

- 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 nach 48h; nach 72-96h; nach 7-10 Tagen
- Schlüsselfrage 3** Welche Sensitivität, welche Spezifität hat der Epikutantest im allgemeinen und allergenbezogen?
- SF3a RDA1 vs. Anamnese
SF3b sync
SF3c Zyklusabhängigkeit
- Schlüsselfrage 4** Beeinflussen hormonelle Einflüsse das Epikutantestergebnis (Zyklusabhängigkeit)?
- Schlüsselfrage 5** Beeinflusst die Einnahme folgender Medikamente das Epikutantestergebnis?
Medikamente: Antihistaminika; syst. Glukokortikoide; Celicept; Cyclosporin; Azathioparin; Methotrexat; Alitretinoin/Acitreth/Isotretinoin; ACE Hemmer; Opioide; Etanercept; Adalimumab; Infliximab; topische Glukokortikoide; Calcineurininhibitoren
- Schlüsselfrage 6** Welche Risiken und Nebenwirkungen bestehen bei der Durchführung eines Epikutantests?

Study characteristics				Methods							Results										Critical Appraisal of Study								
First Author/year	Sources of funding and competing interests	Setting	Aims and Objectives	Study Design	Reference standard test(s) evaluated	Duration of exposure	Application site	Time interval and treatment(s) administered between the tests	Investigator(s) and assessor(s) training	Inclusion criteria	Patients included (n)	Patients (age (mean/range); gender (M/F))	presumed diagnosis	Grading/Classification/Strength of reaction	Definition of outcome	Results I (overall positive reactions)	Results II (reactions at different time points)	Results III (3 most frequently reported substances?)	Accuracy	Reproducibility	Cut-Off determination	Comparison of two or more tests	Adverse effects	Author conclusion	Internal validity	external validity	Evidence level (Oxford)	Other/ Addendum (Optional)	
Barbaud et al. 2001	Source of funding not described Competing interests: not stated	Nancy, France	To determine the causes of non-relevant positive patch tests and ID T with drugs in cutaneous adverse drug reactions (CADR). To establish the threshold of non-relevance for drugs tested by IDT.	Monocentric study, n=196, presumably non consecutive study, retrospective analysis	n/a	not described	upper back	6 weeks to 6 months	n/a	Patients with CADR	800	n/a	CADR	n/a	positive patch tests, positive IDT	n/a	n/a	n/a	n/a	n/a	n/a	IDT/patch test	not reported	Skin tests with drugs are of value in investigating CADR. False positive results should be compared with negative control subjects	Exclusion criteria missing. Patient data missing: mean age, sex strength of patch test reaction missing. No blinding	study population not described	3b	irrelevant criteria missing	
Barbaud 2014	Source of funding not described Competing interests: not stated	literature review	Recommendation of skin testing in non-IgE-mediated drug allergy	expert opinion based on literature review	n/a	not described	n/a	at least 1 month after the resolution of the CADR and during the year following the CADR	n/a	n/a	n/a	n/a	Non-IgE-mediated drug allergy	n/a	positive test results	n/a	n/a	n/a	n/a	n/a	n/a	skin prick test, intradermal test, patch test	n/a	Drug patch tests are safe, positive in only 9-23 % of the reported cases. Drug patch tests may have their best indications in SCAEs such as AGEPEP or DRESS	n/a	n/a	5	systematic literature review	
Bircher et al. 1996	Labor of Dermatochemistry, Strasbourg, Astra Draco, AG Sweden, Ciba Inc. Switzerland, Yamanouchi Europe, N. Glaxo Inc. UK, University Hospital, Geneva, Bral Allergen GmbH, Germany	Basel, Bern, Geneva, Zurich, Lausanne, 10 dermatologists in private practice	To determine the prevalence of positive patch tests to corticosteroids in Switzerland of patients undergoing routine patch tests.	prospective multicentre exploratory cohort study with good reference standards	referring with the screening series and 12 corticosteroids commonly used in Switzerland	48 h	n/a	n/a	n/a	consecutive dermatologic patients with an indication for patch testing	3016 patients	age 42 (6-96); gender: 1189/1826	presumed allergic contact dermatitis (ACD)	International Contact Dermatitis Research Group (IC-DRG)	positive patch tests to corticosteroids	65 patients (2.2 %), 26 male and 39 female with a total of 106 positive reactions to corticosteroids	n/a	31 (1%) reactions to TXP, 30 (1%) reactions to BUD, 29 (1%) reactions to HCB, 16 (0.5 %) reactions to HCA	n/a	70-98 % concordance in retesting	n/a	n/a	n/a	n/a	Corticosteroids should be included in routine patch-testing, as markers of corticosteroid sensitization (especially private, subcutaneous and hydrocortisone butyrate may be suited). Patch test reactions of 2+ or higher have a better reproducibility than 1+ reactions; to establish the clinical relevance in an individual patient a usage test should be performed	n/a	n/a	2b	
