

The logo features a small, thick, magenta vertical bar positioned above the letter 'i' in the word 'VITAZ'. The word 'VITAZ' is rendered in a bold, black, sans-serif typeface.

VITAZ

STERK IN ZORG

Code rood of vals alarm: antibiotica-allergie

Symposium door antibiotherapiebeleidsgroep

The logo for GlaxoSmithKline (GSK) in orange.The logo for VITAZ, featuring a small pink vertical bar above the word "VITAZ" in black, with "STERK IN ZORG" in pink below it.The logo for Pfizer, featuring a blue stylized "P" icon followed by the word "Pfizer" in blue.

Overzicht Programma

1. Introductie

Dr. Pieter Goeminne | Longziekten en allergieën Vitaz

2. Antibiotica-allergie bij kinderen

Prof. dr. Van Gasse Athina | Kinderallergoloog ZAS

3. Antibiotica-allergie bij volwassenen

Prof. dr. Schrijvers Rik | Internist | Allergoloog UZ Leuven

4. Masterproefonderzoek: Bètalactam-allergie labeling en delabeling binnen Vitaz

Apr. Vanderper Vanessa | Antibioticabeleid & HOST Vitaz

5. Vragenronde & receptie

WAT DOET DE ANTIBIOTICABELEIDSGROEP?

1. Therapeutisch **formularium** van antimicrobiële geneesmiddelen.
2. **Aanbevelingen** voor empirische, etiologische en profylactische antimicrobiële behandelingen.
3. Initiatieven om **overmatig gebruik te beperken**.
4. **Opleiding** van (para)medisch personeel (diagnose, microbiologie, epidemiologie en behandeling)
5. Meten van de **implementatie** van formularium en aanbevelingen met feedback
6. Meten van **antibioticaverbruik** en **voorschriftprofielen** met feedback
7. Bewaken van antimicrobiële **resistentie** + feedback
8. Jaarlijks **activiteitenrapport** naar bapcoc

⇒ Iedere vrijdag: **MIMOSA** (Microbiologisch en Infectiologisch Multidisciplinair Overleg ter promotie van Strategisch Antibioticagebruik) : voor alle disciplines toegankelijk!

⇒ Mail casus: antibiotica@vitaz.be OF infectie@vitaz.be



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Immunologie
Allergologie - Reumatologie
Universiteit Antwerpen



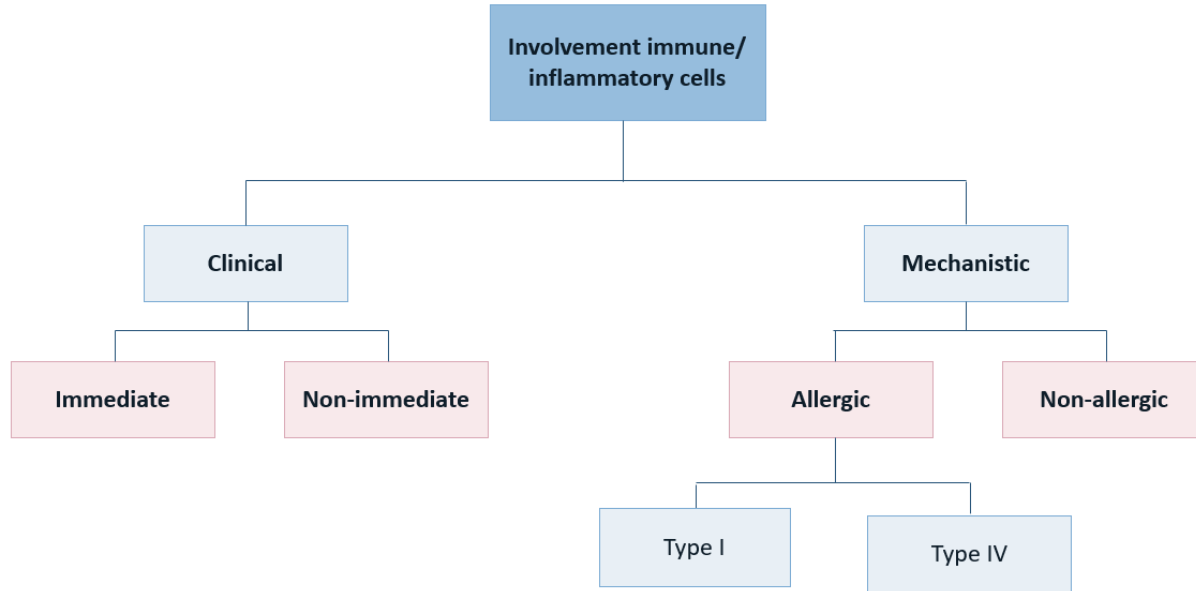
Antibiotica-allergie bij kinderen: focus op penicilline

