stimulate the innate immune system, which then alerts the adaptive immune system. It usually achieves innate immune activation through the generation of reactive oxygen species (ROS)/oxidative stress which then generates danger-associated molecular pattern (DAMP) molecules such as fibronectin and hyaluronan [4]. These DAMP molecules then activate pattern recognition receptors (PRRs) such as toll-like receptors (TLRs) 2 and 4, which leads to the stimulation of pro-inflammatory cytokines, the secretion of chemokines and recruitment of T cells to the skin, and an amplification of the immune response [1].
- Metal contact allergens appear to be unique in having the ability to directly stimulate TLRs, and hence the innate immune system, without generating DAMP molecules [5].
- *Immunological mechanisms* underpinning allergic contact dermatitis have similarities to the immune response to pathogenic bacteria and this explains why apparently evolutionarily wasteful responses (allergic contact dermatitis) have been preserved [1, 6].
- There is strong clinical evidence that the immune response to contact allergy consists of both a tolerizing and a sensitizing response, and that the tolerizing response decays with age at a faster rate than the sensitizing response. This explains why allergic contact dermatitis is more common in the elderly, when the T cell sensitizing response to experimental strong contact allergens such as dinitrochlorbenzene (DNCB) appears to decline [7].
- Exposure to contact allergens in the absence of danger signals should theoretically lead to tolerance. However, once clinical sensitization has occurred it has not so far been possible to reverse it [8].
- *Oral tolerance* to nickel through dental braces has probably occurred in many individuals; however, this effect will usually only happen if the individual has not had their ears pierced prior to dental braces being inserted such that they have significant prior skin exposure [9].
- In everyday life, most allergic contact dermatitis reactions are elicitation reactions and occur within 48 hours of exposure. A main exception to this is reaction to *p*-phenylenediamine in "henna beach tattoos", which is usually a primary sensitizing reaction occurring after 10–21 days, similar to an experimental DNCB sensitizing reaction.

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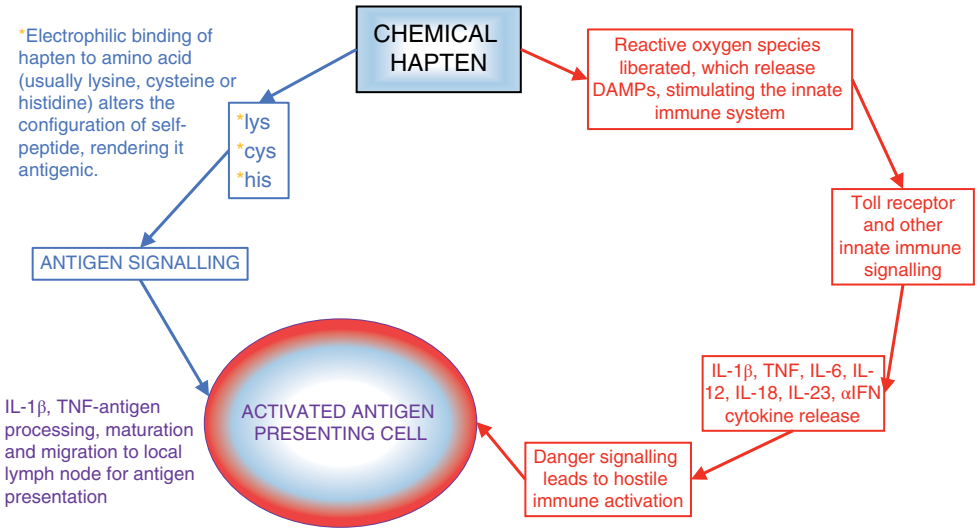

Figure 1.1 Dual signaling by haptens leading to contact sensitization. →, antigen pathway; →, danger pathway.

- By inference, sensitization to everyday agents such as cosmetic allergens are "quiet" events. Elicitation allergic contact dermatitis reactions occur when the threshold for response is surpassed, recognizing that the threshold will depend on the dose/concentration of the allergen factored with the extent/level of sensitization.
- The *level of sensitization* can increase through either repeated exposure to an allergen from a single source (e.g. *p*-phenylenediamine exposure from hair dye repeatedly applied every 1–2 months) or from exposure to an agent from multiple sources (e.g. methylisothiazolinone exposure from cosmetic creams, shampoos, and washing-up liquid).
- The immunological dose can increase through exposure to increased concentrations of an allergen (e.g. changing from blonde to black hair dye can increase the allergen exposure by a factor of 10 [10]), exposure to an allergen in the presence of an adjuvant (e.g. fragrance exposure in the presence of an aluminum salt in a deodorant, the aluminum salt acting as an adjuvant and increasing the danger signals generated), exposure to an allergen on skin which is already inflamed and where danger signals have already been generated (e.g. application of fragrance in an aftershave onto facial skin with seborrheic eczema), or increased time of exposure to an allergen (e.g. increased work hours in a construction unit leading to increased time of exposure to epoxy resin).
- Some contact allergens co-react from immunological cross-reaction due to chemical similarity, e.g. nickel and palladium, *p*-phenylenediamine and benzocaine. Some contact allergens co-react due to sensitization from same-source exposure, e.g. nickel and cobalt from exposure to low-carat gold jewelry.
- In patients with atopic dermatitis, contact sensitization occurs through the Th2 immune system and is therefore less efficient [11]. This may also explain how contact allergens and exposure to irritants can exacerbate atopic dermatitis (i.e. through Th2 stimulation) even without sensitization occurring (chemical atopy) [12].

