“How the uncertainties associated with patch testing, including false positives and negatives, could be minimized”

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Confusion

Contact allergy – allergic contact dermatitis

Contact allergy

No disease

Reaction pattern

Allergic contact dermatitis

Contact allergy

Exposure

Relevance

Contact allergy

Induction - Elicitation

Qualitative - Quantitative aspects

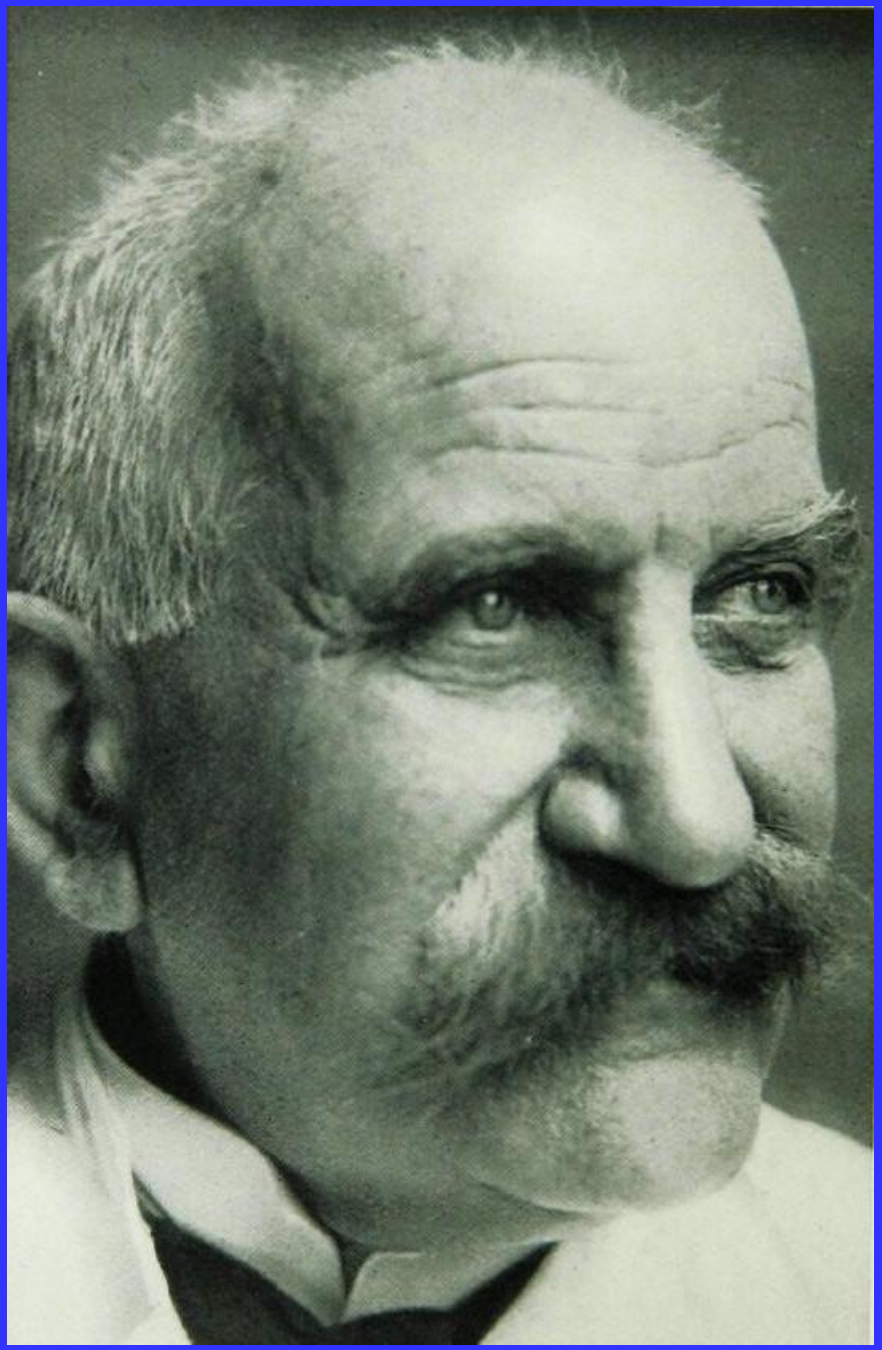
Quantitative aspects

DBS 1% ALK
0.1% ALK
0.01% ALK
0.001 % ALK
0.0001 % ALK

Establishing of contact allergy

In vitro

In vivo



Diagnosis of contact allergy and allergic contact dermatitis

What to patch test with

Every exposure/contactant that can explain the dermatitis under investigation - wholly or partly in case of contact allergy

Patch test preparations

Standard series

Additional series

Patient-supplied products

How to choose test concentration?

As high as possible without causing adverse ractions, particularly active sensitization

How to choose test concentration

- Exposure conditions
- Textbooks

Patch test results

Individual factors

Non-individual factors

Patch test results

Individual factors

Skin condition
Anatomical site
Medication
Tanning
Hormonal status

Patch test results

Non-individual factors

- Test technique
- Test preparation
- Application time
- Application technique
- Dose
- Occlusion time
- Reading times
- Classification