Bircher et al. 2006	n/a	literature review	Clinical and diagnostic aspects and management options of hypersensitivity reactions to antiepileptic drugs	expert opinion based on literature review	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	patients with hypersensitivity to antiepileptic drugs	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	In cell-mediated hypersensitivity reactions, such as erythematous plaques and exanthemas, skin prick or intradermal tests, with e.g. 1:10 or undiluted preparations can be performed. Patch tests, possibly with tape stripping, are less sensitive but may be positive	n/a	n/a	5		
Brockow et al. 2002	n/a	Rostrom based on literature review	Skin test procedures in the diagnosis of drug hypersensitivity	expert opinion based on literature review	n/a	2 days	upper back	3 weeks to 3 months	n/a	n/a	n/a	n/a	presumed drug hypersensitivity	ECDRG	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Some tests have to be applied according to the suspected pathomechanism of the drug hypersensitivity. Skin testing with SPT, IDT and/or patch test is especially recommended in adverse drug reactions to beta-lactams, antibiotics (mainly penicillins, cephalosporins). In non-immediate possibly drug-related reactions patch tests and/or late readings of intradermal tests are recommended	n/a	n/a	5		
Brockow et al. 2013	n/a	European position paper based on systematic literature review	To promote and standardize reproducible skin testing with safe and non-irritant drug concentrations in the clinical practice. Safe and non-irritant drug concentrations with specificity of at least 95 % in diagnosis for drug allergy	Systematic review of literature with data on skin test concentrations for drugs by searching the databases of Medline and Embase, reference lists of identified articles, textbooks, case reports, guidelines, personal experience by members of the task force. Inclusion of observational studies, case series, case reports, personal experience of members of the group when other reliable data were lacking.	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	patients with drug allergy	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	There is paucity of literature on skin drug test concentration and method protocols. For NHR, the patch test has an equal or slightly lower sensitivity than IDT with delayed readings	There is paucity of literature on skin drug test concentration and method protocols. For NHR, the patch test has an equal or slightly lower sensitivity than IDT with delayed readings	Review of the literature and evidence grading established for recommendations	Review of the literature and evidence grading established for recommendations	3a	

Isaksson et al 1999	Source of funding: work supported by grants from The Swedish Foundation for Health Care Sciences and Allergy Research, the Edvard Wallander Foundation and the Frisen Foundation. Budesonide was supplied by Yamanouchi Pharma, Denmark. No competing interests.	University Hospital Leuven Belgium	Patch testing with budesonide: influence of dose, occlusion time, reading time	Prospective one centre non- consecutive study; patch testing with budesonide in serial dilutions	n/a	patch test	48 h, 5 days for 1 column, 24 h for 1 column.	upper back	n/a	patients previously known to be hypersensitive to 1% budesonide tested in ethanol	10	n/a	patients previously known to be hypersensitive to 1% budesonide tested in ethanol	ICDRG	Readings on day 2, 4 and 7	9 of 10 (9/10) patients reacted to budesonide	More patients tested positively to low concentrations of budesonide. The most positive reactors were found when budesonide was tested with 48h occlusion in low concentrations (0.002%) and read on DA.	n/a	n/a	n/a	n/a	n/a	n/a	n/a	One and the same concentration cannot be used to detect contact allergy in all budesonide-allergic patients. With early readings low concentrations may be preferable. With late readings high concentrations may be recommended. There may be therefore an argument for patch testing with 2 concentrations (high and low). As not to miss a contact allergy a late reading after 1	No blinding. Exclusion criteria not defined.	Small sample size	3b
Lammintausta et Kortelango 2006	n/a	Turku University Central Hospital, Finland	To analyse the relevance of skin tests in revealing drug allergy. The relevance of skin test results was evaluated with drug provocation studies.	Retrospective one center study (1989-2001)	Provocation test	Patch test, prick test, intradermal test, oral provocation test	48 h	upper back	Time interval between skin reaction and test: 2 months to 20 years. Was not recorded systematically	Patients with history of suspected cutaneous adverse drug reactions	947	n/a	presumed diagnosis of CADR	n/a	If erythema and infiltration and/or edema had developed, the reaction was interpreted as positive. Macular erythema was regarded as non-significant.	positive patch test reaction in 89 of 826 patients (10.8%); 13 of 16 patch test positive patients (81.3%) developed exanthema after provocation	n/a	beta-lactams, ceftriaxone, trametoprim	n/a	n/a	n/a	n/a	n/a	Time interval between skin reaction and test not recorded systematically. Acute CADRs were seen in only a few cases and the type of the reaction was often based on the history of the patient. IDT was used in only 9/1 cases and it could have been useful more often. No blinding.	no blinding	3b		