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CHAPTER 2

Patch Test Technique

CHAPTER CONTENTS

Patch testing is an *in vivo* standard procedure to detect type IV hypersensitivity reactions to contact allergen(s) and determine the clinical relevance. The results from correct patch test techniques help in identifying and avoiding the true causative allergen(s). A positive patch test detects the immunological state of contact allergy. The diagnosis of allergic contact dermatitis depends on deducing clinical relevance. Patch testing within the context of the process of diagnosing allergic contact dermatitis is discussed in Chapter 3.

Patient expectations should be managed at the pre-patch test stage. In particular, a negative patch test and/or an inconclusive diagnosis at the post-patch test stage should be highlighted as possible outcomes.

Indications

- Where direct exposure allergic contact dermatitis (ACD) is suspected, e.g. to hair dye, perfume, gloves, jewelry.
- Acute or chronic dermatitis which is possibly related to occupational exposure.
- Recalcitrant chronic eczema.
- Hand eczema.
- Worsening of pre-existing eczema or exacerbation of endogenous eczema, such as atopic, seborrheic, or nummular eczema.
- When airborne ACD is suspected, e.g. perfumes, resins, preservatives and plants.
- Atypical, asymmetrical, or unpredictable flares of dermatitis to exclude by proxy ACD.
- Some delayed-type drug eruptions.
- Non-eczematous cutaneous reactions that may be manifestations of contact sensitization, such as lichenoid dermatitis and pseudolymphomatous reactions.
- To differentiate between angioedema and ACD mimicking angioedema.
- Discoid eczema.
- To exclude medicament allergy.
- Mucositis – conjunctivitis, stomatitis, vulvitis where ACD is suspected.
- Implants – loosening, rejection, association with localized or extensive rash [1, 2].

Cronin states "Ideally every patient with eczema should be patch tested and the importance of this investigation is now universally accepted"[3]. However, this statement should be seen as an ideal subject to practical constraint.

Patch test techniques

Patient information

- All patients should be informed about the purpose, procedure, benefits and potential side-effects of patch testing.
- The need to keep the back dry should be emphasized.
- Excessive exercise, wetting the testing areas, and sunlight should be avoided during the procedure. Excessive sunlight exposure in the 4 weeks prior to testing should also be avoided.

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Preparation of patch testing