Patch test results

Non-individual factors

Test technique

Test preparation

Application time

Application technique

Dose

Occlusion time

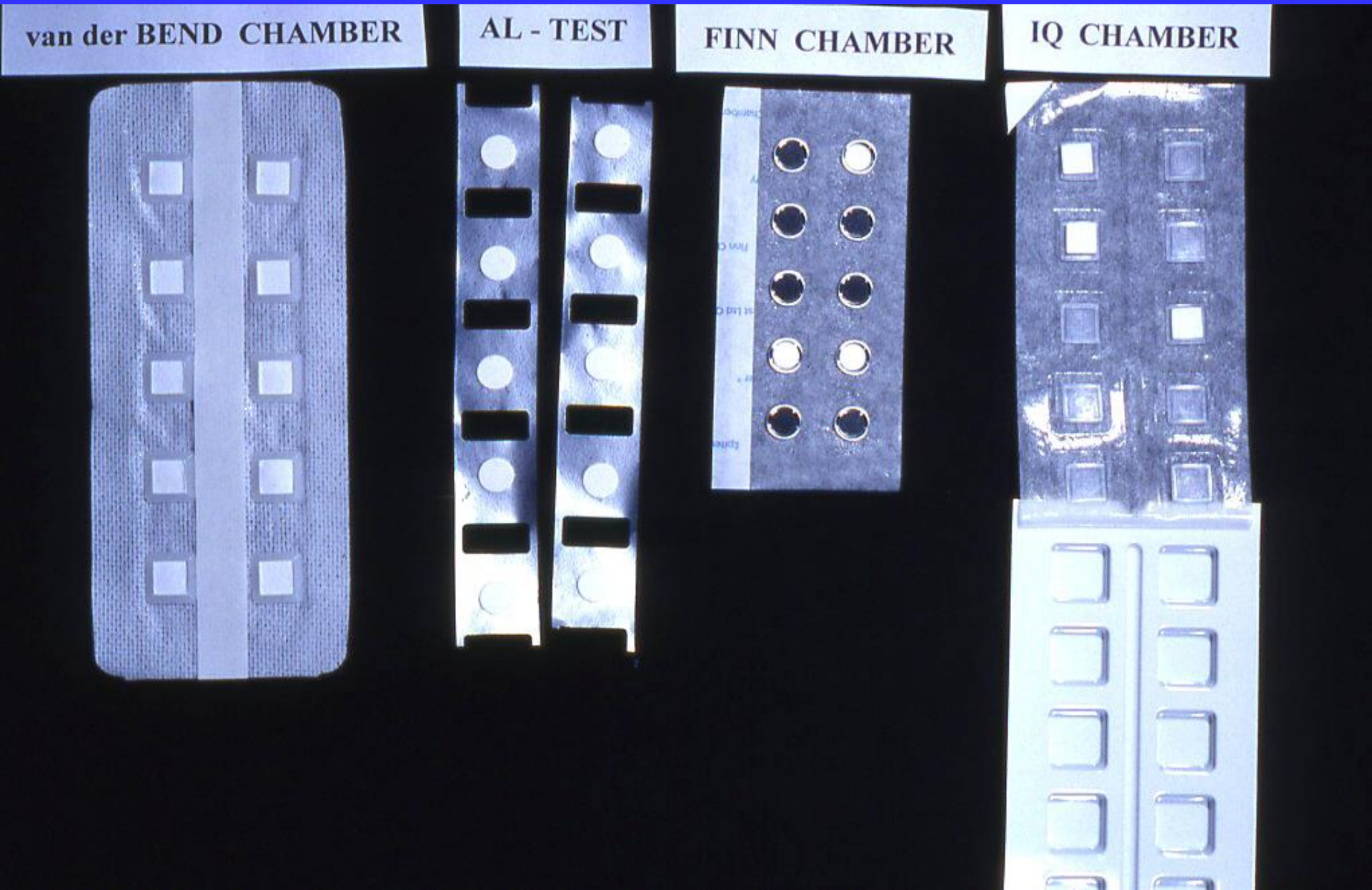
Reading times

Classification

Test technique

units/chambers

occlusive tape

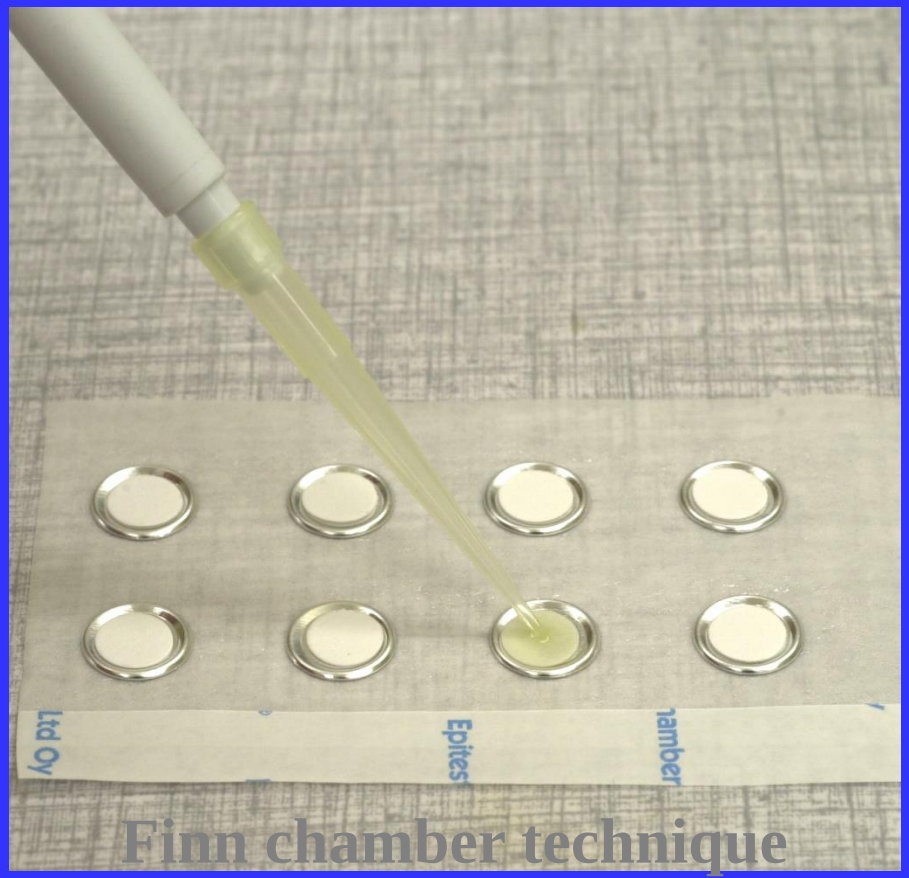

van der BEND CHAMBER
AL - TEST
FINN CHAMBER
IQ CHAMBER

Test technique

Unloaded	Loaded
Al-test	True test
Finn chamber	
Van der Bend chamber	
IQ chamber	

False negative reactions in gold- allergic patients?

Gold trichloride



Finn chamber technique

Test results

Patient	Positive test
Gold allergic	0/13

Patch test results

Non-individual factors

Test technique

Test preparation

Application time

Application technique

Dose

Occlusion time

Reading times

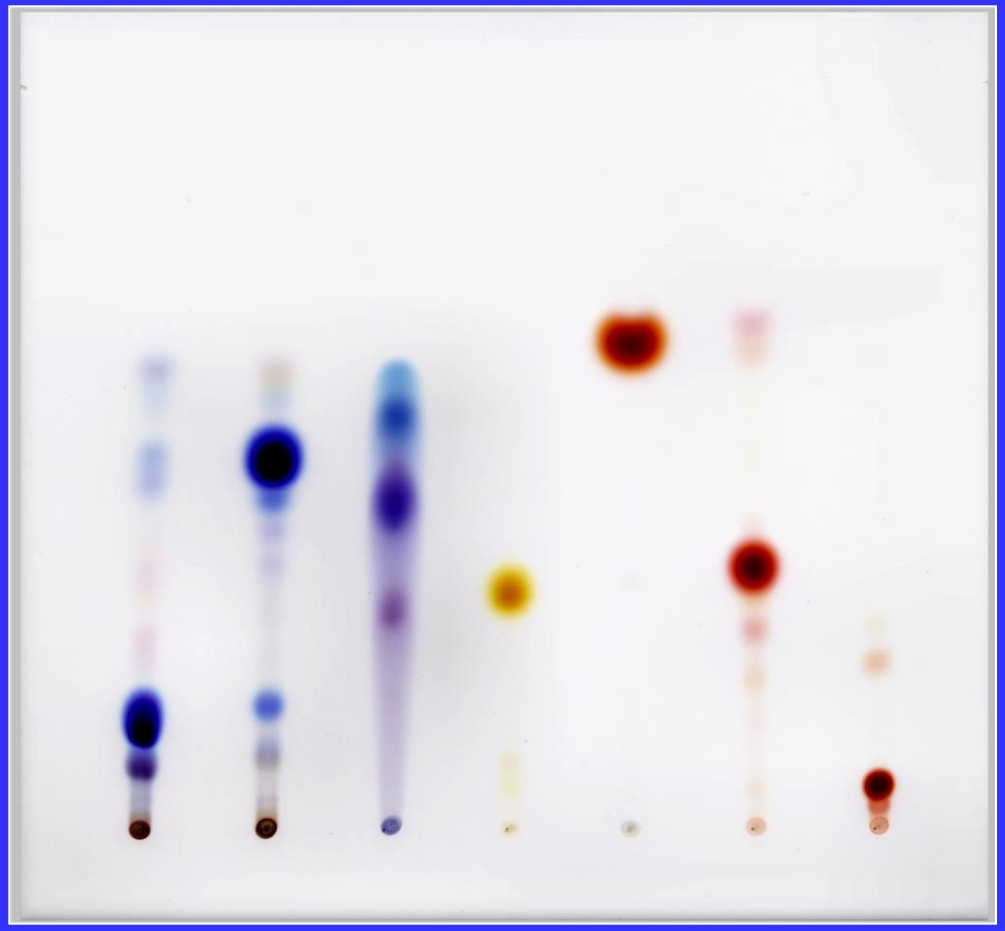
Classification

4,4’-MDI in petrolatum patch test preparations

Stated concentration (%; w/w)	Found concentration (%; w/w)	Ratio between stated/found concentrations
1	0.12	8.3
2	0.095	21.1
2	0.082	24.4
1	0.036	27.8
1	0.026	38.5
2	0.031	64.5
1	0.015	66.7
2	0.024	83.3
2	0.010	200
1	0.001	1000
0.1	<0.0005	>200
2	<0.0005	>4000
2	1.3	1.5
1	0.19	5.3