Lippo et al 2013	n/a	Turku University Central Hospital, Finland	To identify patient cases with multiple delayed-type drug sensitizations by using patch testing.	n/a, presumably consecutive patients (n=11) with suspected cutaneous adverse drug reactions (CADR)	n/a	n/a	n/a	upper back	n/a	general dermatology patients with suspected CADR in a 9 year period	811	n/a	suspected drug allergy	interpretation performed according to the international criteria for patch testing, ESCD	number of patients with positive patch test reactions and patch test reactions to multiple drugs at 48 and 96 h	Positive patch test reactions of drugs were found in 34/811 patients	Multiple delayed drug sensitizations were found in 434 patients (12% of those patients with positive results in drug patch testing. All these patients had clinical CADR.	They were all sensitized to one or more antibiotic drugs. Co-sensitization to other drugs was seen in 3 of 4 patients. Patients with multiple sensitizations: Amoxicillin, cephazolin, Pseudoephedrine, Opioids	n/a	n/a	n/a	n/a	n/a	Drug patch testing is useful in cutaneous adverse drug reactions where multiple drugs are suspected. Importance of testing all culprit drugs. Multiple sensitizations can be found in a proportion of patients who have delayed drug allergies.	Small sample size. Concentrations of the pharmacological y active ingredients used in the studied patients. No blinding. Frequency of testing per test substance not stated.	unclear whether all tested patients had experienced clinical symptoms	3b	
Osawa et al 1999	The work was partially supported by Grants-in-Aid for Scientific Research (0167070) from the Ministry of Education, Science and Culture, Japan. No competing interests declared.	Department of Dermatology, Yokohama City University School of Medicine, Yokohama, Japan.	Evaluation of the usefulness of intradermal testing and patch testing in patients with various types of eruptions caused by many kinds of drugs.	Retrospective monocentric, non-consecutive study	provocation test	Intradermal test, Patch test	patch test: 48 h	patch test: upper back	n/a	patients with generalized drug eruptions	242	age: 47.2 (1-85); MF = 87:145	suspected non-immediate drug eruption. Patients with delayed type drug eruptions: maculopapular erythematous type (MP), erythema multiforme type (EM), erythrodermic type (ED), acrodermatitis type (ECo), lichenoid type (LP), fixed type (FD).	ICDRG	positive, delayed reaction at 48 and 72 h	Positive skin test reactions were found in 31.3% of the cases patch tested. Patients with anticonvulsants induced eruptions showed a relatively high positive rate in patch testing (sodium valproate most frequently, but should be tested with less than 5% in petrolatum).	n/a	n/a	n/a	n/a	n/a	n/a	Patch testing is valuable but it is still not thought to be as useful as intradermal tests because of low responsiveness to sensitized drugs, except in ED type, ECo type, and anticonvulsant-induced drug eruptions. Intradermal testing and patch testing are useful in vivo assays for detection of drug allergy, because there is still no reliable in vitro assay. The intradermal	n/a	n/a	3b		
Watson et al 2009	The study was sustained by funds of regional research of University Hospital of Nancy. No competing interests.	One centre, retrospective study, University Hospital Nancy, France	To evaluate the negative predictive value of drug skin tests.	One centre, retrospective exploratory study	Provocation test	Patch test, prick test, intradermal test, oral provocation test	patch test: 48 h	According recommendation (ESCD)	At least 6 weeks after complete disappearance of the CADR	Patients with cutaneous adverse drug reactions	200	mean age: 43.8 years, 72 males, 128 females	cutaneous adverse drug reactions	ESCD	positive: strong drug causality or positive oral provocation test; negative: negative oral provocation test.	42 of 403 rechallenges were positive, thus the negative predictive value of drug skin tests in our unit was 89.6%. (negative skin test (Patch, prick, IDT) 200 oral provocation test: negative predictive value 89.6%; 143 substitution test: negative predictive value 89.5%.	n/a	antibiotics, paracetamol, Neost, corticosteroids	n/a	n/a	n/a	n/a	skin prick test, intradermal test, patch test and oral provocation	Negative drug skin tests do not eliminate the responsibility of a drug in drug reactions, and must be followed by drug re-administration under hospital surveillance. The rechallenge can be positive even with low drug causality assessment and negative drug skin tests. All the drugs taken	no blinding	n/a	2b	