1. Patch testing systems
   Patch testing is performed by applying chemical substances under occlusion on the patient's skin under standardized conditions. There is still no definite evidence to show which testing system is superior. Nowadays, there are many different systems available, including:
   - aluminum disks mounted on a non-occlusive hypoallergenic acrylic-based adhesive tape [4]
   - plastic chambers on hypoallergenic tape (Figure 2.1)
   - pre-packaged tests mounted on an acrylic-based adhesive tape.
2. Allergen selection
   - Standard/baseline series should be applied to all patients [5, 6].
   - The addition of a specific allergen, based on the history and clinical presentation of the dermatitis, may be needed [7, 8].
   - Extra series, when available, can be added to increase the sensitivity of the test if deemed clinically appropriate (e.g. hairstyling series in a beautician).
3. Vehicles
   The properties, solubility, and pH of an allergen determine the most suitable vehicle for use.
   - Petrolatum (pet.) can be mixed with most chemicals. First, petrolatum is stable. Second, it can prevent or decrease degradation, oxidization, and polymerization of the combined allergen [9, 10]. Third, it is inexpensive. Finally, it provides good occlusion. In general, water-insoluble agents are diluted in petrolatum. Acetone, methyl ethyl ketone, ethanol, and olive oil can be used as alternatives. Petroleum samples can be applied from a syringe to form a "snake" covering the maximum diameter of the chamber.
   - Aqueous solutions are more suitable vehicles for some substances, such as water for formaldehyde, methylchloroisothiazolinone, and methylisothiazolinone (MI). These are usually applied using a paper disc fixed onto the chamber with a small amount of pet. The application of too much petroleum may smother the upper layer of the disc on application of the patch to the back, thereby leading to a false-negative result.
4. Concentrations
   - Commercial test substances are preferred.
   - A dilution series of allergens could be tested when investigating
     - a low number of highly suspected agents
     - new allergens.
   - Appropriate concentrations for patch testing of allergens in various preparations are shown in Table 2.1.
     Note: Testing patients' own products is only helpful when positive as there may be low sensitivity, e.g. a moisturizer may have MI at a concentration of 100 ppm, whereas the ideal concentration for MI for patch testing is 2000 ppm in aqueous solution.
   - Mixes of allergens
     Some allergens in the standard series, such as fragrances and rubber compounds are tested as mixtures. If practicable, subsequent additional testing to individual agents on the first reading should be performed if the patch test to the mix is positive.
   - Patch testing of a patient's own substance(s)
     - The important necessary information includes the patient's own sample(s), information leaflets, safety data sheets, and/or lists of ingredients, e.g. International Nomenclature of Cosmetic Ingredients (INCI) lists. This information may be found on the Internet or requested from the manufacturers.
     - Patch testing must not be done with unknown chemicals or extremely hazardous substances such as poisonous agents.
     - Strong acids or alkaline chemicals should be buffered in order to decrease the risk of cutaneous irritation and to allow allergen preparation in higher concentrations – in practice this will be outside the expertise of most centers.
     - Negative results may occur due to too low concentrations, whereas too high concentrations may lead to cutaneous irritation and active sensitization.
5. Storage
   In general, substances for patch testing should be kept at 2–8 °C and protected from light. A contact allergen with a particular property may need special storage conditions. For example, some diisothiocyanates should be stored at −18 °C. The expiry dates must be checked regularly [11, 12].
   Fragrances and acrylates are particularly volatile substances and should be stored in refrigerators in closed syringes. Preparation of these for patch testing should be performed immediately before application as prolonged exposure to air will lead to a theoretical lowering of allergen concentration.

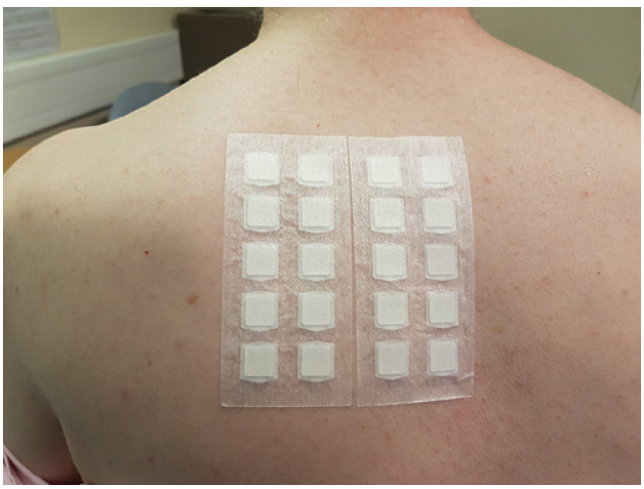

Figure 2.1 Patch test application using IQ® chamber system.

Patch test application

1. Anatomical site
   - The upper back is the preferred site. Its flat surface is suitable for occlusion and a number of allergens can be tested due to an available large area.

Table 2.1 Different preparations of commonly used products and suitable concentrations for patch testing [20].

Preparation	Examples	Tested concentration	Notes
Leave-on products	Cosmetic preparations, protective creams, topical medicaments	"as is", i.e. undiluted	—
Rinse-off products	Liquid soap, shampoos, shower gels	1–10% in aq., depending on the formulation	—
Metal-working fluids	The most important allergens are biocides, rust preventives, emulsifiers, and tall oil derivatives	Test the metal-working fluid "as is" taken from the machine or a fresh dilution prepared from the concentrate	Testing only fluids may miss preservative and fragrance allergies
Water-based fresh metal-working fluids	The workplace concentration of water-based metal-working fluids is usually 4–8% in the circulatory system	5% concentration in aq. Adjusting the pH, the used water-based 4–8% metal-working fluids taken from the circulatory system can be tested if necessary	Other possible sources of impurities (e.g. oil) can be evaluated separately
Oil-based metal-working fluids		50% in olive oil (fresh and used)	—
Solid materials	Paper, textile, plastic, rubber, metal specimens of suitable shape, wood dust	"as is" Note: Samples can be fixed to the chambers with small amounts of pet.	Consider the use of large 12 mm diameter chambers —
Powdery materials, ground dust, scrapings or small cut pieces			Tested in chambers (first moistened with water or organic solvents)
Larger pieces	Glove material, textiles	"as is" Consider larger chambers	Test semi-open, cover with surgical test tape without a chamber
Plants		Concentrations of commercially available plant materials include sesquiterpene lactone mix 0.1% pet., primin 0.01% pet., tulipaline A 0.01% pet., and diallyl disulfide 1.0% pet. Fresh or dried plant material: use "as is" Plant materials (flower, leaf, or stem): patch test plant material "as is" with a drop of saline water or ethanol for each part of the plant because either water-soluble or alcohol-soluble allergens, or both, may be present	Consider the use of larger 12 mm chambers Some plants cause irritant reactions Active sensitization is a possible theoretical risk Plant material generally has more allergens during the summer compared to winter
Miscellaneous	Textiles, plastics, food, plants, perfumes, drugs, and grease	Thin-layer chromatograms, paper, "as is" [27]	Available only in a few centers in Europe
Unidentified material brought by patient			Do not test as may be caustic, noxious, or poisonous