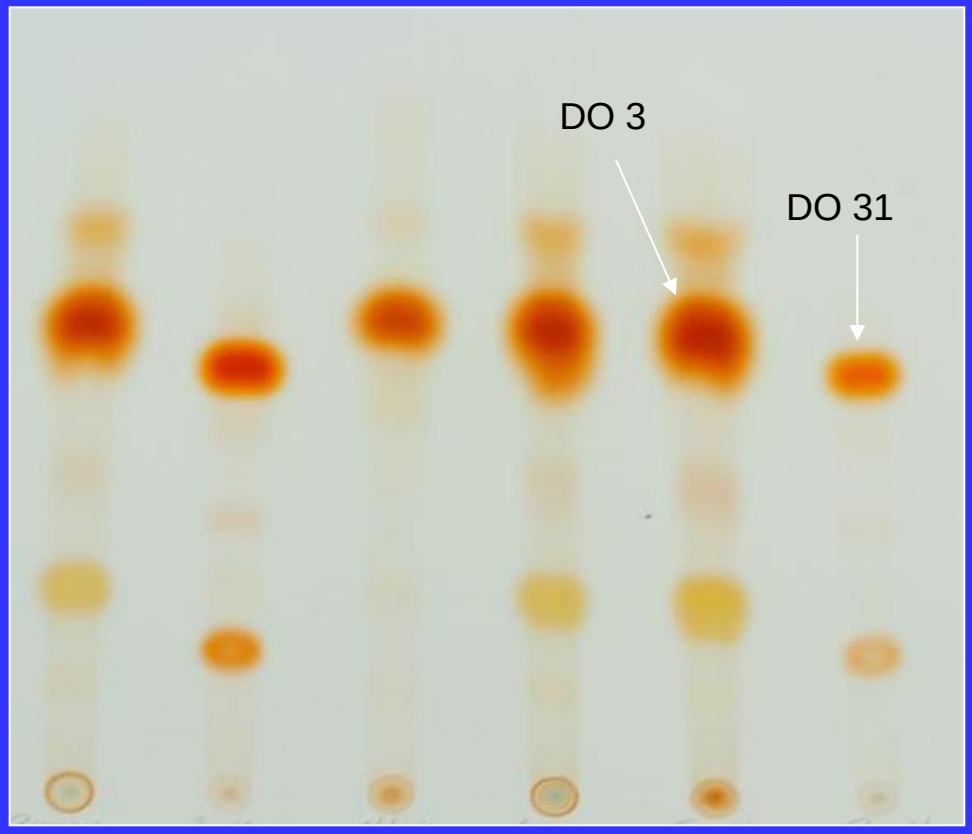
Frick et al. Contact Dermatitis 2004: 51: 73-78