Barboud 2005	n/a	literature review	Are patch tests helpful in drug allergy?	expert opinion based on literature review	n/a	Patch test, Prick-test, intradermal test	patch test: 48 h	back	during the 6 months following the CADR	n/a	n/a	n/a	CADR	ICDRG	according ICDRG	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Drug patch tests can be helpful in determining the cause of CADR. They induce only rarely adverse reactions. They can be done with any commercialized form of a drug. A negative patch test does not exclude its role in causing a CADR. Sensitivity of patch test seems lower than with IDT. Patch test can be positive in patients with negative IDT.	n/a	Specificity and their negative predictive value of patch tests have not been determined.	5	

Barbaud 2009	n/s	literature review	skin testing in delayed reactions to drugs	expert opinion based on literature review	n/a	Patch test, Prick test, IDT	patch test: 48 h	back	during the 6 months following the CADR	n/a	n/a	n/s	delayed reactions to drugs	ICDRG	patch test according ICDRG	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Drug sensitivity cannot be helpful in determining the cause of a CADR caused by a delayed hypersensitivity. Drug skin tests can induce adverse reactions, however rare. The results of drug skin tests depend on the clinical features of the CADR and on the tested drug. It is advised to perform drug skin tests during the 6 months following the CADR. Patch tests and prick tests can be done with any	n/a	n/a	5
Barbaud et al 2013	n/s	French multicentre study Nancy, Dijon, Bordeaux, Creteil, Lille, Angers, Reims, Clermont-Ferrand, Besancon, Suresnes, Thionville, Lomme	To determine the value and safety of drug patch tests in patients with SCAR (DRESS, ASEP, SJS/TEN)	Prospective 3-year french multicentre exploratory cohort study of the "Tademiad" group of the French Society of Dermatology	n/a	Patch test (Prick test IDT)	patch test: 48h	upper back	within the 12 months following the resolution of SCAR	Patients with SCAR	134	mean age: 51.7 years (range 3-94 years); 48 male, 86 female.	SCAR	according ESCDG guidelines	value and safety of drug patch tests in SCAR	tests positive in 64 % (DRESS), 55 % (ASEP), 24 % (SJS/TEN)	n/a	beta lactams (22 cases), pristinamycin (11 cases), purpura thrombotique (five cases)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	One relapse of ASEP during patch testing	Patch tests conducted with commercialized forms of some drugs diluted to 30 % in petrolatum are of value and safe for investigating ASEP and DRESS. As any inflammatory stimulation could be responsible for virus reactivation in DRESS, we propose conducting patch tests 6 months after the onset rash in DRESS	Few or no controls. No blinding	No quality-control measures.	2b
Brahmi et al. 2010	n/s	francophone french study: Paris (Hopital St-Jacques), Colmar, Montpellier, Rouen, Nancy, Clermont-Ferrand, Tours, Paris, Metz, Brest, Caen, Reims, Paris (Hopital Saint-Louis), Guadeloupe, Limoges, Bordeaux, Poitiers, Paris (Hopital Pasteur), Paris (Hopital Drouot)	to retrospectively collect and analyse well informed cases of fixed drug eruptions observed in a hospital setting.	Retrospective multicentric French nationwide 3-year-period descriptive non-interventional study (2005-2007).	n/a	patch test	n/s	inconsistently mentioned whether patch test was done on involved or normal skin or both	n/s	patients with fixed drug eruption	59	mean age: 59 years (8-93); W 51 ± 1.35 (M 4 ± 2.21 m)	fixed drug eruption	n/s	characteristics of fixed drug eruptions	tests positive in 12 cases	n/s	paracetamol > piroxicam > Amoxicillin, Carbocystein, > Hydrocortison, Thiocticin, pharmacological groups: NSAIDs > antibiotics	n/a	n/a	n/a	n/a	n/a	n/s	NSAID are common causes of FDE. Based on FDE pathogenesis, which is a lymphocyte CD8-mediated reaction, it has been proposed that the offending drug may induce local reactivation of memory T-cell lymphocytes localized in epidermal and dermal lesions and initially targeted by the viral infection.	no blinding, small number;	retrospective descriptive study	3b		
Duong et al. 2010	n/s	one center, Hopital Henri Mondor, Creteil, France	Sensitivity of patch tests in different SCARs	Retrospective one center study, Hopital Henri Mondor, Creteil, France	n/a	patch test	n/s	n/s	3 to 6 weeks after recovery of drug reaction	patients with SCAR (AGEP, DRESS, FDE, SJS/TEN)	111	Mean age: 53 years (21-89); sex ratio: 1.3 (FM);	SCAR	n/s	sensitivity of patch test	46/111 (41 %);	n/s	AGEP (83%), DRESS (95 %), FDE (17 %), SJS/TEN (26 %)	n/a	n/a	n/a	n/a	n/a	n/s	Patch test with suspected drug: weak sensitivity. But is very useful tool in assessing the drug responsibility in adverse drug reaction. Sensitivity of patch test is higher with ASEP than with SJS/TEN. Nevertheless an negative patch test will not eliminate the suspected culprit drug.	Inclusion and exclusion criteria specified. No control group. Force of patch test reactions Reactions/starke 1 not mentioned. No information about occlusion time.	n/a	4		