- The outer surfaces of the upper arms or thighs can be used as alternatives.

2. Occlusion time

The latest International Contact Dermatitis Research Group (ICDRG) recommendation recommends an occlusion time of 2 days.

Patch test reading

1. Reading times

Patch test reactions must be evaluated over at least two readings. Many options of reading times can be arranged with different levels of recommendation, as shown in Table 2.2.

2. Patch test reading

The ICDRG reading criteria, which scores according to the morphology of patch test reactions, is used as a standard (Table 2.3 and Figure 2.2).

- Contact allergy is demonstrated with positive patch test reactions (reactions of at least 1+) at day 3 and/or later.
- Where necessary, a dose-response relationship between the strength of allergic reactions and a variety of concentrations differentiates a true positive result from an irritant reaction.
- Questionable reactions (?+) can sometimes be clinically relevant in an individual patient [6, 13] and may need further investigations such as repeated patch testing with different concentrations or a repeat open application test.
- False-positive reactions can give an appearance of skin which has been rubbed with "soap" (Figure 2.3). Pustular and follicular reactions may be either false or true positive reactions (Figures 2.4 and 2.5).

Table 2.2 Schedules of patch test reading and levels of recommendation [20].

Levels of recommendation	Days of patch test reading				Notes
	Day 2	Day 3	Day 4	Day 7	
Optimum (ideal), but may be least practicable	✓	✓ (day 3 or day 4)		✓	A reading between day 5 and day 10 is necessary for some allergens, such as corticosteroids and aminoglycosides A reading around day 7 will pick up additionally 7–30% of contact allergies [28–30]
Fair alternative	X	✓ (day 3 or day 4)		✓	
Acceptable	✓	✓ (day 3 or day 4, prefer day 4)		X	False-negative results may occur
Possible but not generally recommended	X	X	✓	X	In order to increase detection of contact allergies, two readings on days 4 and 7 were required [28] A day 2 reading as the only single reading is not appropriate [31]

Table 2.3 The ICDRG patch test reading criteria [32].

Symbol	Morphology	Assessment
–	No reaction	Negative reaction
?+	Faint erythema only	Doubtful reaction
+	Erythema, infiltration, possibly papules	Weak positive reaction
++	Erythema, infiltration, papules, vesicles	Strong positive reaction
+++	Intense erythema, infiltrate, coalescing vesicles	Extreme positive reaction
IR	Various morphologies, e.g. soap effect, bulla, necrosis	Irritant reaction

- Positive reactions to corticosteroids can sometimes give an "edge" effect, with the periphery more raised and palpable than the center of the positive patch test reaction (Figure 2.6).
- A large blister reaction may indicate either a strong true "positive" reaction or a strong irritant "false" reaction to an inappropriately diluted agent.
- Rarely a non-eczematous true reaction may occur (e.g. an erythema multiforme-like reaction to *p*-phenylenediamine) which may be relevant to the morphology of the presenting dermatitis. At the first reading appointment equivocal patch test reactions, and surprisingly positive or surprisingly negative patch test reactions should be repeated.

Special considerations

False-negative and false-positive reactions

Although there is no definite contraindication for patch testing, physicians must be aware of the possibility of false-negative and/or false-positive reactions in some special situations. Patch testing, if necessary, could still be performed in these patients. Repeat patch testing may, however, give more information. The following may promote false-negative reactions:

- *Individual factors*. Immunosuppression [14–16], tanning, very active atopic dermatitis [17], active dermatitis
- *Environmental factors*. Ultraviolet (UV) light/sun exposure [18] – significant natural ultraviolet B (UVB) or therapeutic UV exposure to the back within the past 4 weeks or between the first and second readings.
- Medications:
  - systemic immunosuppressive drugs, e.g. corticosteroids more than 15 mg per day; azathioprine and cyclosporine – proceed with caution but if unsuspected negative test, consider re-testing when off immunosuppression [19].
  - Topical corticosteroids influence patch testing results only when they are applied to the patch test sites.
  - Antihistamines, disodium cromoglycate [19], and non-steroidal anti-inflammatory drugs (NSAIDs) usually have no effects on allergic patch test reactions [20].

