Bijlage 4: Tabellen en figuren

Tabel 2 ALDEN score, uit Sassolas B et al. ALDEN, an algorithm for assessment of drug causality in Stevens-Johnson Syndrome and toxic epidermal necrolysis: comparison with case-control analysis. Clin Pharmacol Ther. 2010 Jul;88(1):60-8

Table 5 Details of the algorithm of drug causality for epidermal necrolysis (ALDEN)

Criterion	Values	Rules to apply	
Delay from initial drug component intake to onset of reaction (index day)	Suggestive +3	From 5 to 28 days	−3 to 3
	Compatible +2	From 29 to 56 days	
	Likely +1	From 1 to 4 days	
	Unlikely −1	>56 Days	
	Excluded −3	Drug started on or after the index day	
		In case of previous reaction to the same drug, only changes for: Suggestive: +3: from 1 to 4 days Likely: +1: from 5 to 56 days	
Drug present in the body on index day	Definite 0	Drug continued up to index day or stopped at a time point less than five times the elimination half-life[a] before the index day	−3 to 0
	Doubtful −1	Drug stopped at a time point prior to the index day by more than five times the elimination half-life[a] but liver or kidney function alterations or suspected drug interactions[b] are present	
	Excluded −3	Drug stopped at a time point prior to the index day by more than five times the elimination half-life[a], without liver or kidney function alterations or suspected drug interactions[b]	
Prechallenge/rechallenge	Positive specific for disease and drug: 4	SJS/TEN after use of same drug	−2 to 4
	Positive specific for disease or drug: 2	SJS/TEN after use of similar[c] drug or other reaction with same drug	
	Positive unspecific: 1	Other reaction after use of similar[c] drug	
	Not done/unknown: 0	No known previous exposure to this drug	
	Negative −2	Exposure to this drug without any reaction (before or after reaction)	
Dechallenge	Neutral 0	Drug stopped (or unknown)	−2 or 0
	Negative −2	Drug continued without harm	
Type of drug (notoriety)	Strongly associated 3	Drug of the "high-risk" list according to previous case–control studies[d]	−1 to 3
	Associated 2	Drug with definite but lower risk according to previous case–control studies[d]	
	Suspected 1	Several previous reports, ambiguous epidemiology results (drug "under surveillance")	
	Unknown 0	All other drugs including newly released ones	
	Not suspected −1	No evidence of association from previous epidemiology study[d] with sufficient number of exposed controls[c]	
		Intermediate score = total of all previous criteria	−11 to 10
Other cause	Possible −1	Rank all drugs from highest to lowest intermediate score	−1
		If at least one has an intermediate score >3, subtract 1 point from the score of each of the other drugs taken by the patient (another cause is more likely)	
Final score −12 to 10			

<0, Very unlikely; 0–1, unlikely; 2–3, possible; 4–5, probable; ≥6, very probable.

ATC, anatomical therapeutic chemical; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.

[a]Drug (or active metabolite) elimination half-life from serum and/or tissues (according to pharmacology textbooks, tentative list available in complementary table), taking into account kidney function for drugs predominantly cleared by kidney and liver function for those with high hepatic clearance. [b]Suspected interaction was considered when more than five drugs were present in a patient's body at the same time. [c]Similar drug = same ATC code up to the fourth level (chemical subgroups), see Methods. [d]See definitions for "high risk," "lower risk," and "no evidence of association" in Methods, ref. 15 (detailed list available in complementary table).

Tabel 3 EuroSCAR score, uit Sidoroff A, Halevy S, Bavinck JN, Vaillant L, Roujeau JC. Acute generalized exanthematous pustulosis (AGEP)--a clinical reaction pattern. J Cutan Pathol. 2001 Mar;28(3):113-9.