Soria et al. 2011	the work (M. Baeck) was partly funded by the Foundation Saint-Luc, Cliniques Universitaires Saint-Luc from Belgium (M. Baeck) le Groupe d'Etudes de la Recherche en Dermatologie-Allergologie (GERDA), France. A. Soria was supported by a grant from Institut Sclerose from France. No competing interests declared.	3 centers: Brussels (Belgium), Leuven (Belgium), Lyon (France)	To compare the test results obtained with patch, prick and intradermal testing, to assess the most sensitive method for diagnosing corticosteroid hypersensitivity	3 centre study	n/a	patch test, prick test, intradermal test	8 h, 24 h, 48 h, 96 h	upper back	n/s	subjects with positive patch test reactions to corticosteroids; 3 control subjects	19 patients (positive to corticosteroids); 3 patients (control subjects)	11 women: mean age 55 years; 8 men: mean age 49 years; control subject: 2 women, 54 and 64 years old; 1 men, 66 years old	patients with corticosteroid sensitization, diagnosed by patch test	ICDRG	positive skin test (patch, prick, ICT),	patch and intradermal results were concordant in 11 of 15 patients.	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/s	patch tests most often positive when removed after 48 h and read on day 4 and/or day 7. The intradermal tests gave positive results earlier than patch tests in 11 of 15 subjects, at the same time point in 2 subjects and later than the patch tests in 1 subject.	Prick tests were not in ethanol: dilution showed to be the most adequate and effective way of detecting delayed corticosteroid hypersensitivity. Removing the patch tests at D2 (or D4), with later readings between 3 and 7 days, provided optimal detection of delayed hypersensitivity to corticosteroids. The use of intradermal tests allows the detection of additional contact allergy cases.	Small sample size; Exclusion criteria not defined; No blinding	3b (study without consistently applied reference standard)	3b	
Tanno et al. 2011	n/s	two centers: Sao Paulo, Brazil	To determine sensitivity and specificity of drug patch test in severe, cutaneous adverse reactions	Prospective two center study, Sao Paulo, Brazil	History of NHR to drugs based on adapted ENDA questionnaire	patch test	48 h	n/s	at least 6 weeks after recovery. Mean delay of 3.7 months between adverse reaction and patch testing	patients with SCAR (SJS/DRESS), 20 with history of maculo-papular exanthema 15 with DRESS 10 with SJS 7 with macular exanthema 3 with multiform erythema 3 with phototoxicity 2 with fixed eruption 1 with late urticaria	Patients: 58 females, 3 males, mean age: 48.6 years	mean age: 48.6 years, 92.7 % were women.	patients with SCAR (DRESS, SJS)	European Environmental Contact Dermatitis Research Group	positive patch test reactions on 48 and/or 72 h.	Sensitivity of patch test in all NHR: 37 %; Specificity of patch test in all NHR: 100 % Positive predictive value: 100 % Negative predictive value: 20 % Sensitivity of patch test in SCAR: 83.5 %	n/s	aromatic anticonvulsants > antibiotics > NSAID, Sulfonamides.	n/a	n/a	n/a	n/a	none	Patch test may be an useful and safe diagnostic method in assessing the drug involved in NHR, particularly in SCAR, but low sensitivity	Inclusion and exclusion criteria specified. Control group not specified. Force of patch test reactions (Reactions/starke 1 not mentioned). No blinding	n/a	3b			

Wolkenstein et al 1995	n/s	One center, Department of Dermatology, Hôpital Henri Mondor, Créteil, France	To study patch testing in severe ADRs (SUS/TE, AGEF, other severe cutaneous ADRs resulting in hospitalization)	one center study, exploratory cohort with good reference standard	History of severe CADR, scoring system of likelihood for each drug at occurrence of rash	patch test	48 h	back	n/s	Patients with experienced CADRs	69, 20 control subjects (healthy volunteers)	mean age 49 (r=15), age 23-85 years, 30 females, 20 males	Patients with experienced CADRs	ICKDRG	n/s	Proportion of relevant positive tests significantly higher in AGEF. The proportion of antibiotics among the culprit drugs was significantly lower in SUS/TE than in AGEF. The proportion of NSAID among the culprit drugs was significantly higher in SUS/TE than in AGEF.	n/s	SUS/TE: Determination of culprit drug: SUS/TE (n=22), artemisinin n=7, NSAR n=7, sulfonamide n=4, miscellaneous n=4. 1 positive test to sulfonamide. SUS/TE, AGEF or other cutaneous ADRs could be linked to the clinical type of eruption, but to the different spectrum of the culprit drug.	n/a	n/a	n/a	n/a	n/s	1 - Patch testing has a weak sensitivity in SUS/TE2. Patch testing seems to be rather specific in SUS/TE1. Patch testing seems to be more specific to other cutaneous ADRs, such as AGEF4. One can hypothesize that the difference of sensitivity of patch testing in SUS/TE, AGEF or other cutaneous ADRs could be linked to the clinical type of eruption, but to the different spectrum of the culprit drug.	Small sample size. Exclusion criteria not specified (e.g. prior therapy with immunosuppressants, phototherapy, topical/systemic corticosteroids, etc.); no blinding	2b