Special groups

- Atopic dermatitis
  - Indications for patch testing are the same as for other patients.
  - Beware of false-positive/irritant reactions, especially to metals.
- Children
  - Indications for patch testing are the same as in adults [21].
  - A smaller selection of some contact allergens may be needed because of a smaller back.
  - Unless there is a history of exposure, exclude *p*-phenylenediamine and epoxy resin to reduce the possibility of active sensitization.
- Drug eruptions

  According to some types of drug eruptions, positive patch test results can confirm the culprit drug(s), whereas negative reactions cannot exclude the responsible medication. These include:

  1. delayed cutaneous adverse drug reactions (CADRs), including maculopapular exanthema, drug reaction with eosinophilia and systemic symptoms (DRESS),

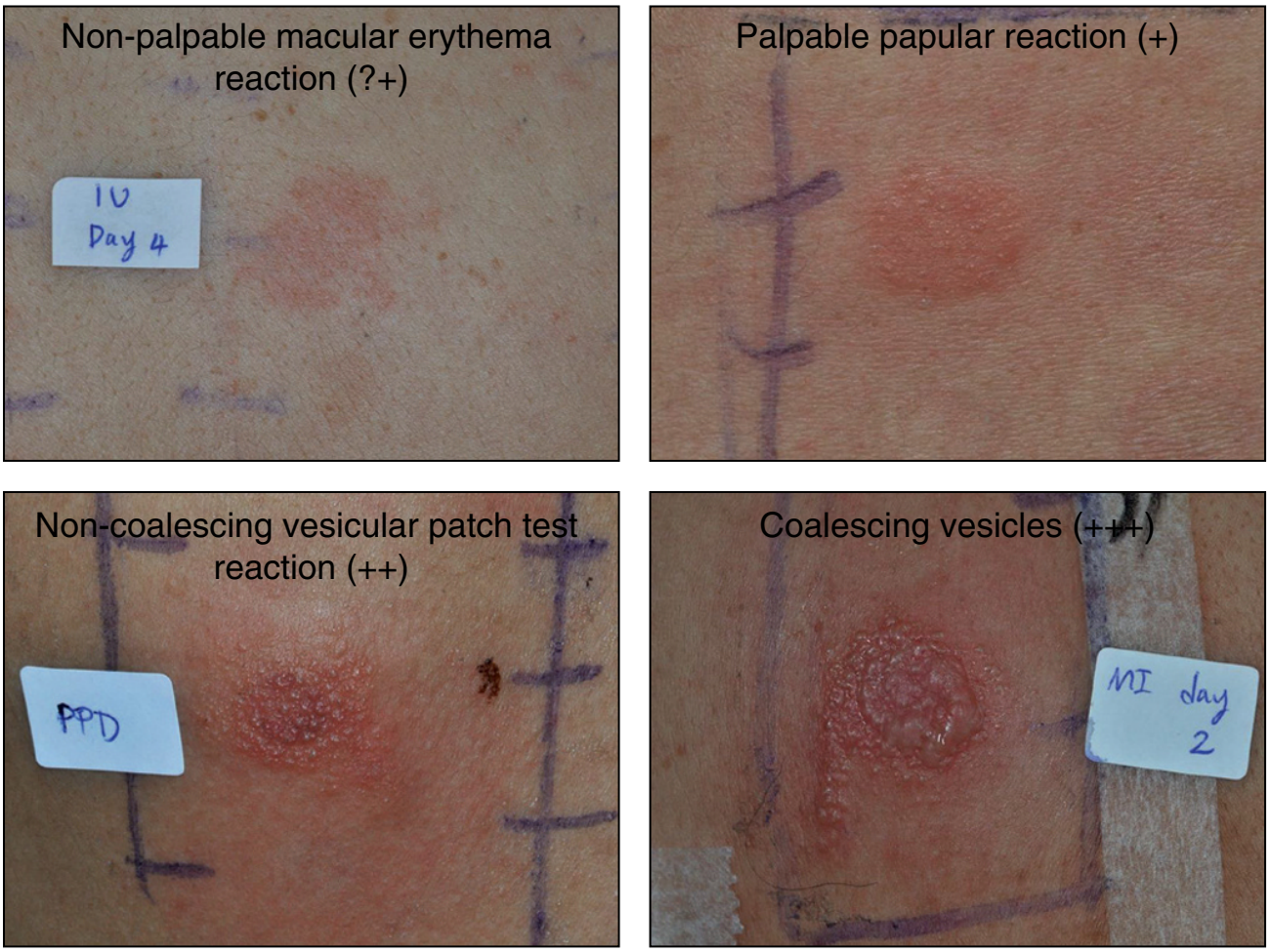

Figure 2.2 ICDRG criteria for scoring patch test reactions.