Dr. Athina Van Gasse

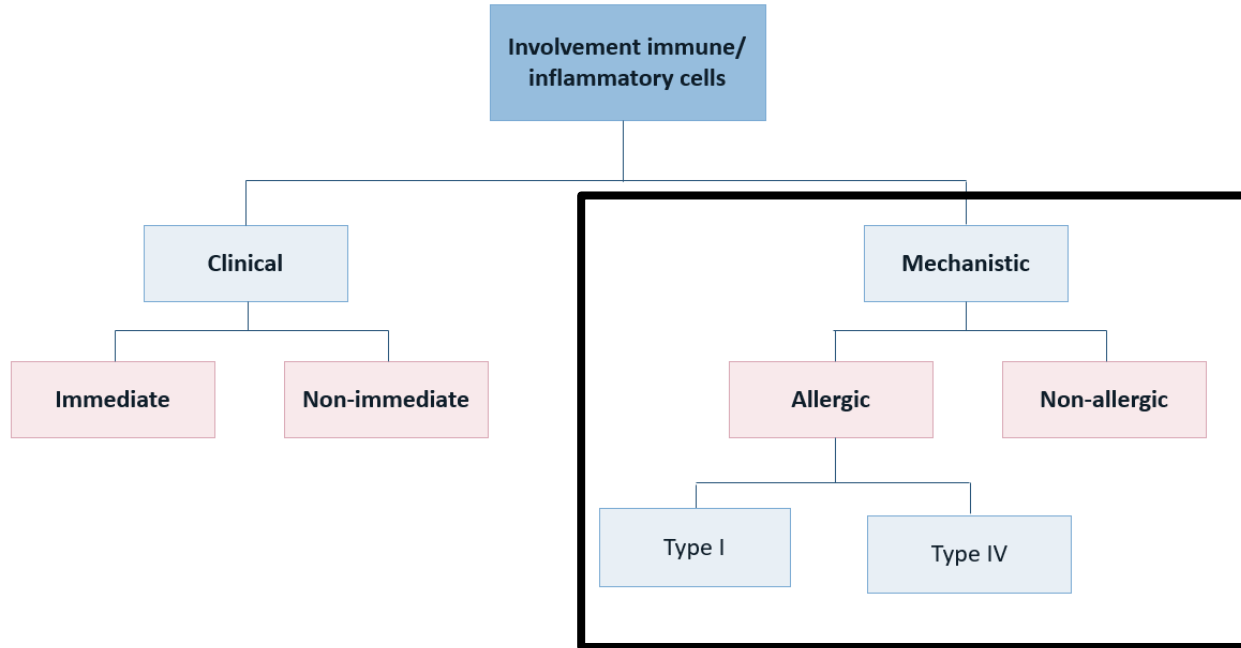
Adverse drug reactions

- = unintended, harmful effects resulting from exposure to a compound for diagnostic, prophylactic, or therapeutic purposes
- Pharmacological properties <-> hypersensitivity

Drug hypersensitivity reactions (DHR)



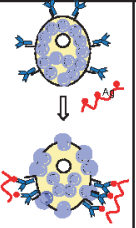
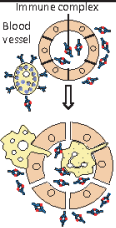
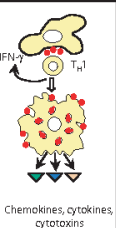
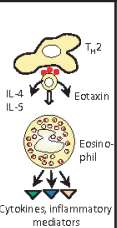
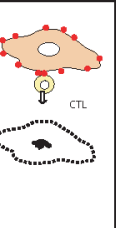
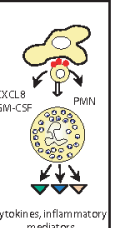
Drug hypersensitivity reactions (DHR)