Disperse dyes



Ryberg et al. Contact Dermatitis 2008: 58: 199-209

D Orange 3

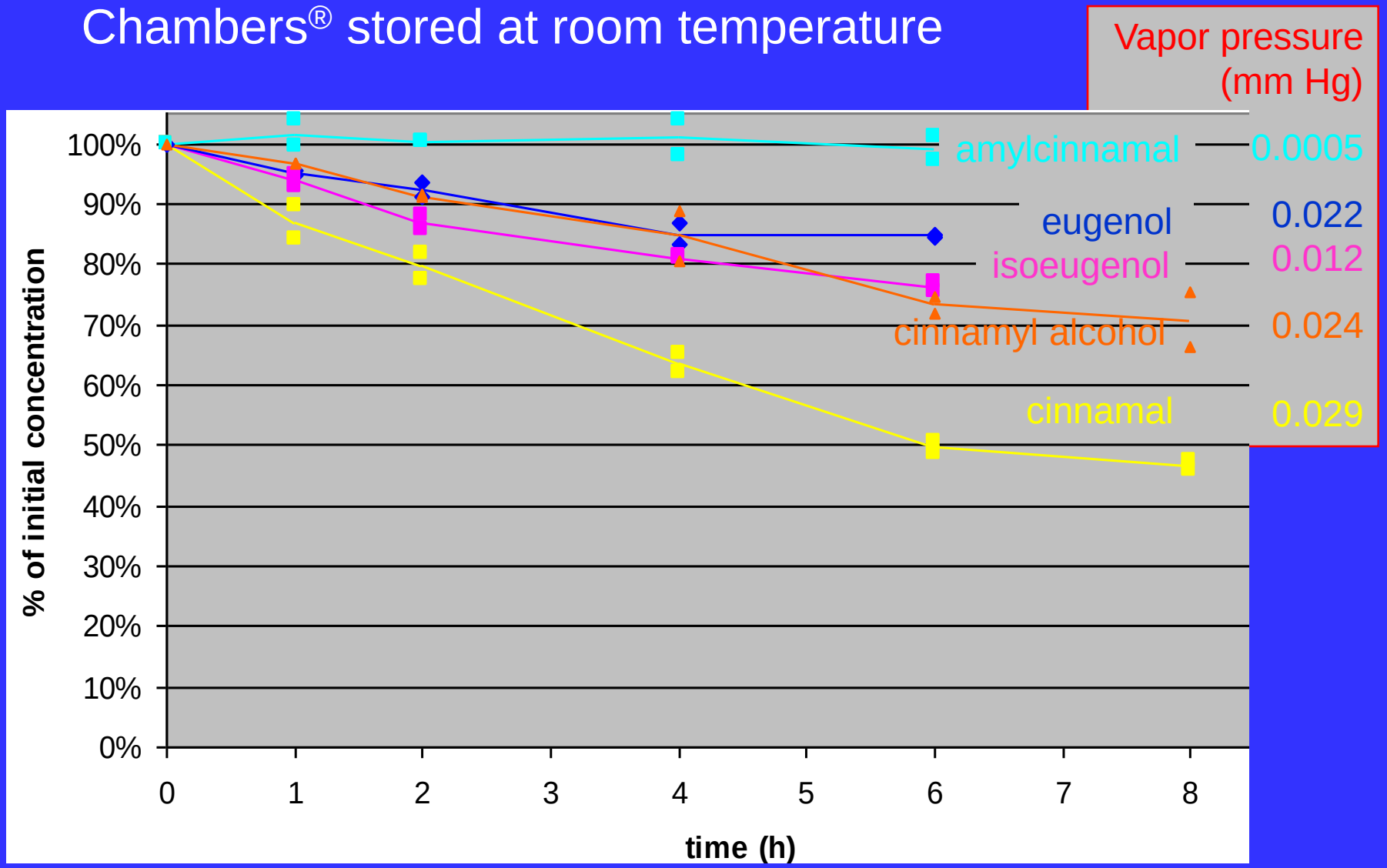


Patch test results

Non-individual factors

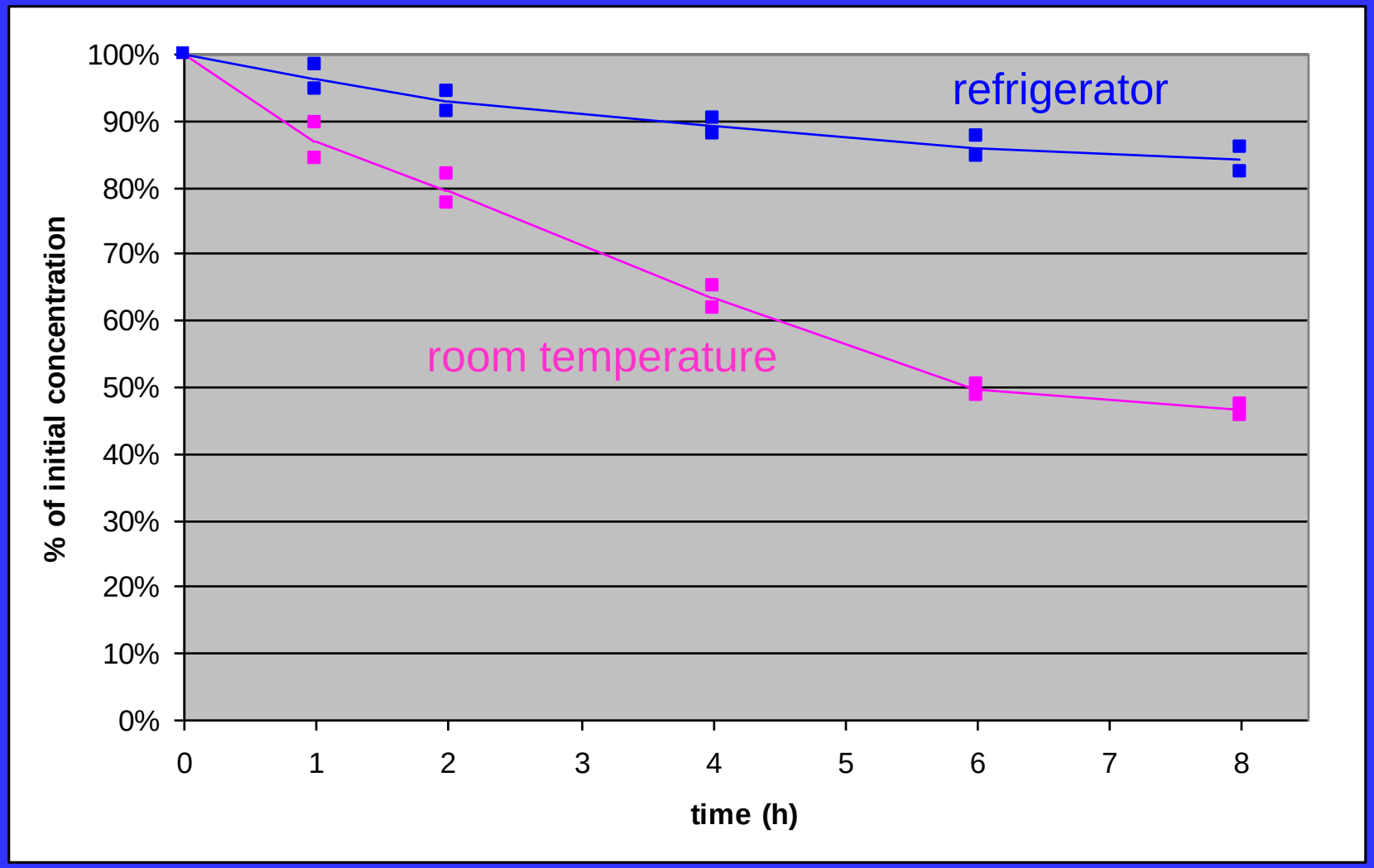
Test technique
Test preparation
Application time
Application technique
Dose
Occlusion time
Reading times
Classification

