Schlüsselfrage 1: Für welche Indikationen wird der Epikutantest (ECT) empfohlen, kann empfohlen bzw. erwogen werden oder nicht empfohlen werden?

SF1a: Arzneimittel
SF1b: weitere Indikationen

Schlüsselfrage 2: Welche Expositionsdauer (24h versus 48h), welcher Expositionsort und welche Ablesezeitpunkte sind überlegen im Nachweis einer bestehenden Sensibilisierung?

SF2a: Expositionsdauer
SF2b: Expositionsort
SF2c: Ablesezeitpunkte (nach 48h; nach 72-96h; nach 7-10 Tagen)

Schlüsselfrage 3: Welche Sensitivität, welche Spezifität hat der Epikutantest im allgemeinen und allergenbezogen?

SF3a: ROAT vs. Anamnese
SF3b: sync
SF3c: Zyklusabhängigkeit

Schlüsselfrage 4: Beeinflussen hormonelle Einflüsse das Epikutantestergebnis (Zyklusabhängigkeit)?

Schlüsselfrage 5: Beeinflusst die Einnahme folgender Medikamente das Epikutantestergebnis?

Medikamente: Antihistaminoide; Ciclosporin; Etanercept; Adalimumab; Infliximab; Methotrexat; Sulfasalazin; Nielsen; Topische Glukokortikoide; Calcineurinhibitoren

Schlüsselfrage 6: Welche Risiken und Nebenwirkungen bestehen bei der Durchführung eines Epikutantests?
<table>
<thead>
<tr>
<th>First author and year</th>
<th>Journal and publisher</th>
<th>Study Design</th>
<th>Methods</th>
<th>Aims and Objectives</th>
<th>Reproducibility</th>
<th>Reference no.</th>
<th>Source of funding</th>
<th>Competing interests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brockow et al. 2014</td>
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<tr>
<td>Barbaud 2014</td>
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<td>Brockow et al. 2014</td>
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<td>Barbaud et al. 1995</td>
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<td>Bircher et al. 2013</td>
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**Aims and Objectives**

1. To determine the causes of non-relevant positive patch test reactions.
2. To determine the prevalence of positive patch test reactions in patients with drug allergies.
3. To compare the performance of patch test and Intradermal test with delayed reaction (CADR).

**Methods**

- **Study Design:** Systematic literature review
- **Inclusion:** Patients with drug allergies
- **Exclusion:** Patients with non-drug-related reactions

**Results**

- **Percentage of non-relevant positive patch test reactions:** 65% in diagnosis for drug allergies
- **Prevalence of positive patch test reactions:** 2.2% in a total of 106 patients
- **Intradermal test:** 31 (1%) reactions to drugs in Cutaneous Adverse Reaction (CADR) and during the patch test.

**Discussion**

- Skin tests have to be performed. Patch tests, possibly with SPT, IDT and/or patch test is performed. The main advantage of patch test is the better reproducibility and exanthemas, skin drug test and method of the pathomechanism of the drug allergy.
- Skin tests with drugs have to be performed. Patch tests and/or late reaction with negative control are of value in SCARs investigation.
- In cell-mediated drug reactions such as AGEP or delayed-type hypersensitivity, Skin tests are of value in individual patient a reaction, especially if the tests are performed in a consecutive manner and the Skin prick test, patch test and/or patch test is performed. The main advantage of +3 points) is the better reproducibility and exanthemas, skin drug test and method of the pathomechanism of the drug allergy.

**Conclusion**

- There is paucity of evidence grading evidence grading +3 points for drugs by reference lists of private practice. More reliable evidence grading evidence grading +3 points for drugs by reference lists of private practice.
<table>
<thead>
<tr>
<th>Study Authors and Year</th>
<th>Country and Hospital</th>
<th>Study Design and Setting</th>
<th>Patients and Diagnoses</th>
<th>Treatment and Protocol</th>
<th>Main Findings and Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lammintausta et al. (1999)</td>
<td>Finland</td>
<td>Retrospective analysis of patch test data</td>
<td>Patients with suspected drug eruptions</td>
<td>Patch test: 48 h, 5 days for contact dermatitis</td>
<td>Patch test can be useful in diagnosing suspected drug eruptions.</td>
</tr>
<tr>
<td>Barbaud et al. (2005)</td>
<td>France</td>
<td>Prospective study of patients with drug eruptions</td>
<td>Patients with suspected drug reactions</td>
<td>Patch test, prick test, and ILAC-MIC test</td>
<td>Patch test is more sensitive than prick test and ILAC-MIC test in detecting drug reactions.</td>
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<tr>
<td>_lookup_2009</td>
<td>Germany</td>
<td>Retrospective study of patients with drug eruptions</td>
<td>Patients with suspected drug reactions</td>
<td>Patch test, prick test, and ILAC-MIC test</td>
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<td>_lookup_2010</td>
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<td>Patch test is more sensitive than prick test and ILAC-MIC test in detecting drug reactions.</td>
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</table>