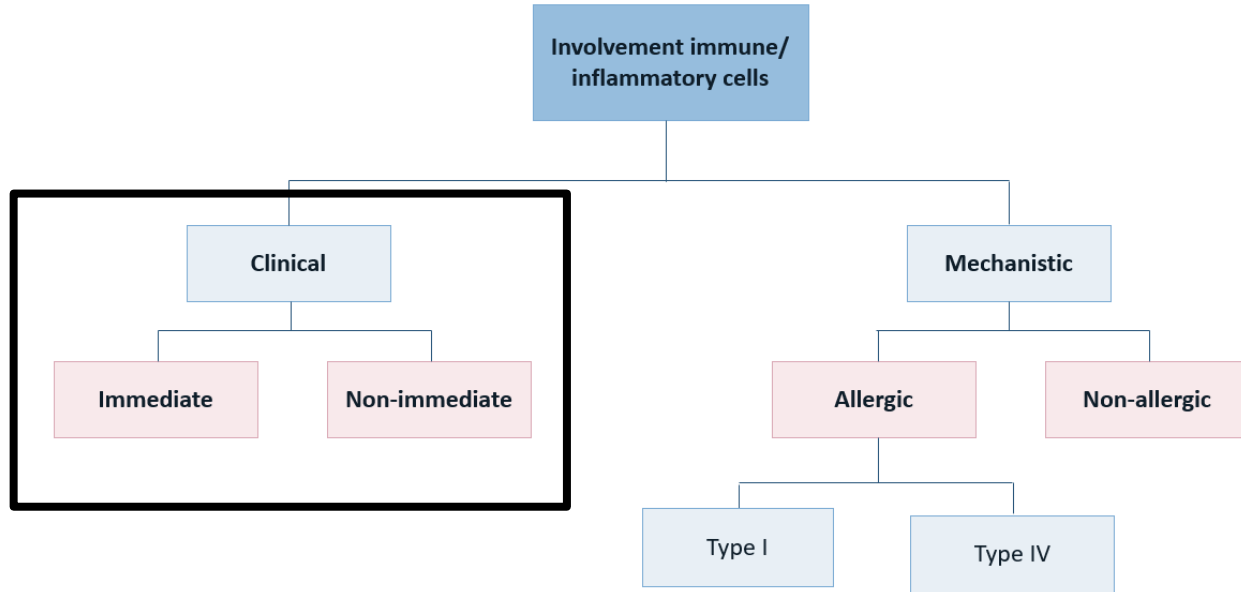
Drug hy

Antibody (I–III) and T-cell orchestrated hypersensitivity reactions (IV a–d)

DHR)

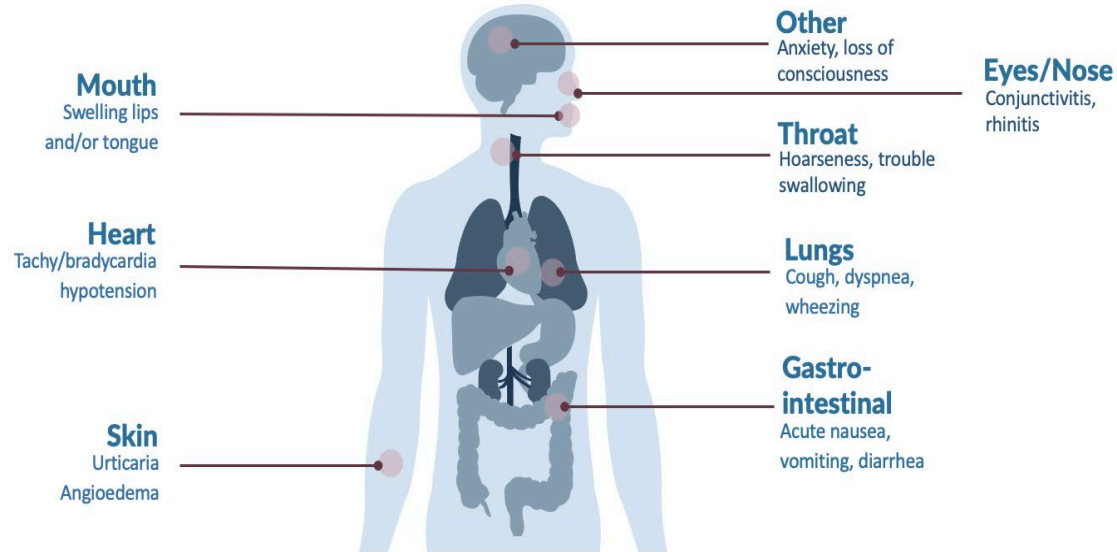
	Type I	Type II	Type III	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	IgE	IgG	IgG	IFN- γ , TNF- α (T _H 1 cells)	IL-5, IL-4/IL-13 (T _H 2 cells)	Perforin/granzyme B (CTL)	CXCL8, GM-CSF (T cells)
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Soluble antigen	Antigen presented by cells or direct T-cell stimulation	Antigen presented by cells or direct T-cell stimulation	Cell-associated antigen or direct T-cell stimulation	Soluble antigen presented by cells or direct T-cell stimulation
Effector	Mast cell activation	FcR+ cells (phagocytes, NK cells)	FcR+ cells Complement	Macrophage activation	Eosinophils	T cells	Neutrophils
							