Test preparations applied in Finn Chambers® stored at room temperature

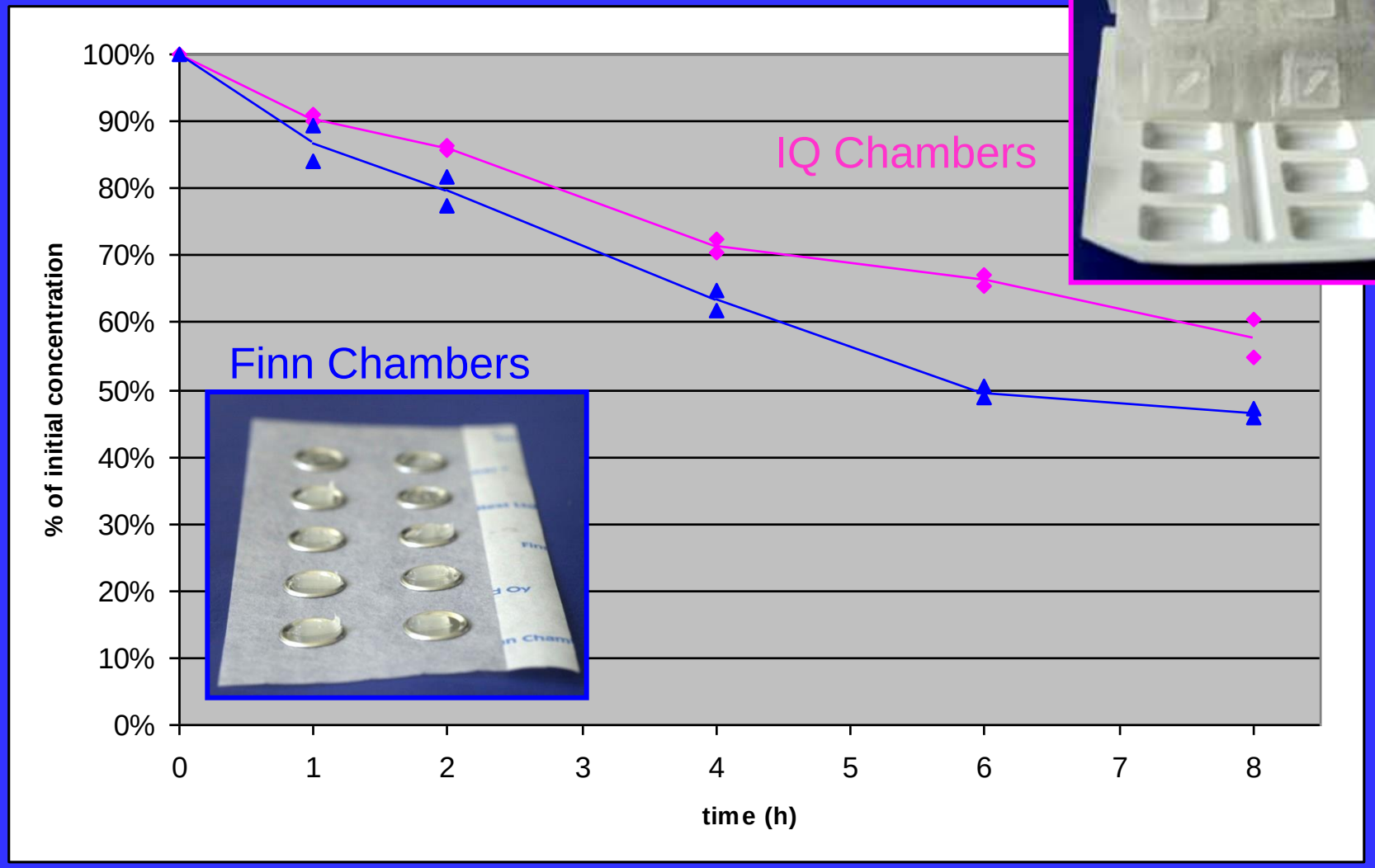


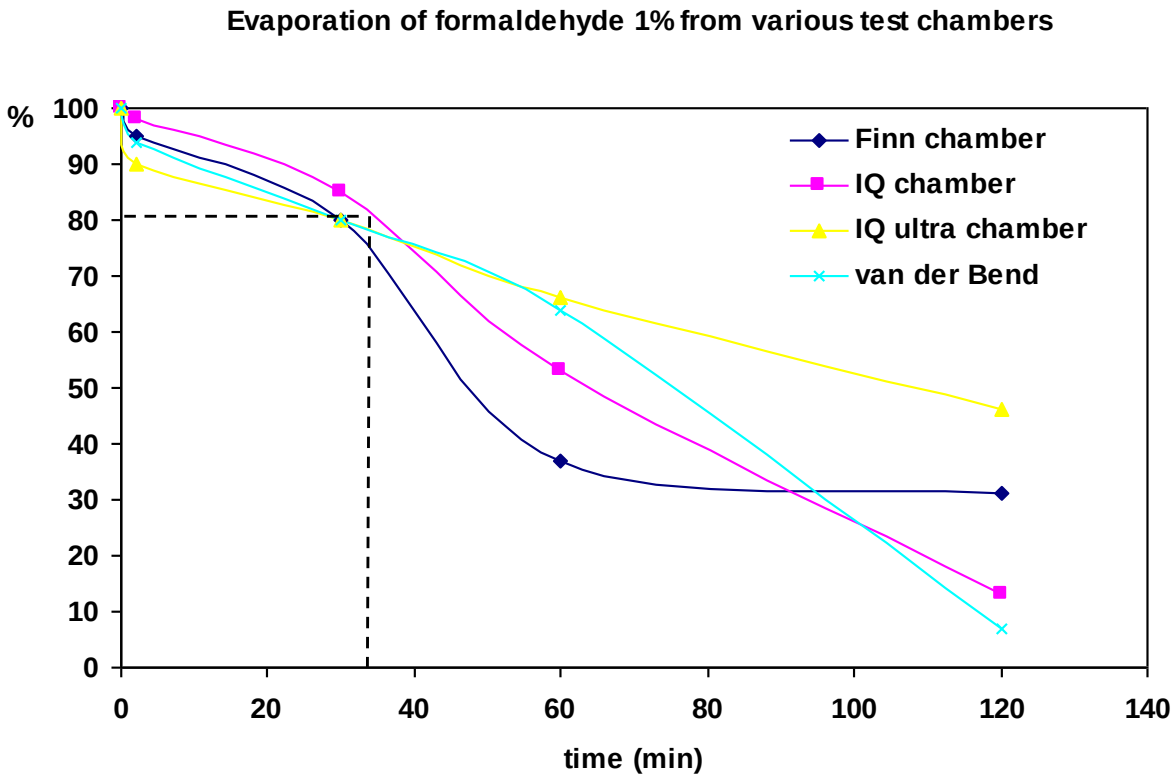
Mowitz et al. Br J Dermatol 2012: 167: 822-7

Cinnamal applied in Finn Chambers® stored at room temperature and in refrigerator



Cinnamal in Finn Chambers® and IQ Chambers® stored at room temperature

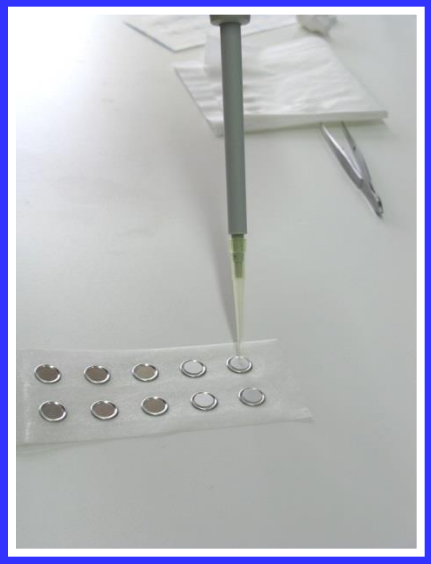



Evaporation of formaldehyde 1% from various test chambers
%
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
140
time (min)
Finn chamber
IQ chamber
IQ ultra chamber
van der Bend

Patch test results

Non-individual factors

- Test technique
- Test preparation
- Application time
- ***Application technique***
- Dose
- Occlusion time
- Reading times
- Classification