Note: Table shows a summary of various studies on the use of patch tests in diagnosing drug eruptions. The studies included retrospective and prospective analyses of patients with suspected drug eruptions. Patch test was found to be more sensitive than other tests in detecting drug reactions.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Type of Study</th>
<th>Study Design</th>
<th>Population</th>
<th>Methodology</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbaud et al. 2012</td>
<td>2012</td>
<td>Prospective study</td>
<td>Descriptive non-interventional study (2005-2007)</td>
<td>58 French patients with SCAR</td>
<td>Patch test: 46/111 (41%); n/a patch test n/s n/s n/s n/s n/s</td>
<td>Patients with SCAR: 53.5% patch test positive; 24% (SJS/TEN)</td>
<td>Sensitivity of patch test in SCAR: 53.5%; Specificity of patch test: 94%</td>
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<tr>
<td>Martin et al. 2013</td>
<td>2013</td>
<td>Prospective study</td>
<td>Retrospective study</td>
<td>103 patients with SCAR</td>
<td>Patch test: 46/111 (41%); n/a patch test n/s n/s n/s n/s n/s</td>
<td>Patients with SCAR: 53.5% patch test positive; 24% (SJS/TEN)</td>
<td>Sensitivity of patch test in SCAR: 53.5%; Specificity of patch test: 94%</td>
</tr>
<tr>
<td>Ferrand et al. 2013</td>
<td>2013</td>
<td>Prospective study</td>
<td>Descriptive non-interventional study</td>
<td>32 patients with SCAR</td>
<td>Patch test: 46/111 (41%); n/a patch test n/s n/s n/s n/s n/s</td>
<td>Patients with SCAR: 53.5% patch test positive; 24% (SJS/TEN)</td>
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</table>

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Study Design</th>
<th>Population</th>
<th>Intervention</th>
<th>Control</th>
<th>Outcome</th>
<th>Comparison</th>
<th>Duration</th>
<th>Findings</th>
</tr>
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<tbody>
<tr>
<td>Kleinhans et al. 1996</td>
<td>1996</td>
<td>n/s Study</td>
<td>100 patients</td>
<td>Celebrex in petrolatum</td>
<td>n/a</td>
<td>Patch test results</td>
<td>2b</td>
<td>The proportion of positive results was significantly lower in patients who were sensitized to Celebrex than in controls.</td>
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<tr>
<td>Brockow et al. 2005</td>
<td>2005</td>
<td>n/s Literature review</td>
<td>Nancy and the French Minister of Health</td>
<td>Comparison of cutaneous ADRs, such as SJS/TEN, with other cutaneous ADRs</td>
<td>n/a</td>
<td></td>
<td>2b</td>
<td>The investigation of skin prick test results, patch test results, and intradermal test results showed that skin prick tests and patch tests are more sensitive than intradermal tests in detecting cutaneous hypersensitivity reactions.</td>
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<tr>
<td>Barbaud et al. 1998</td>
<td>1998</td>
<td>n/s</td>
<td>Hypersensitivity reactions to contrast media</td>
<td>Intradermal test</td>
<td>n/a</td>
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<td>The proportion of positive results was significantly lower in patients who were exposed to contrast media than in controls.</td>
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</tbody>
</table>
To give guidance for diagnostic procedures in the diagnosis of cutaneous adverse drug reactions

**Literature review and expert consensus**

- **Skin prick test**, **Intradermal test**, **Patch test**, in vitro tests (spec. IgE, CAST, LTT, Elispot)
  - PT: n/s readings after 20 minutes, 48h, (72h), 96h, if negative: also after one week.
  - Upper back, in FDE also previous site of drug eruption 6 weeks to 6 months

**Patients with cutaneous adverse drug reactions**

- The results of drug skin tests also depend on the clinical features of the CADR. The use of appropriate control patients is necessary to avoid false-positive results.
- To determine the sensitivity and specificity of drug skin tests in investigating CADR, it is necessary to organize multicentre studies using the same guidelines.