Barbaud et al 1998	The work was supported in part by grants from the Clinical Research Commission of the University Hospital of Nancy and the French Minister of Education and Research. Competing interests not stated.	One center study, University Hospital Nancy, France	The use of skin testing in the investigation of cutaneous adverse drug reactions	one center study, exploratory cohort with good reference standard	Clinical feature of the CADR documented at time of drug rash	Patch test, Prick-test, IDT	48 h	upper back	6 weeks after onset of CADR	Patients with delayed drug eruptions	72 patients	Mean age 52.3 years, SD 21.4 years; 24 men, 48 women	delayed drug eruptions	ICKDRG	n/s	Positive results were obtained in 43 % (prick-test), 24 % (patch), 67 % (IDT).	n/s	n/a	n/a	n/a	n/a	n/s	define the value of the relatively safe drug skin tests in order to avoid, whenever possible, drug challenges. Drug patch test results depend on clinical feature (especially in T-cob-mediated	Inclusion criteria different. Statistical analysis. Control subjects	2b	
Brockow et al 2009	n/s	European multicentre study; München/Germany, Rome and Tronafoglio, Graz/ Austria, Basel/Switzerland, Nancy/France, Vercelli, Comba/Portugal, Breda/Dutchland, Porto/Portugal, Seixal/Portugal, Montpellier/France, Oslo/Norway	To determine the specificity and sensitivity of skin tests in patients who have experienced hypersensitivity reactions to isolated contrast media.	Prospective European multicentre study, exploratory cohort with good reference standard	History of a typical drug hypersensitivity recorded using the ENDA drug allergy questionnaire	Skin prick test, Intradermal test (IDT), Patch test (PT)	patch test: 48 h	back	minimum delay of 1 week and median delay of 6 months after the CM-induced hypersensitivity	patients with reported previous hypersensitivity reactions after CM exposure	220, 82 control patients	Median age at the time of the diagnostic testing: 54 years (age range 10-83 years) for immediate group and 58 years (age range 10-80 years) in non-immediate group; 80 females, 57 males	hypersensitivity reactions to isolated contrast media	ESCO	n/s	Patch tests were conducted in 19 patients with non-immediate reactions; 22 were tested, positive. About 50 % of patients in the immediate and non-immediate group could be diagnosed by standardized skin tests, if testing was conducted within 2-6 months after the reaction; 50 % of the hypersensitivity reactions to RCM are caused by an immunological reaction. Specificity of delayed IDT and PT were both 100%.	n/a	n/a	n/a	n/a	n/a	At least 50 % of hypersensitivity reactions to contrast media are caused by an immunological mechanism. Skin testing appears to be a useful tool for diagnosis of contrast medium allergy and may play an important role in selection of a safe product in previous reactors. Skin testing seems to be a useful tool for diagnosis of CM allergy and may play an important role in selection of a safe product in previous reactors. Specificity of skin tests is as high as 96-100 %. Further studies are required to establish their negative predictive value.	Recruitment bias possible (reacting patients with higher reactions). No provocation: > skin test sensitivity cannot be determined with certainty. No blinding. Negative predictive value has yet to be determined.	Control group (71 never exposed subjects, 11 under reactions). Subjects who had tolerated contrast medium exposure). Negative predictive value has yet to be determined.	2b	
Brockow et al 2006	n/s	literature review	Clinical and diagnostic aspects of hypersensitivity reactions to isolated contrast media.	expert opinion based on literature review	n/a	Skin prick test, Intradermal test, Patch test	patch test: 48 h	back	n/a	n/a	n/a	n/a	hypersensitivity reactions to isolated contrast media	n/s	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Specify and sensitivity of skin testing in contrast media allergy remains to be established.	n/a	n/a	5	
Kleinans et al 2002	n/s	One centre study, University Hospital Frankfurt	to evaluate tolerability of Celebrex in NSAID-sensitive patients using patch test, scratch test and oral provocation	consecutive patients and/or dry cohort with good reference standard	single blind placebo controlled oral provocation test	Patch test with homogenized Celebrex undiluted (?), 5% and 10% in pet and oral provocation	48 h	n/a, presumably back	n/s	patients with history of NSAID sensitivity (symptoms within 6 h after ingestion and other components of the drug subsequently tolerated)	14	6 males, 8 females, age 18-72 years	presumed NSAID sensitivity	International Contact Dermatitis Research Group (IC-DRG)	non irritant patch test concentration of Celebrex	Patch test with homogenized Celebrex 8 of 10 patients + at D2 with decrease between D2 and D3. In 9 control patients without NSAID-hypersensitivity similar reactions in patch test.	n/a	n/a	n/a	n/a	n/a	scratch tests with homogenized Celebrex (undiluted ?) was negative, as was oral provocation	When performing patch tests with Celebrex, high concentrations of about 10 % homogenized Celebrex in petrolatum should be used.	Small sample size. Exclusion criteria not defined. No blinding	it is not clear whether nonirritant skin test concentrations are able to detect sensitization to COX-2 inhibitors	2b