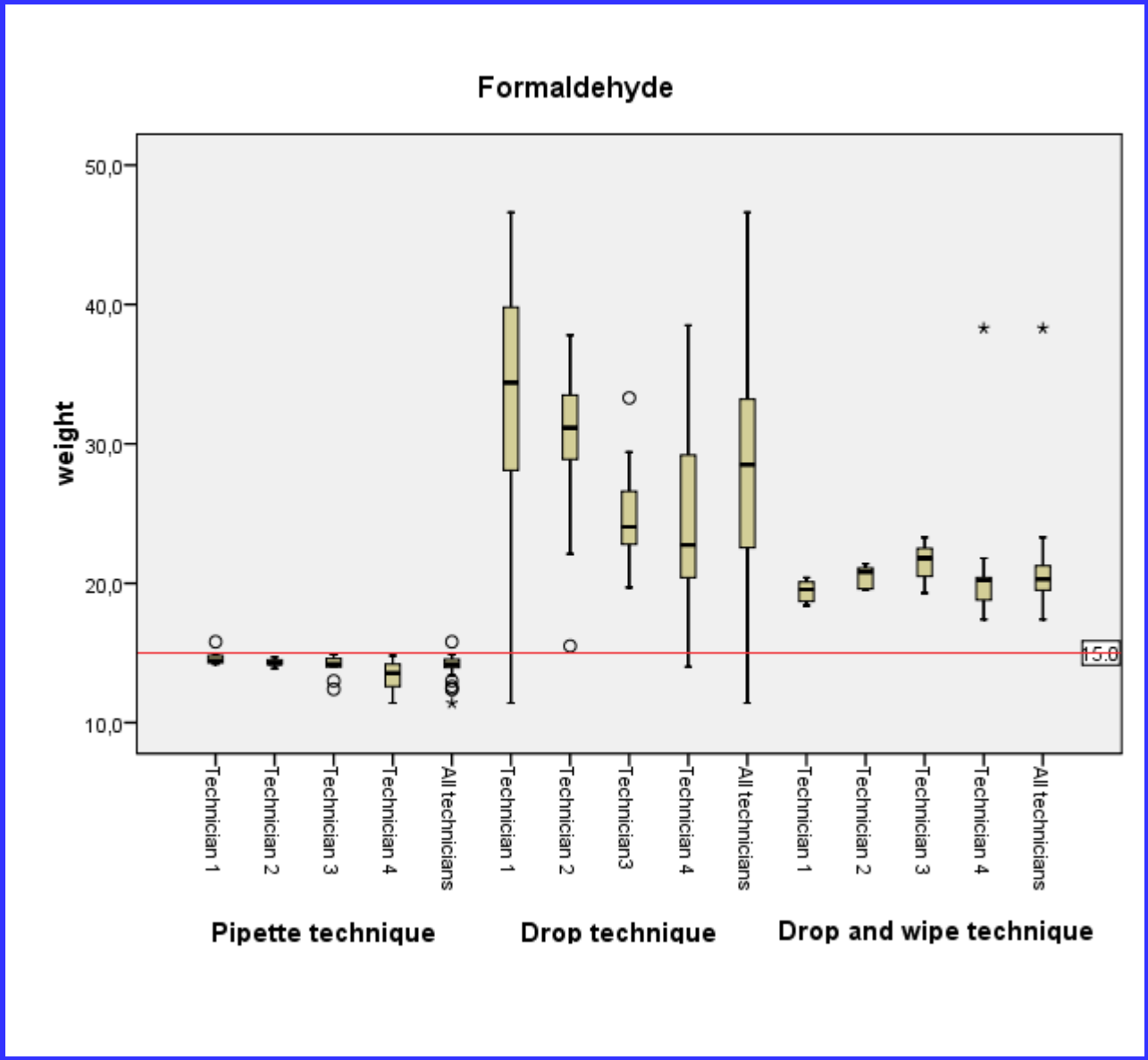
Micro-pipette technique

Drop technique

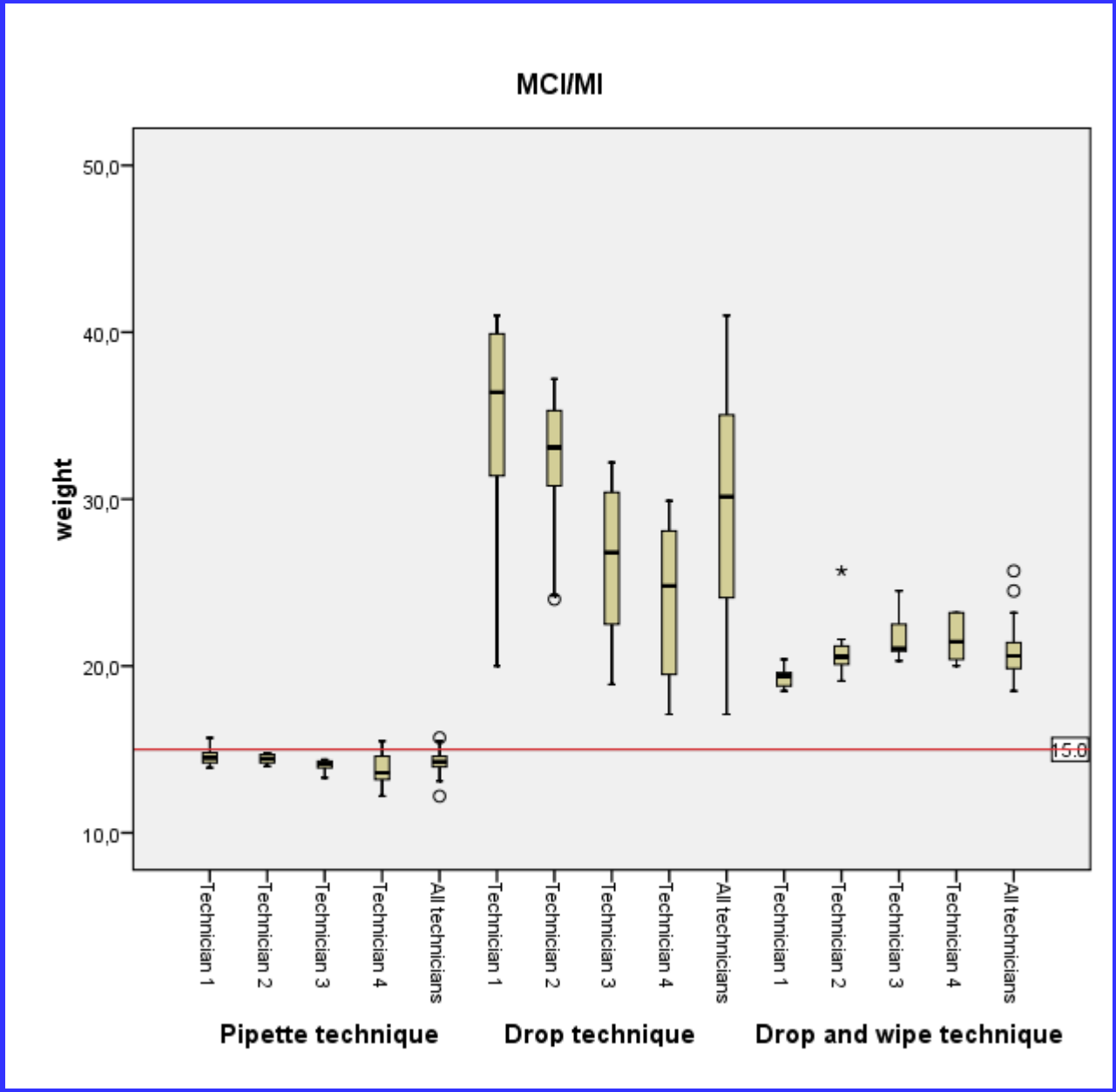
Drop and wipe technique

Frick -Engfeldt et al. Contact Dermatitis: 2010: 63: 284-8

Results:


Formaldehyde
weight
50,0
40,0
30,0
20,0
10,0
15,0
Technician 1
Technician 2
Technician 3
Technician 4
All technicians
Technician 1
Technician 2
Technician3
Technician 4
All technicians
Technician 1
Technician 2
Technician 3
Technician 4
All technicians
Pipette technique
Drop technique
Drop and wipe technique

Results:


MCI/MI
weight
50,0
40,0
30,0
20,0
10,0
15,0
Technician 1
Technician 2
Technician 3
Technician 4
All technicians
Technician 1
Technician 2
Technician 3
Technician 4
All technicians
Technician 1
Technician 2
Technician 3
Technician 4
All technicians
Pipette technique
Drop technique
Drop and wipe technique

Patch test results

Non-individual factors

Test technique
Test preparation
Application time
Application technique
Dose
Occlusion time
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Classification

The dose is determined by the

Concentration

Volume/amount applied

Petrolatum

Convenient to use

Prevents degradation,
oxidation and polymerization but not evaporation

Difficult to apply a fixed dose

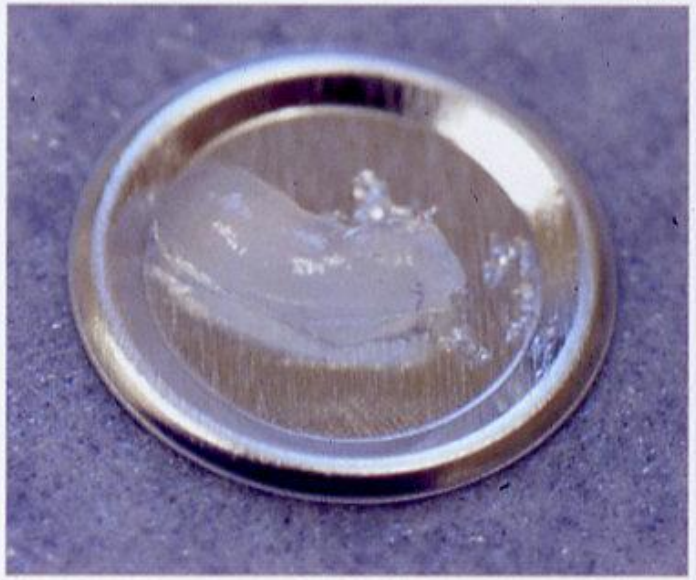
Intraindividual variation

	Weight (mg)*		
	Technician 1	Technician 2	Technician 3
Mean	16.2	28.7	20.5
95% Confidential interval for mean	15.4-17.1	27.5-29.9	19.6-21.4
Median	15.9	28.4	20.3
Standard deviation	2.94	4.28	3.06
Range	11.1-27.0	21.0-45.8	14.4-27.3
Coefficient of variation (%)	18.1	14.9	14.9

*Calculated by subtracting the weight of a loaded Finn chamber® with the average weight of the unloaded chambers, i.e. 54.2 g.

Bruze et al. Contact Dermatitis 2007: 56: 38-42

Dose

Test conc.	0.3%	0.5%
Applied amount		
	33 mg	20 mg
Dose	0.2 mg/cm^2	0.2 mg/cm^2

Results all 3 occasions

• 30 mg	0 neg, 36 pos,	21 major spreading
• 25 mg	0 neg, 36 pos,	15 major spreading
• 20 mg	1 neg, 35 pos,	9 major spreading
• 15 mg	3 neg, 33 pos,	8 major spreading
• 10 mg	12 neg, 24 pos,	4 major spreading

Bruze et al. Contact Dermatitis 2007: 56: 281-5

Does the dose matter?