**Patch testing**

- Patch testing is a safe procedure, even in patients with severe CADRs, apart from exceptional cases of reactivation of the CADR.

**Drugs skin test results**

- Although drug hypersensitivity cannot be reliably ruled out even by applying all available test methods, they do make better risk assessment easier.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Reference</th>
<th>Diagnostic test(s)</th>
<th>Duration of assessment</th>
<th>Outcome</th>
<th>Methods</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Conclusion</th>
<th>Authors' conclusion</th>
<th>Internal validity</th>
<th>External validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cohort study</td>
<td>n/a</td>
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<td>n/a</td>
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<td>2</td>
<td>Case series</td>
<td>n/a</td>
<td>n/a</td>
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<td>3</td>
<td>Expert opinion</td>
<td>n/a</td>
<td>n/a</td>
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<td>4</td>
<td>Case report</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
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<td>n/a</td>
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</table>

**Table Notes:**
- **Diagnostic test(s):** patch testing or history of metal allergy.
- **Duration of assessment:** includes pre- and post-patch testing.
- **Outcome:** results of patch testing or self-reported symptoms.
- **Methods:** includes type of patch testing and control methods.
- **Advantages:** benefits of patch testing for diagnosis.
- **Disadvantages:** limitations of patch testing and potential risks.
- **Conclusion:** summary of findings and recommendations.
- **Authors' conclusion:** expert opinion on the effectiveness of patch testing.
- **Internal validity:** factors affecting the internal consistency of the study.
- **External validity:** factors affecting the generalizability of the study.

**Table Data:**
- **Patients [age]:** mean age of participants.
- **Gender:** distribution of male and female participants.
- **Grading/Classification:** severity of condition.
- **Diagnosis helped:** clinical relevance of patch testing.
- **Early improvement:** positive impact on quality of life.
- **Symptoms and treatment:** further management of allergic reactions.
- **Costs of disease:** financial implications of allergic reactions.
- **Evidence level:** level of evidence based on the Oxford Centre for Evidence-Based Medicine.
### Methods

- **Technologies**: *Ministry of Technology, Information, and Communications, Singapore*.
- **Database**: *Network of Departments of Dermatology*, *Clinic, Singapore*.

### Study Characteristics

- **Duration**: *18 centers of the Network of Departments of Dermatology*, *Dermatology Department of Stockholm, Department of Dermatology, Clinic, Singapore*.
- **Sample Size**: *9946 patients*.
- **Setting**: *17 centers of the Ministry of Technology, Information, and Communications, Singapore*.

### Objectives

- **Questions**: To determine the exposure time of allergic reactions and to investigate the influence of the occlusion.
- **Methods**: To use patch test data from the IVDK (15.553 patients) to analyze the characteristics of allergic reactions (at least one positive reaction at the patch test) in patients with at least one allergic reaction in the patch test.

### Results

- **Positive Reactions**: *9.946 patients*.
- **Irritant Reactions**: *48h (n=36)*.
- **Concordant**: *48h occlusion (n=19)*.
- **Discordant**: *48h occlusion (n=22)*.

### Conclusions

- *In all but 3 cases, allergic reactions positive in the patch test showed positive reaction at least one allergen (in 10 distinct allergens)*.
- *Concordant / discordant*: *37/43 (86%) concordant 48h vs. 48h exposure (comparison: 26% discordant)*.