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis	Hemolytic anemia, thrombocytopenia (e.g., penicillin)	Serum sickness, Arthus reaction	Tuberculin reaction, contact dermatitis (with IVc)	Chronic asthma, chronic allergic rhinitis, Maculopapular exanthema with eosinophilia	Contact dermatitis, Maculopapular and bullous exanthema, Hepatitis	AGEP, Behçet's disease

Drug hypersensitivity reactions (DHR)



Immediate DHR

- Immediate = <1h



Cave anaphylaxis !!

Immediate DHR

- Urticaria



Urticaria: The 1-1-1 Criterion for Optimized Risk Stratification in β -Lactam Allergy Delabeling



Vito Sabato, MD, PhD^{a,b,c,*}, Francesco Gaeta, MD, PhD^{d,*}, Rocco Luigi Valluzzi, MD^e, Athina Van Gasse, MD, PhD^a, Didier Gaston Ebo, MD, PhD^{a,b,c}, and Antonino Romano, MD^f *Ghent and Antwerpen, Belgium; and Rome and Troina, Italy*

Imme

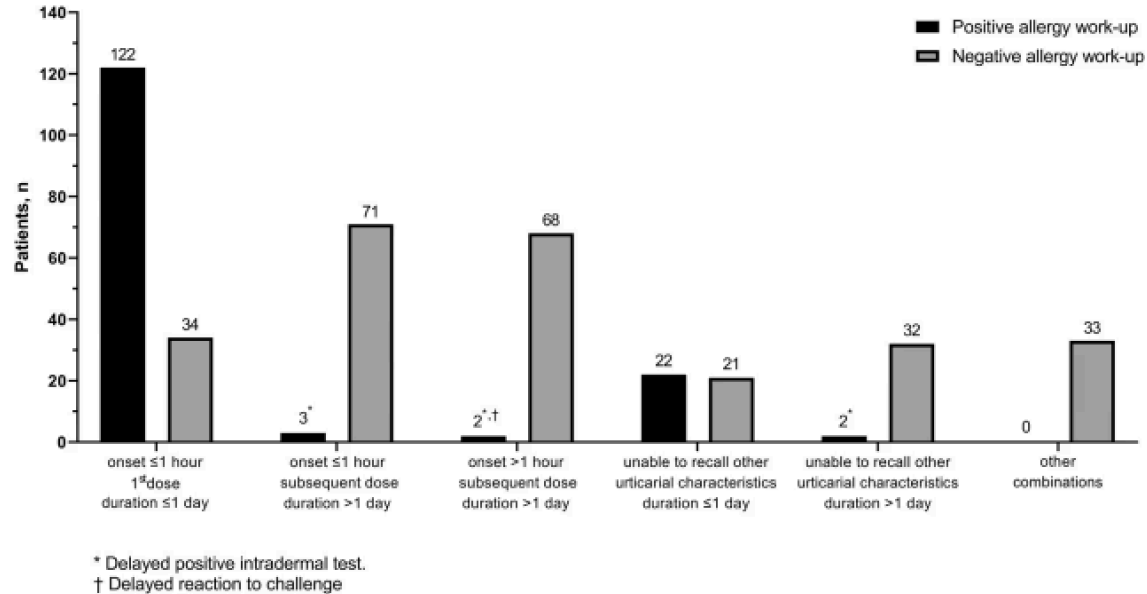


FIGURE 3. Characteristics of urticarial eruptions in patients with positive (n = 151) and negative (n = 259) allergy workup. Twenty-two patients refused the drug