Significance of patch test dose

+ or (+) patch test reaction on D 3/4 to fragrance mix, Myroxolon Pereira or methyldibromoglutaronitrile in 47 patients

Retest

Read on D 3/4 (”D7”)

Significance of patch test dose

Results

Previous	Present	10 mg	20 mg	40 mg
(+)	+	10%	15%	25%
+	+	14%	29%	56%

P=<0.05

Patch test results

Non-individual factors

Test technique
Test preparation
Application time
Application technique
Dose
Occlusion time
Reading times
Classification

Occlusion time

48h

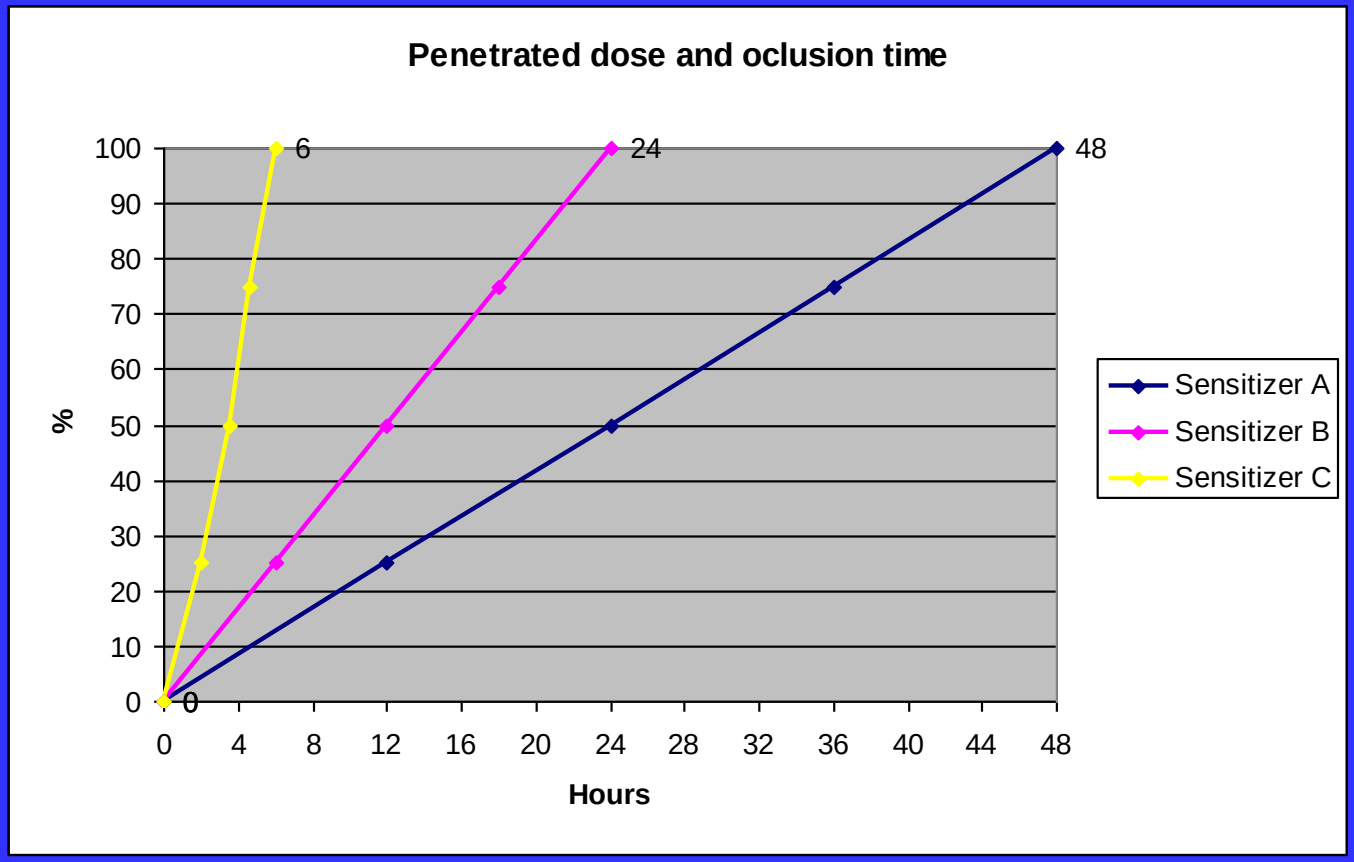
Number of molecules/ unit area skin

Test technique

Dose

Occlusion time

Penetrated dose and occlusion time



Number of molecules/ unit area skin

Nickel sulphate

5% and 48h occlusion = 30% and 5h occlusion

Bruze. Acta Derm Venereol 1988: 68: 361-364

Patch test results

Non-individual factors

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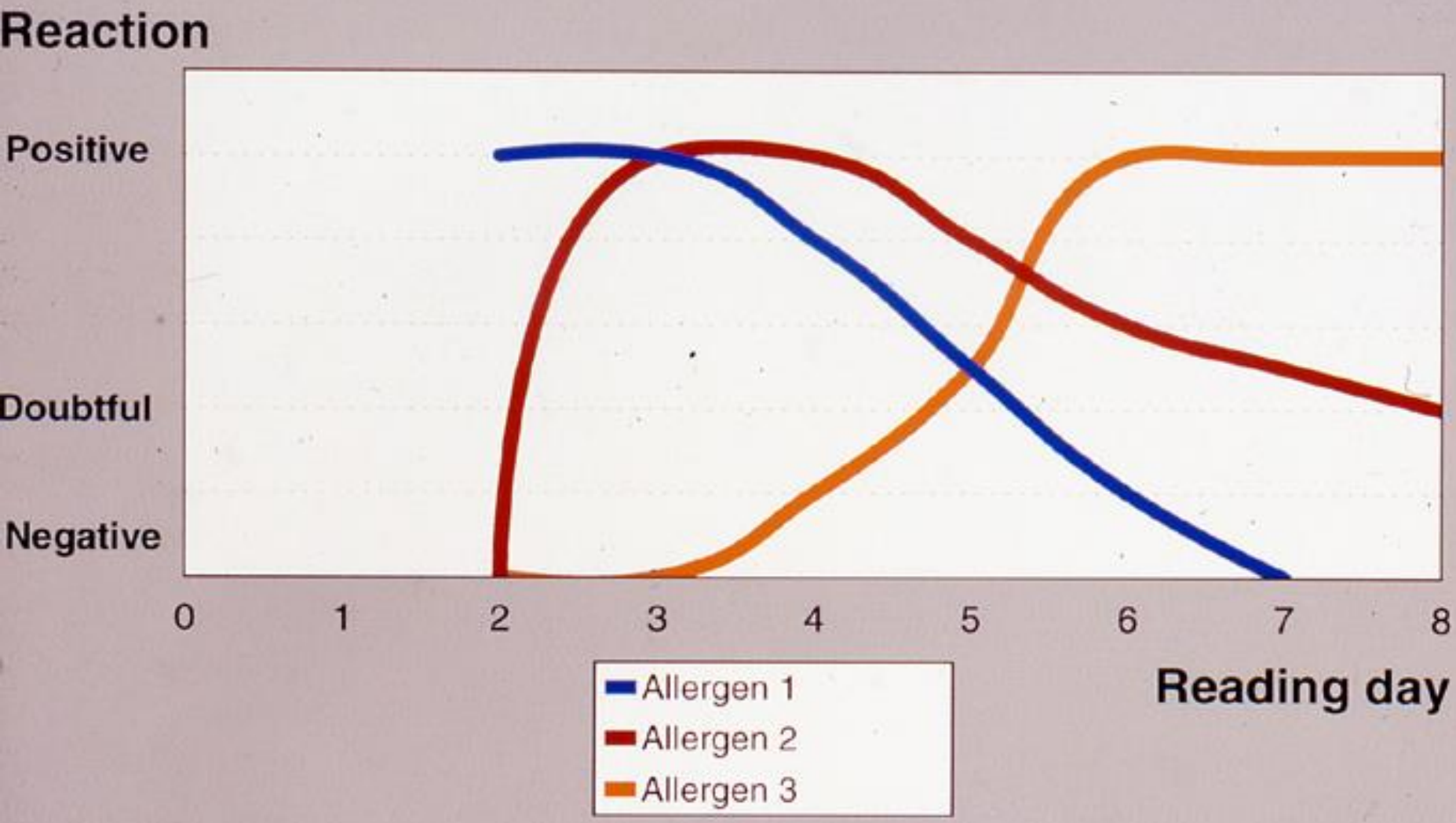
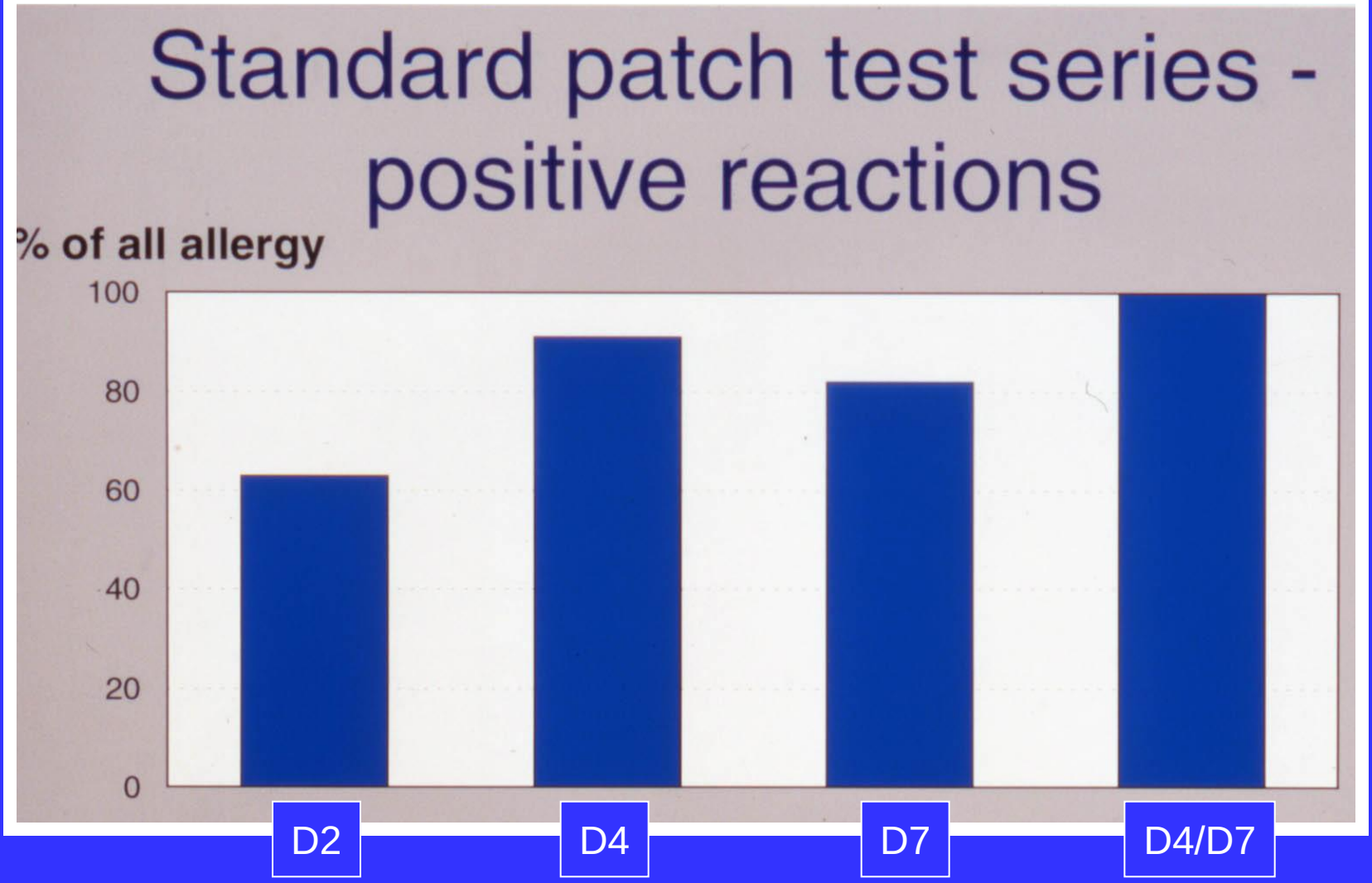
Reading times