Barboud et al. 2001	n/s	guideline	To give guidance for diagnostic procedures in the diagnosis of cutaneous adverse drug reactions	literature review and expert consensus	n/a	Skin prick test, Intradermal test, Patch test, In vitro tests (specifically, 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	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	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	n/a	n/a	5
Johansen et al. 2015	individually stated for each author	guideline	To give guidance for diagnostic patch testing recommendations on best practice including the diagnosis of drug eruptions	literature review and expert consensus	n/a	PT, ROAT, Semi open test, Photo-PT	D2 and D3 or D4 and around D7 (optimum).	Upper back (same as for the investigation of allergic contact dermatitis, except for fixed drug eruption; additional test: patch testing is advised)	at least 4-6 weeks after complete resolution of the CADR		Patients with cutaneous adverse drug reactions	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Patch testing is a safe procedure, even in patients with severe CADRs, apart from exceptional cases of reactivation of the CADR	n/a	n/a	5
Brockow et al. 2015	n/s	guideline	To give guidance for diagnostic procedures in the diagnosis of drug hypersensitivity	literature review and expert consensus	n/a	Skin prick test, Intradermal test, Patch test, In vitro tests (specifically, CAST, LTT, Elispot)	PT: in cases with reported exanthema: 24h or 48h; in case of previous anaphylactic reactions: reading after exposure of 20 or 30 minutes	n/s	n/a		Patients with drug allergy	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Although drug hypersensitivity cannot be reliably ruled out even by applying all available test methods, they do make better risk assessment easier.	n/a	n/a	5

n subgroup/ study population
N total number of patients
m mean
n/s not stated
n/a not applicable
MF male /female

Study characteristics				Methods										Results										Critical Appraisal of Results									
First author year	Research and reporting reference	Setting	Aims and Objectives	Question addressed	Study Design	Reference selection criteria	Eligibility criteria inclusion exclusion	Duration of exposure	Application site	Excluding times	Time interval and sequentially assessing time	Investigatory and sequentially assessing time	Inclusion criteria	Exclusion criteria	Patients excluded	Patients aged gender M:F	Interventive Diagnosis	Control Diagnosis	Outcomes Primary Secondary	Definition of Outcome	Results (Number n/N)	Results (Percentage)	Accuracy	Reproducibility	Cost- effectiveness	Comparison with best practice	Adverse effects	Author credibility	Author bias	Internal validity	External validity	Confidence interval	Other Information Desirable
McGowan 2004	16	University of Hull The Netherlands	To establish the response of male patients to therapy as described in the literature	prophylactic control	NS	The design is clearly stated and the patient population is well defined and included in the analysis	1- High 2- High 3- High 4- High	2 sites	1- High 2- High 3- High 4- High	NS	NS	patients who had a high level of inclusion criteria in the study	2 patients	2 patients	714, aged 1-70, M:F	NS	Observational Control Research Group Control Research Group Control Research Group	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High
McGowan 2004	16	University of Hull The Netherlands	To assess if patients in the study were able to understand the study and participate in the study	prophylactic control	NS	The design is clearly stated and the patient population is well defined and included in the analysis	1- High 2- High 3- High 4- High	2 sites	1- High 2- High 3- High 4- High	NS	NS	patients who had a high level of inclusion criteria in the study	2 patients	2 patients	714, aged 1-70, M:F	NS	Observational Control Research Group Control Research Group Control Research Group	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High
McGowan 2004	16	University of Hull The Netherlands	To investigate whether patients understand the study and participate in the study	prophylactic control	NS	The design is clearly stated and the patient population is well defined and included in the analysis	1- High 2- High 3- High 4- High	2 sites	1- High 2- High 3- High 4- High	NS	NS	patients who had a high level of inclusion criteria in the study	2 patients	2 patients	714, aged 1-70, M:F	NS	Observational Control Research Group Control Research Group Control Research Group	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High