### Funding and Interests

- *Research Group Dermatitis Research Group Dermatitis (Germany)*.
<table>
<thead>
<tr>
<th>Study Design</th>
<th>Objectives</th>
<th>Aims and Questions</th>
<th>Study Population</th>
<th>Internal Validity</th>
<th>Duration of Exposure</th>
<th>Site of the Antigen and Application</th>
<th>External Validity</th>
<th>Results</th>
<th>Reading Times</th>
<th>Sources of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective cohort</td>
<td>To compare the variations in regional reactivity variations in skin reactions to nickel sulfate on the back</td>
<td>nickel-sensitive patients undergoing patch test</td>
<td>24 patients</td>
<td>not reported</td>
<td>3 months</td>
<td>different areas of the back</td>
<td>not reported</td>
<td>not stated</td>
<td>not applicable</td>
<td>Memon 1996, Lindelöf 1992, Simonetti 1998, Van Strien 1994</td>
</tr>
<tr>
<td>Prospective cohort</td>
<td>The allergen to nickel was applied in routine patch test on different sites containing coins and fuerarm (n=6).</td>
<td>nickel-sensitive individuals</td>
<td>21 patients</td>
<td>not reported</td>
<td>2 days</td>
<td>forearm (n=6), thigh (n=3), upper left side (n=3), neck (n=3), 1. chin, 2. neck, 3. upper arm, 4. lower arm, 5. back, 6. thigh, 7. forearm, 8. palm</td>
<td>not reported</td>
<td>not stated</td>
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<td>Memon 1996, Lindelöf 1992, Simonetti 1998, Van Strien 1994</td>
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<td>Study Characteristics</td>
<td>Study Design</td>
<td>Study Group</td>
<td>Study Population</td>
<td>Study Duration</td>
<td>Allergens</td>
<td>Reading Times</td>
<td>Results</td>
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<tr>
<td>To investigate the optimal patch test reading time with repeated nickel patch test readings</td>
<td>Retrospective</td>
<td>International Contact Dermatitis Research Group</td>
<td>18 centers of the Information Network</td>
<td>1989-2005</td>
<td>15 standard allergens (lanolin, neomycin, p-phenylenediamine)</td>
<td>D2, D3, D4, D5, D6, D7, D8</td>
<td>1. D2 (48h) negative day 3 and positive later on - found reactions 2. D3 (72h) negative day 3 and positive later on - found reactions 3. D7 (10 days) negative day 3 and positive later on - found reactions</td>
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<tr>
<td>To assess the necessity of late readings and discuss the consequences of delayed positive reactions</td>
<td>Retrospective chart</td>
<td>Mayo Clinic, Rochester, USA</td>
<td>Retrospective data</td>
<td>1999-2000</td>
<td>17 standard allergens (lanolin, neomycin, p-phenylenediamine)</td>
<td>D2, D3, D4, D5, D6, D7</td>
<td>1. D2 (48h) negative day 3 and positive later on - found reactions 2. D3 (72h) negative day 3 and positive later on - found reactions 3. D7 (10 days) negative day 3 and positive later on - found reactions</td>
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<tr>
<td>To analyse the results of the standard series and to quantify the proportion of delayed-positive reactions</td>
<td>Retrospective cohort</td>
<td>North American Contact Dermatitis Group</td>
<td>Prospective cohort</td>
<td>2004-2005</td>
<td>17 standard allergens (lanolin, neomycin, p-phenylenediamine)</td>
<td>D2, D3, D4, D5, D6, D7</td>
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</table>

Table 1: Summary of patch test studies.
<table>
<thead>
<tr>
<th>Study characteristics</th>
<th>Investigator-prospective, chart review of study</th>
<th>Study design</th>
<th>Patients</th>
<th>Total patients</th>
<th>Provocation protocol</th>
<th>Patch test materials</th>
<th>Concentrations</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Outcome criteria</th>
<th>Results</th>
<th>Clinical relevance here</th>
<th>Cut-Off</th>
<th>Comparison</th>
<th>Effects</th>
<th>Imputabililty in simple and relevant cases</th>
<th>Patients meeting the criteria</th>
<th>Results can be transferred to other cases</th>
<th>Other</th>
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<tr>
<td>Aschenbrenner et al.</td>
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<td>Hauksson et al.</td>
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<td>R. Christiansen et al.</td>
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<td>Pavord et al.</td>
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<td>Barbaud et al.</td>
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<td>Study Design</td>
<td>Population</td>
<td>Methodology</td>
<td>Exposure</td>
<td>Outcomes</td>
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<tr>
<td>Johansen et al.</td>
<td>2005</td>
<td>Denmark</td>
<td>Prospective cohort study</td>
<td>1701 patients</td>
<td>Patch testing</td>
<td>Fragrance mixtures</td>
<td>Allergic contact dermatitis</td>
<td>The prevalence of fragrance allergy was high.</td>
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<tr>
<td>Goksel et al.</td>
<td>2005</td>
<td>Ankara, Turkey</td>
<td>Prospective cohort study</td>
<td>1701 patients</td>
<td>Questionnaire, patch testing</td>
<td>Fragrance products</td>
<td>Allergic contact dermatitis</td>
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</table>

*Note: The table is truncated for brevity.*
**Sources of funding and competing interests**

- EU Commission: QLK4-CT-1999–01558

**Setting**

- 'Fragrance chemical allergy: a major environmental and consumer problem in Europe.'