	D2	D3/4	D7
Internationally	+	+	(+)
Sweden		+	+

Contact allergy - course





Macfarlane et al. Contact Dermatitis 1989: 20: 127-132

Patch test results

Non-individual factors

Test technique
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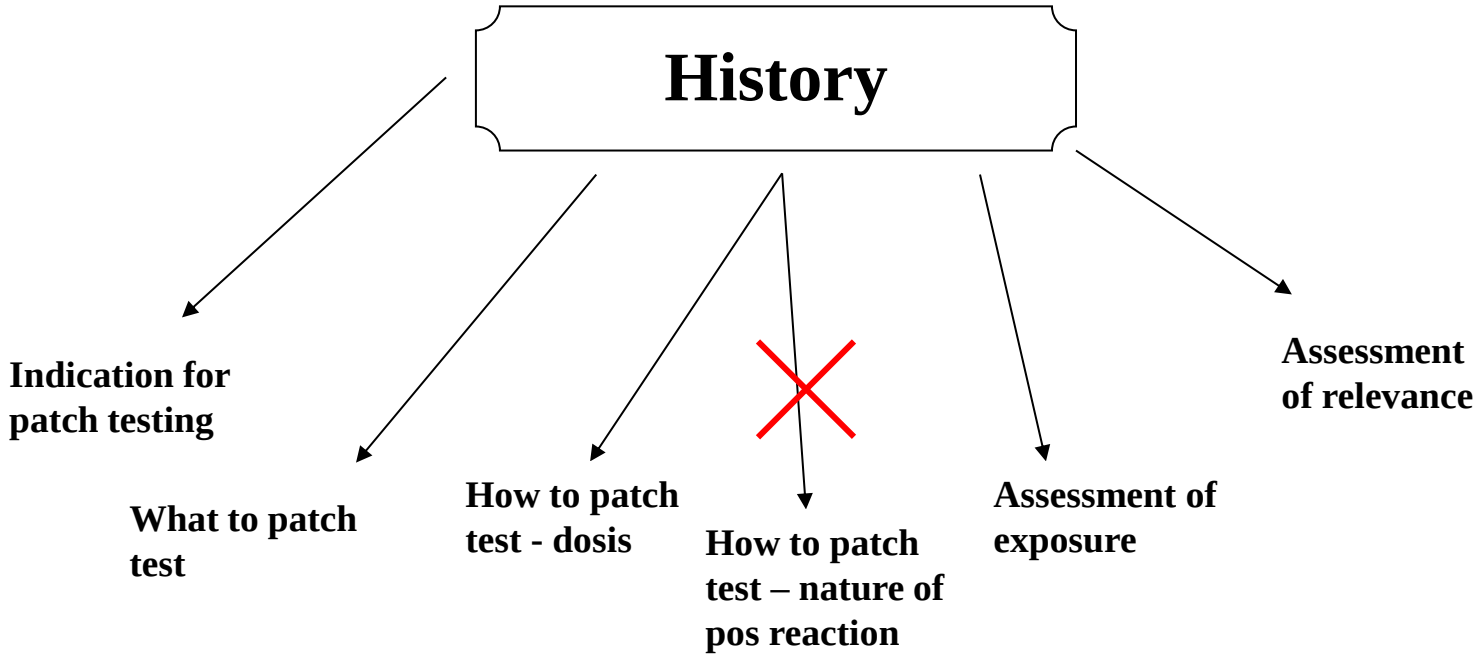
DBS 1% ALK
0.1% ALK
0.01% ALK
0.001 % ALK
0.0001 % ALK

Clinical impact of different thresholds for allergic reactions

Low thresholds	false-positive reactions increases
High thresholds	false-negative reaction increases

Use of history for diagnosis of contact allergy and allergic contact dermatitis



Doubtful reactions

Re-test

- Higher concentration
- Lower concentration
- Other vehicle

Intracutaneous test

New sensitizer?

True positive (allergic) – false positive (irritant)

Patch testing in controls

Positive reaction

Individual patient	20 controls
Group of patients	Fisher’s exact test