McGowan 2004	16	University of Hull The Netherlands	To compare the effect of therapy on the quality of life of patients	prophylactic control	NS	The design is clearly stated and the patient population is well defined and included in the analysis	1- High 2- High 3- High 4- High	2 sites	1- High 2- High 3- High 4- High	NS	NS	patients who had a high level of inclusion criteria in the study	2 patients	2 patients	714, aged 1-70, M:F	NS	Observational Control Research Group Control Research Group Control Research Group	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High	Comparison of 1- High 2- High 3- High 4- High

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N
m
ns
na
NA

subgroup study population
total number of patients
mean
not stated
not applicable
male/female

Rosch et al. 2006	EU Commission (2004-CT-1999-02558) Programme – chemical safety: a major environmental and consumer problem in Europe	6 European departments	Does the FM identify additional patients with a previous history related to FM? Is it necessary to add FM to the European safety?	prospective cohort of patients	a reported 'history' of previous FM is necessary to add FM to the European safety	Prospective test with baseline series with FM (8% vs. 2.8%, 14%, 14%, 14%)	2 days	back	PT after interview	Consecutive patients eligible for patch testing	1701 patients	Median age 44, range 15-86, 62.2% female	suspected allergic contact dermatitis	ICD9G (according to chapter 168)	positive patch test D3 or D4	60 of 1701	not stated	not applicable	23 pos. PT with pos. history, 17 pos. PT with neg. history, 252 neg. PT with pos. history, 1350 neg. PT with pos. history	the new FM is added additional to previous FM	results can be transferred to patients meeting the inclusion criteria	4
Rosch et al. 2006	EU Commission (2004-CT-1999-02558) Programme – chemical safety: a major environmental and consumer problem in Europe	6 European departments	Does the FM identify additional patients with a previous history related to FM? Is it necessary to add FM to the European safety?	prospective cohort of patients	a reported 'history' of previous FM is necessary to add FM to the European safety	Prospective test with baseline series with FM (8% vs. 2.8%, 14%, 14%, 14%)	2 days	back	PT after interview	Consecutive patients eligible for patch testing	1701 patients	Median age 44, range 15-86, 62.2% female	suspected allergic contact dermatitis	ICD9G (according to chapter 168)	positive patch test D3 or D4	111 of 1701	not stated	not applicable	50 pos. PT with pos. history, 10 pos. PT with neg. history, 821 neg. PT with pos. history, 1364 neg. PT with pos. history	the number of new positive reactions is more with FM than with FM	results can be transferred to patients meeting the inclusion criteria	4
Gohar et al. 2011	Ardara University Commission of Sports Research Project (2006-09-20-0229793)	Ardara, Turin	To evaluate the prevalence of CM in competitive athletes ... and the role of skin testing in its diagnosis	prospective cohort series	observation or skin prick test administration of CM	1000, 100, and 10-100 dilutions of the subject CM in saline	2 days	back	not applicable	Patients with immediate hypersensitivity reactions to CM	24, only 6 with non-immature reactions (aged 18 months)	mean age 19, range 10-34 years, 6 males, 18 females	atopy-like reaction after administration of CM	European Society of Contact Dermatitis (on drug testing: Reichel et al., CDD 2001: 45-52, 2008)	positive patch test D3 or D4 or D5 or D6	11 of 8 patients	not stated	not applicable	1 pos. PT with pos. history, 2 neg. PT with pos. history, 21 controls (neg. history) had none PT test with control	Skin testing with CMs has a high sensitivity, but its role is limited by a low specificity to test its relevance to reactions to CM	results can be transferred to patients meeting the inclusion criteria	26
Johansen et al. 1997	Phd. Neale Fignin Foundation, Danish Board of Health and Danish EPA	Denmark	To investigate the relationship between patients' own perception of the use of personal products and the prevalence of allergic skin diseases	prospective cohort series	skin prick test and patch testing with the use of personal products (Fragr., Cosm., Hyg., Perf., etc.)	Patch test with baseline series with FM (8% vs. 2.8%, 14%, 14%, 14%)	2 days	back	PT after questionnaire	Consecutive patients eligible for patch testing	622 consecutive patients invited, but 673 females participated	age range 18-67, 21 males, 673 females	suspected allergic contact dermatitis	ICD9G (according to WHO code at 687)	positive patch test D3 or D4	18 pos. to FM, 32 pos. to M, never to G	not stated	not applicable	60 pos. PT with pos. history, 204 neg. PT with pos. history, 143 pos. PT with neg. history, 422 neg. PT with neg. history	... most negative reactions were positive patients are aware that the use of essential products may relate with history	results can be transferred to patients meeting the inclusion criteria	4

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n/s
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MF