**Aims and Objectives**

- "Does the FM II identify additional patients with a positive fragrance history missed by FM I? Is it necessary to add FM II to the European standard series?"

**Study Design**

- Prospective cohort of patients
- Patch test with baseline series with FM II (2.8%; 14%; 28% pet.)

**Reference standard test**

- 2 days back simultaneous

**Diagnostic test(s)**

- Consecutive patients eligible for patch testing
- 1701 patients

**Duration of exposition**

- Median age 44, range 13-96; 62.2% female

**Application site**

- Suspected allergic contact dermatitis

**Time interval and treatment(s) administered between the tests**

- ICDRG (according to textbook chapter "Contact Dermatitis" 2001 edition)
- Positive patch test D3 or D4
- 50 of 1701 not stated

**Inclusion criteria**

- 36 pos. mix and single ingredients (SI); 5 neg. mix, pos. SI; 14 pos. mix, neg. SI, 1646 neg. mix, neg. SI

**Patients included [n]**

- Not applicable

**Patients [age (mean/range); gender (M/F)]**

- Not applicable

**Presumed Diagnosis**

- Suspected allergic contact dermatitis

**Grading/Classification/Strength of reaction**

- Definition of outcome

**Results I (overall positive reactions)**

- Testing with individual constituents is positive in about 50% of cases reacting to either 14% or 28% FM II
- No blinding

**Results II (reactions at different time points)**

- Results II (3 most frequently reported substances?)

**Accuracy**

- Results can be transferred to patients meeting the inclusion criteria

**Reproducibility**

- Not stated

**Cut-Off determination**

- Not applicable

**Comparison of two or more tests**

- Not applicable

**Adverse effects**

- None reported

**Author conclusions**

- Internal validity
- External validity

**Evidence level (Oxford)**

- Other/Addendum (optional)

---

**Legend of Study Characteristic:**

- A: Journal study selection
- B: Internal number of patients
- C: Exclusions
- D: Unclear
<table>
<thead>
<tr>
<th>Study design</th>
<th>n/a</th>
<th>n/a</th>
<th>n/a</th>
<th>n/a</th>
<th>n/a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Critical appraisal of study
- Patch testing: none
- At least ++ reaction to nickel sulfate

Methods
- Subgroup/study population

Rohold 1994 n/s
- Hindsen 199
- Tamer 2003 n/s
- Bonamonte 2005

Supported by
- Faculty of Medicine, Hospital, Denmark
- and Gynaecology, Malmö, Sweden
- Educational and Anaesthesia, Ankara Numune Dermatology, Pamukkale Italy

Nickel sulphate patch tests in women at different points of menstrual cycle and whether the adequacy of luteal phase is related to the possibility that sensitization mechanisms differ markedly on the basis of testing with nickel dilutions.
- The response characteristics of patch test reactivity was particularly observed on the progestin phase in 29 patients.

Inclusion criteria
- Control group (both days 7-10; day 20-24) n=15, group 1 (day 7-10; day 20-24) n=13
- Inclusion criteria were: Controls: age n/s; Female nickel allergy; Visual scoring comparison of reactions.

Time point of randomisation
- 7-10 vs 20-24
- Age n/s; Female nickel allergy

Duration of exposition
- 48-72 h upper back 5% nickel sensitivity
- 5% of menstruation
- Regular menstrual cycle

Reference
- n/a
- Patch testing 2 days upper back 5% - 0.0013%
- n/a Standard patch testing
- n/a

Diagnostic test(s)
- Reference
- n/a

Cut-off
- Reference
- n/a

Accurancy
- Reference
- n/a

Other
- Reference
- n/a

Evidence level
- IIIb

Other
- Reference
- n/a

---

Statistics
- Accuracy
- Other
Inclusion criteria

- Positive patch test

Authors' conclusion

- Degree of infiltration of positive Tine test

Evidence level (Oxford)

- Not specified

Study preparations

- Supported by a grant from SIDAPA and UCB Pharma Nanterre
- Schering Plough provided the study preparations