Table 2. AGEP validation score of the EuroSCAR study group

Morphology	
Pustules	
Typical*	+2
Compatible**	+1
Insufficient***	0
Erythema	
Typical	+2
Compatible	+1
Insufficient	0
Distribution/pattern	
Typical	+2
Compatible	+1
Insufficient	0
Postpustular desquamation	
Yes	+1
No/insufficient	+0
Course	
Mucosal involvement	
Yes	−2
No	0
Acute onset (≤10 d)	
Yes	0
No	−2
Resolution ≤15 days	
Yes	0
No	−4
Fever ≥38 °C	
Yes	+1
No	0
PNN ≥7000/mm^3	
Yes	+1
No	0
Histology	
Other disease	−10
Not representative/no histology	0
Exocytosis of PNN	+1
Subcorneal and/or intraepidermal *non* spongiform or NOS pustule(s) *with* papillary edema or subcorneal and/or intraepidermal *spongiform* or NOS pustule(s) *without* papillary edema (NOS=not otherwise specified)	+2
Spongiform subcorneal and/or intraepidermal pustule(s) *with* papillary edema	+3

Interpretation: ≤0: no AGEP, 1–4: possible, 5–7: probable, 8–12: definite.
Remarks: Patients are not included in the study, if only localized pustules are reported, the pustular rash already lasts longer than 3 weeks or a clear alternative diagnosis has been made by a dermatologist.
*Typical: typical morphology as described in the "clinical features" section
**Compatible: not typical, but not strongly suggestive of other disease.
***Insufficient: lesions can not be judged (mostly because of late stage of the disease or poor quality of pictures).

Tabel 4 Gebruik van huidtesten (intradermale testen, plakproeven en systemische provocatietesten), uit Phillips EJ, Bigliardi P, Bircher AJ, Broyles A, Chang YS, Chung WH, et al. Controversies in drug allergy: Testing for delayed reactions. J Allergy Clin Immunol. 2019 Jan;143(1):66-73.

TABLE III. Use of delayed skin prick testing/IDT, patch testing, and systemic provocation for delayed reactions[18,19,32,33]*

	Patch tests†	Prick tests	IDT‡	Systemic provocation
Maculopapular rash	Useful (positive in 10% to 40%)	Potentially useful	Potentially useful, but direct oral provocation might be indicated in low-probability situations	After negative skin test results with delayed readings in low-probability situations; NPV of 90%
Generalized eczema (contact reaction)	Useful	Potentially useful	Potentially useful	After negative delayed skin test result with delayed readings; NPV is unknown
Baboon syndrome or SDRIFE	Useful (positive in 52% to 82%)	Potentially useful	Potentially useful	After negative skin test results with delayed readings; NPV is unknown
Fixed drug eruption	Useful with *in situ* application in area of previous reaction (up to 40% positive)	Unknown	Unknown	At full dose when patch tests or repeated application test results are negative; NPV is unknown
Photosensitization	Photopatch tests with a 5-J exposure to UVA, irradiation at 48 h	No value	No value	No value without exposure to UV
AGEP	Useful; sensitivity depends on the specific implicated drug (up to 58%)	Unknown	Potentially useful	Systemic provocation of suspected drug or cross-reactive drugs is contraindicated
DRESS	Useful (positive in 32% to 64%) dependent on drug Advised 6 mo after disappearance of rash and other sequelae	Described delayed positive at 24 h but unknown utility	Delayed reading at 24 h Currently unknown safety	Systemic provocation with the highly suspected drug and cross-reactive drugs contraindicated
SJS/TEN	Low sensitivity (<30%); can be considered if there is benefit of diagnostic information obtained§	Considered contraindicated	Considered contraindicated	Systemic provocation with suspected drug is contraindicated
Drug-induced liver disease (or another single-organ phenotype)	Low sensitivity if no cutaneous involvement	Low sensitivity if no cutaneous involvement	Low sensitivity if no cutaneous involvement	Systemic provocation with suspected drug is contraindicated

SDRIFE, Symmetrical drug-related intertriginous and flexural exanthema.

*Practices differ significantly between the United States and Europe and parts of Asia at this time. In Europe both allergists and dermatologists perform skin testing, patch testing, and systemic provocation. In the United States allergists perform mainly skin testing and oral provocation, and there are few canters where delayed testing is offered. Drug patch testing and delayed IDT is not frequently offered in the United States by either allergists or dermatologists and is offered in select centers only.

†Initial read at 48 hours; reading occurs at 72 and 96 hours and 1 week if initial result is negative.

‡Read at 48 hours if 24-hour result is negative.

§For allopurinol and its metabolite oxypurinol, patch testing has had 0% sensitivity.