challenge. Multivariable analysis showed that the 1-1-1 criterion has sensitivity, specificity, negative predictive value, and positive predictive value of 85%, 85%, 80%, and 90%, respectively.

Nonimmediate DHR

- Nonimmediate = >1h

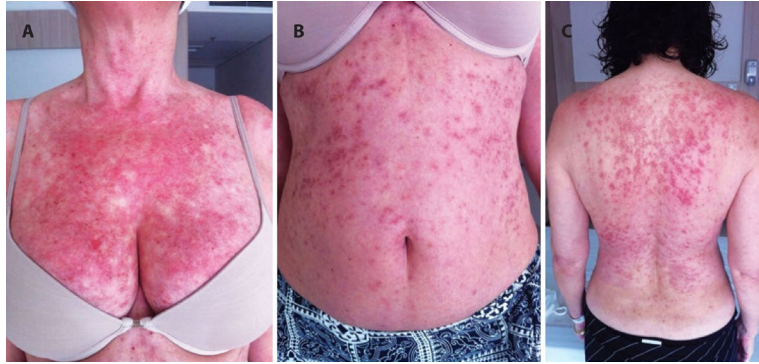


Maculopapular exanthema (MPE)

Nonimmediate DHR



AGEP
(Acute gegeneraliseerde
exanthemateuze pustulose)



DRESS
(Drug rash with eosinophilia and systemic symptoms)

SCAR



SJS-TEN
(Steven-Johnson Syndrome
Toxische Epidermale Necrolyse)

Nonimmediate DHR

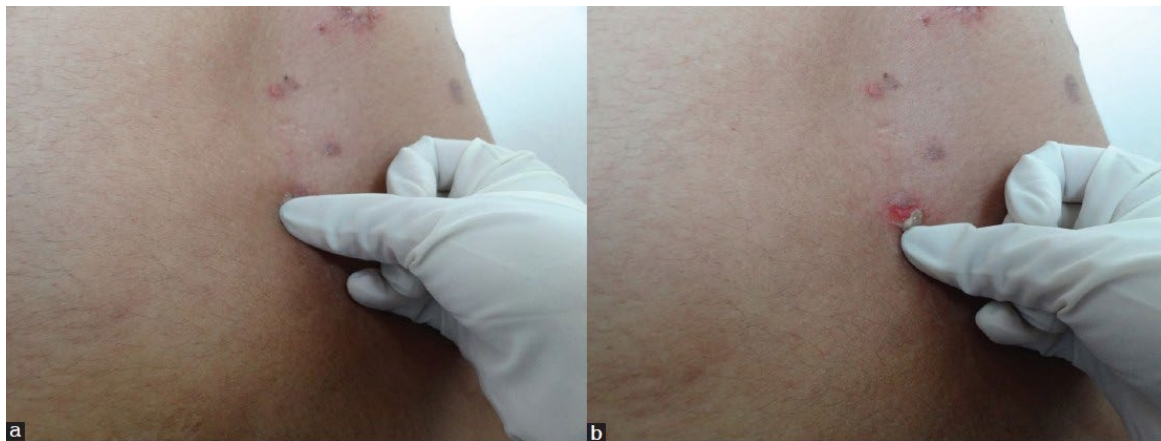
- Danger signs

Nonimmediate reactions

- Intense facial involvement
- Atypical target lesions
- Bullous lesions
- Widespread dark-red erythema
- Extensive pustulosis
- Painful skin
- Mucosal involvement
- Generalized lymphadenopathy
- Elevated liver enzymes
- Impaired renal function tests
- Fever > 38.5°C
- Alterations in blood cell counts (i.e., anemia, granulocytopenia, thrombocytopenia, neutrophilia, eosinophilia)
- Hypocomplementemia
- Hepatitis, nephritis, pneumonitis