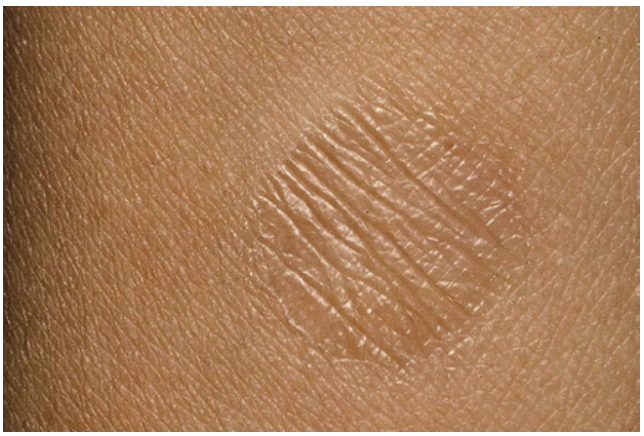

Figure 2.3 False-positive reactions with "soap" appearance.

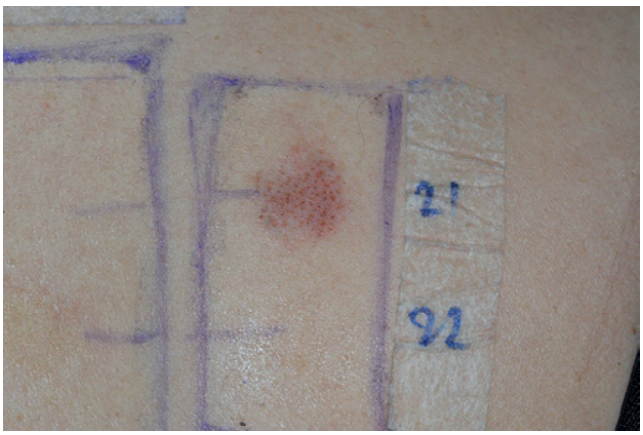

Figure 2.4 Irritant follicular patch test reaction to cobalt, most commonly seen in patients with atopic dermatitis.

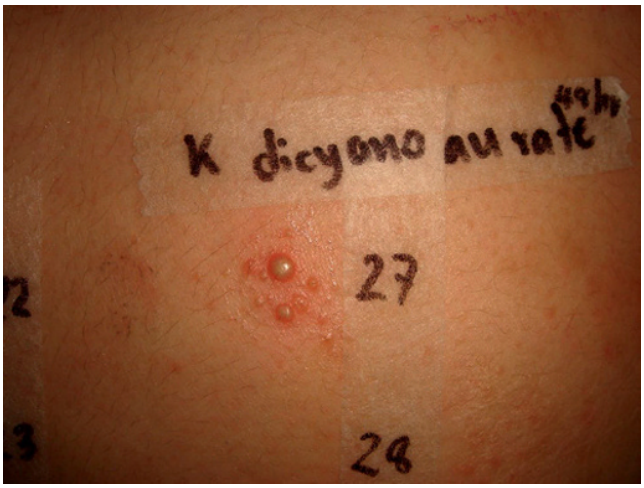

Figure 2.5 Pustular patch test reaction, most commonly seen with metals, which may be either true or false-positive reactions.

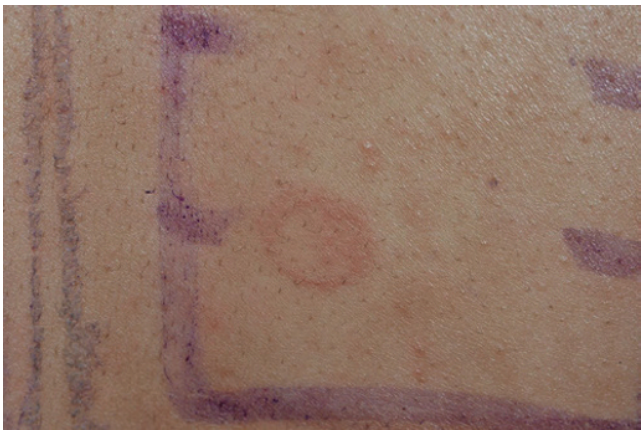

Figure 2.6 Edge effect, commonly seen in positive steroid patch test reactions.