Study characteristics

- Protein purified derivative candidin (CD), tuberculin
- Results of skin tests with nifedipine could influence the tuberculin-induced DTH channel antagonist on oral antihistamines on PR threshold for patch test reactions
- Patches applied for 48h and reading
- Patches applied for 24h and reading
- The patches were applied for 2 days
- The patches were applied for 48
- The patches were applied for 48
- Application
- Identical patches applied on both upper forearms, 4 to 8

Investigator(s) and

- Nickel allergy
- Nickel or chromate
- Allergy
- Nickel or chromate
- Rietschel 1985
- Wee et al (2010)
- Di Nardo 1997
- Clark & Rietschel (1982)

Diagnostic test(s)

- Determining skin fold thickness
- Test of tuberculin antigens (tetanus, streptodornase (SK/SD), streptokinase/penicillin)

Results of skin tests with streptokinase/penicillin were negative.

- Test reactivity at the same urushiol was also measured using laser Doppler
- Decrease from +++ to ++ in 3/7 VIP, methiotepine and ICS-205-930. With VIP a reduction of Leu by the verapamil
- Significant inhibition of calcium entry blockers
- The presence of Toxicodendron allergens

- Reaction in PT to Nickel
- Sensitization to urushiol
- To examine whether the treated arm was identical to the test reactivity was also measured using laser Doppler
- Decrease from +++ to ++ in 3/7 VIP, methiotepine and ICS-205-930. With VIP a reduction of Leu by the use of clobetasol corticosteroids prior to nickel PT reactions.
- Nickel allergy
- Nickel or chromate
- Allergy
- Nickel or chromate
- Rietschel 1985
- Wee et al (2010)
- Di Nardo 1997
- Clark & Rietschel (1982)

Diagnostic test(s)

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Results of skin tests with streptokinase/penicillin were negative.
<table>
<thead>
<tr>
<th>First author/ year</th>
<th>Study Design</th>
<th>Internal validity</th>
<th>Sensitization only</th>
<th>Prevalence</th>
<th>Accuracy</th>
<th>Threshold dose eliciting a reaction</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verma et al (2016b)</td>
<td>observational study</td>
<td>n.s.</td>
<td>48h duration n.s. / Reading at 72h</td>
<td>n.a.</td>
<td>n.s.</td>
<td>none</td>
<td>11</td>
</tr>
<tr>
<td>O'Quinn &amp; Isbell (1969)</td>
<td>observational study</td>
<td>n.s.</td>
<td>48h duration n.s. / Reading at 72h</td>
<td>n.a.</td>
<td>n.s.</td>
<td>none</td>
<td>11</td>
</tr>
<tr>
<td>Condi &amp; Adams 1973</td>
<td>observed</td>
<td>n.s.</td>
<td>48h duration n.s. / Reading at 72h</td>
<td>n.a.</td>
<td>n.s.</td>
<td>none</td>
<td>11</td>
</tr>
</tbody>
</table>

**Diagnostic test(s)**
- PT reaction and strength

**Assessor(s) training**
- n.a.

**Addendum**
- n.a.

**Grading/Classification/Strength and size of the PT reaction**
1. + erythema with infiltration
2. + + erythema with infiltration
3. + + + erythema with infiltration
4. + + + + erythema with infiltration

**Clinical improvement of the dermatitis**
- n.a.

**Hormonal determinations**
- testosterone propionate
- 10 mg daily does not induce any change.

**Comment**
- A systematic review and meta-analysis of clinical trials assessing the efficacy of systemic CyA treatment of 5 to 6 years duration in the treatment of chronic GVHD and cutaneous GVHD.
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Setting</th>
<th>Methods</th>
<th>Duration</th>
<th>Clinical Details</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mancuso 1999</td>
<td>n/s</td>
<td>Mancuso 1999</td>
<td>n/s</td>
<td>n/s</td>
<td></td>
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<tr>
<td>Isaksson 2002</td>
<td>n/s</td>
<td>Isaksson 2002</td>
<td>n/s</td>
<td>n/s</td>
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<tr>
<td>Möller 2002</td>
<td>n/s</td>
<td>Möller 2002</td>
<td>n/s</td>
<td>n/s</td>
<td></td>
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</tr>
</tbody>
</table>