Table 2.4 Allergen preparation in drug patch testing.

Allergen	Base	Control	Notes
Commercially available allergens such as antibiotics, anticonvulsants [33]	10% in pet.	Not required	—
Patient's own drug(s)	Mix with pet. until 10% wt/wt dilution[a] Very low concentration: mix with 30% pet.[a]	Required [34]	The powder form (intravenous or capsules) is preferred over tablets

[a] Grind to a fine powder before mixing with pet.

acute generalized exanthematous pustulosis (AGEP), and Stevens–Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) [22, 23]

2. ACD such as topical application or during manufacture/handling.

Some particular techniques are applied when performing patch testing for drug eruptions:

- Optimal time (seek specialist advice for DRESS and SJS/TEN)
  - At least 4–6 weeks after complete recovery from the CADRs.
  - A longer period may be required in DRESS [23].
- Allergen preparations are summarized in Table 2.4.
- Patch test reading
  - The morphology of reactions described in the ICDRG criteria, as well as other patterns resembling acute CADR(s), may be the presentation of positive patch test reactions [24].

Some special methods are applied only in fixed drug eruptions, including the following:

- Test sites: patch testing should be performed on two sites:
  - a resolved previous lesion (lesional patch test)
  - uninvolved skin, usually on the back (control)
- Duration: patch tests should be applied under occlusion for 6–24 hours.
- Reading time: at 24 and 48 hours (possibly at 6 hours).

Postponing patch testing

Patch tests, if possible, should be postponed in the following situations:

- severe and/or widespread active dermatitis
- systemic immunosuppressive drugs during tapering dosage: if on prednisolone of more than 15 mg per day postpone; if on other immunosuppressive proceed but note the immunosuppression the patient was on in the final summary of his/her patch test results
- recent topical corticosteroid application on the patch testing areas within the past 7 days [25]
- recent (4 weeks) natural sun with UVB or therapeutic ultraviolet exposure of the patch test sites
- active dermatitis at the test area
- pregnancy and lactation – patch testing during pregnancy and lactation is not known to be harmful but most dermatologists postpone during this time as a general precaution.

Interpretation

An assessment of contact allergy consists of two main steps. Step 1 is the interpretation of patch test reactions (Figure 2.7) and step 2 is the evaluation of clinical relevance (Table 2.5).

Adverse effects of patch testing

These adverse reactions can occur, even when the patch tests are performed correctly:

- pruritus
- irritant reactions
- transient localized hyper- or hypopigmentation
- occlusion folliculitis

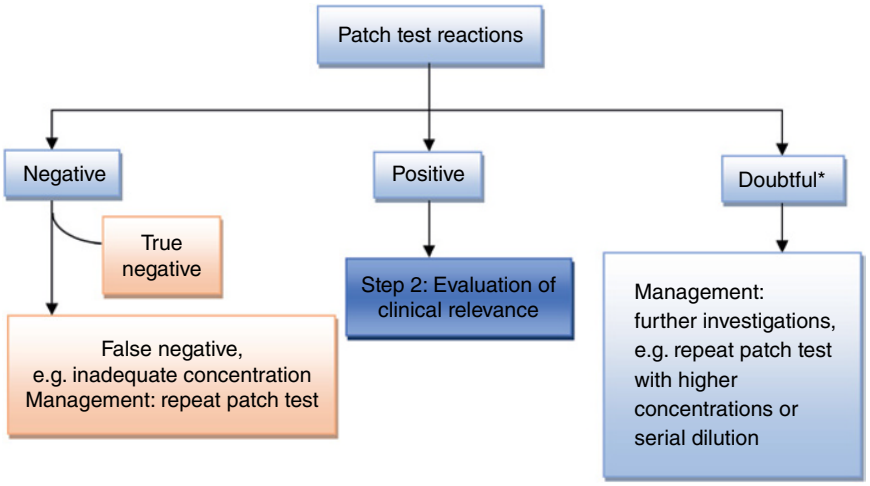

Figure 2.7 Interpretation of patch test reactions.

Table 2.5 The second step in the assessment of contact sensitization: evaluation of clinical relevance.

Clinical relevance	Interpretation
Present (current)	Gives the diagnosis of allergic contact dermatitis
Past	The patient has a past history of clinical contact dermatitis related to the positive patch test allergens
Unknown	Definite correlation cannot be confirmed due to inadequate information Management: re-evaluation of history, clinical examination, worksite visit Further investigations: use test, spot test, chemical analysis
Cross-reaction(s)	Sometimes (not always!) weaker patch test reaction than primary allergen Can occur without previous exposure or sensitization

exposure to allergen without reaction noted as 'exposed'

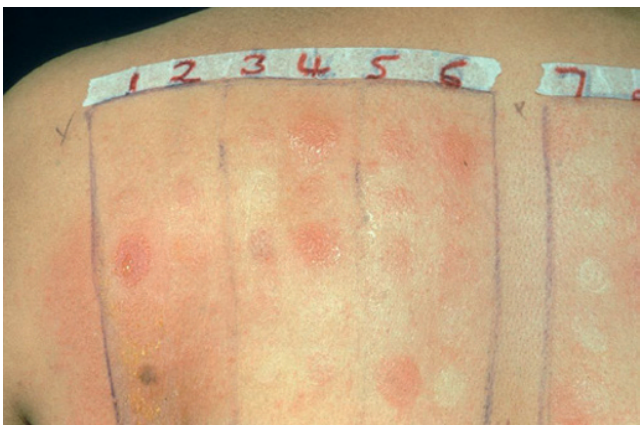

Figure 2.8 Angry back reaction. This is more likely to occur when the patient's dermatitis is extensive and active.

- scarring (very rare)
- flare-up of previous dermatitis

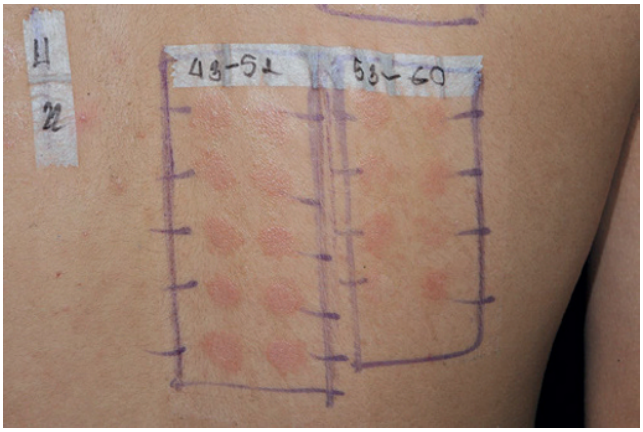

Figure 2.9 Uniform positive reactions in aluminum allergy (from aluminum in Finn Chambers®). Sometimes the reactions are annular in nature.

- persistence of patch test reactions which may last up to several weeks
- "angry back reaction": a non-specific inflammatory reaction with either sheeted inflammation or the appearance of multiple (false)-positive reactions (Figure 2.8). This is particularly likely to happen when the patient's dermatitis is active. Most chamber sites react, which may indicate contact allergy to the aluminum in Finn Chambers® (Figure 2.9).
- active sensitization
  - a positive patch test reaction after 2 weeks of an initially negative result at the same testing area indicates a late reaction which may be active sensitization or a late elicitation reaction.
  - diagnosis: no history of significant exposure and/or reaction. A quicker positive response at repeat patch testing may suggest the diagnosis of active sensitization [26].

Other *in vivo* tests

Other *in vivo* tests are shown in Table 2.6.

Table 2.6 Other *in vivo* tests.

Technique	Repeated open application test (ROAT) [35]	Semi-open test [36]	Open test [20]
Indication	A useful test for clarifying the clinical relevance of positive and doubtful patch test results	To test a patient's own product with suspected irritant properties, such as shampoos, detergents, and cooling fluids	Recommend as the first test for a poorly characterized substance
Techniques	Site: flexural area of the forearm below the antecubital fossa Frequency: 2 times/day Duration: until the patient develops a reaction or up to 2–4 weeks Size: 3 × 3 to 5 × 5 cm Amount: apply over the whole test area	Apply approximately 15 µl of a suspected allergen to an area of 1 × 1 cm using a cotton swab Wait until the substance is completely dry Look for wheals and flares (signs of contact urticaria) Cover with a permeable tape	Site: The volar forearm is usually tested, although the upper back and the upper arm are more reactive. Allergens: • "as is" or • dissolved in water or • some organic solvent (e.g. ethanol or acetone) Methods: 1. Drip a test substance onto the skin 2. Wait until the substance is dry. No occlusion
Reading	Positive reactions often start with follicular papules Erythema and vesicles can also be developed [37, 38]	Same as patch testing	First reading: evaluate at regular intervals during the first 30–60 minutes Second reading: at D3–D4 A negative open test may be due to inadequate penetration, therefore occlusive patch testing may be undertaken
Notes	Because it uses the principle of simulation of a real-life use situation, ROAT is sometimes the only demonstrable positive test in a patient with contact allergy	These two less standardized tests should be performed only by experienced clinicians who fully understand the hazards of the applied chemicals	

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