**Study characteristics**
- **Physicians (n/s)**
- **Single center in Sweden (FIOH)**
- **Two centers in Denmark**
- **Columbia**
- **Novo Nordisk, Finland, Pharma**
- **Smith**
- **Sweden, Finland**, **sterland**, **GIRDACA**
- **European Foundation**

**Objectives**
- **Identify possible hypersensitive to hydrocortisone**
- **Duration of the allergic patch side-effects**
- **Generalized possible contact dermatitis**
- **Whether sensitization to hydrocortisone is caused by these drugs**

**Methods**
- **Epicutaneous allergen series;**
- **Hyposensitization to hydrocortisone;**
- **Sensitization to 2-HEMA or acrylics series**
- **Dilution series.**

**Results**
- **Objective data:**
- **Symptoms:** Flare-up, headache, pruritus or mild superinfection
- **Reactions:** 66% of patients responded to PT, 96.1% of patients responded to T.R.U.E. test
- **Negative:** 52 patients tested negative, 31 patients tested positive
- **Positive:** 4 patients were positive, 5 patients were negative
- **Time interval:** 6-18 years
- **Race of study subjects:** Gender: 3/12, age: 34-76 (mean 47)
- **Gender:** 3/12 women, 10/12 men
- **Hyper-susceptibility:** 4/12 patients
- **Previous positive test:** 6/12 patients reported previous positive tests
- **Reaction:** 1x, budesonide vs placebo, 1x, budesonide vs placebo

**Conclusion**
- **Study:** The study was designed to identify allergic reactions to hydrocortisone and other related compounds. The results showed a significant response to the allergen series, with 66% of patients testing positive. The T.R.U.E. test was also reliable and safe, with a high sensitivity rate of 96.1%. The study concluded that hydrocortisone and other related compounds can cause allergic reactions in a significant number of patients, and that further research is needed to understand the mechanisms behind these reactions.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Methodology</th>
<th>Exposure</th>
<th>Controls</th>
<th>Outcome</th>
<th>Follow-up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>Case-control</td>
<td>1000 patients</td>
<td>Patch test</td>
<td>Gold</td>
<td>Placebo</td>
<td>Sensitization</td>
<td>6 months</td>
<td>Positive reactions seen in 20%</td>
</tr>
<tr>
<td>Study 2</td>
<td>Prospective</td>
<td>500 patients</td>
<td>Intradermal test</td>
<td>Colophony</td>
<td>None</td>
<td>Positive reactions</td>
<td>2 years</td>
<td>Positive reactions in 10%</td>
</tr>
<tr>
<td>Study 3</td>
<td>Retrospective</td>
<td>2000 patients</td>
<td>Patch test</td>
<td>PPD</td>
<td>None</td>
<td>Positive reactions</td>
<td>1 year</td>
<td>Positive reactions in 15%</td>
</tr>
</tbody>
</table>

**Notes:**
- PPD: Pure Protein Dermatosis, a common allergen.
- Colophony: A plant resin, used as an adhesive.
- Gold: A common allergen in patients with dermatitis.
- Intradermal test: A test used to determine the presence of allergens.
- Sensitization: The body's reaction to an allergen.
- Follow-up: The period after the initial exposure to assess outcomes.
- Results: The percentage of patients showing positive reactions.
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Study Design</th>
<th>Study Population</th>
<th>Baseline Information</th>
<th>Methods</th>
<th>Reactions</th>
<th>Interpretation</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1985</td>
<td>Germany</td>
<td>Prospective</td>
<td>4386 SL mix cases</td>
<td>3 cases</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
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<tr>
<td>2</td>
<td>1986</td>
<td>Germany</td>
<td>Retrospective</td>
<td>24. 1998-1990: 100</td>
<td>3 cases</td>
<td>2%</td>
<td>2%</td>
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<tr>
<td>3</td>
<td>1987</td>
<td>Germany</td>
<td>Prospective</td>
<td>1998-1990: 100</td>
<td>3 cases</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
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</tbody>
</table>

**Subgroup/Study Population**

- IV: subpopulation
- IV: subjects (out of)  
- N/A: not applicable
- N/S: not stated

**Male/Female**

- M/F: n/a
- N/A: n/a
- N/S: n/a

**Testing**

- Compositae mix (CM)
- SL mix 0.1%
- SL-Mix 0.1%
- Epitel Ltd.
- Selenos (three patients)
- Trolab
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- THIRD, (German)
- TRUE Test, Hamburg
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