Nonimmediate DHR

- Nikolsky's sign



Diagnosis of DHR

- Misdiagnosis = problem
 - Underdiagnosis = risk for life-threatening re-exposure
 - Overdiagnosis = epidemic of 'false allergies' (penicillin!!)
 - Label of penicillin allergy: 8-10% general population; 15-20% hospitalized patients
 - Label of penicillin allergy in children: 5-10%

Penicillin is the **most** commonly reported drug allergy?

YET...



9 out of 10 patients are **not** truly allergic

Diagnosis of DHR

> [Allergy](#). 2020 Aug;75(8):2111-2115. doi: 10.1111/all.14292. Epub 2020 Apr 24.

Prevalence of self-reported and confirmed penicillin allergy in a Belgian outpatient population

Athina L Van Gasse^{1 2}, Redouane Oulkadi¹, Zakaria Mousati¹, Didier G Ebo¹,
Anca M Chiriac^{3 4}, Marie-Line M Van Der Poorten^{1 2}, Margo M Hagendorens^{1 2},
Margaretha A Faber¹, Jessy Elst¹, Christel M Mertens¹, Leander De Puyseleir¹,
Samuel Coenen⁵, Vito Sabato¹

Affiliations + expand

PMID: 32243598 DOI: [10.1111/all.14292](#)

Diag

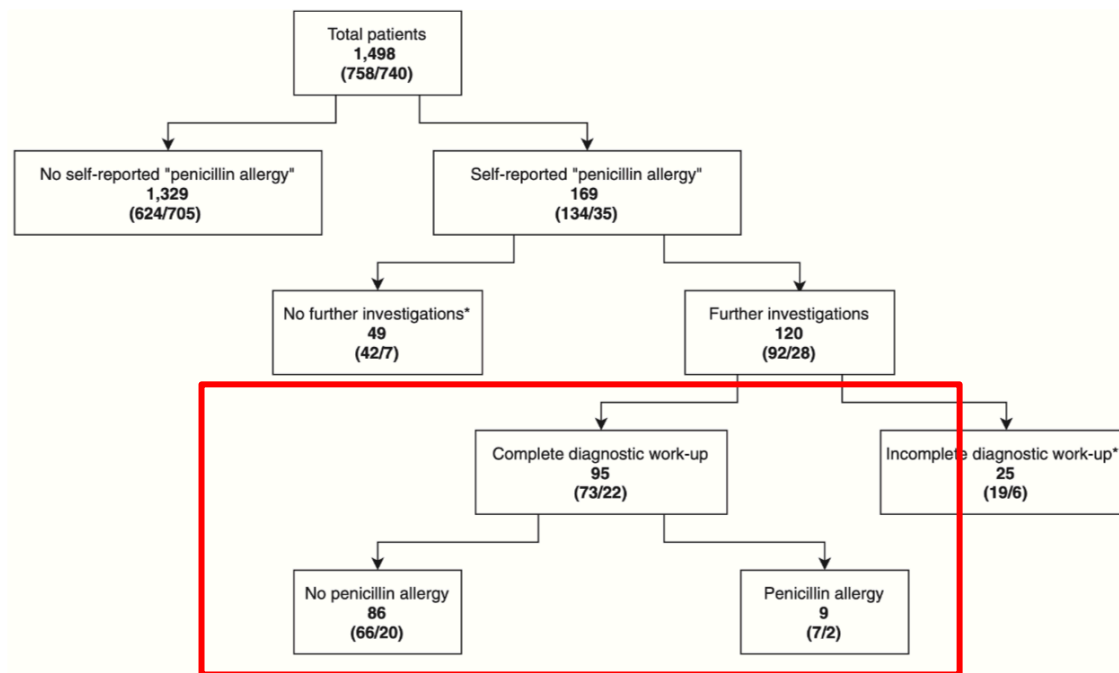


FIGURE 1 This flowchart gives an overview of the study population. The information in brackets displays the number of adults/children. *No further investigations were planned because either the patient considered the "penicillin allergy" to lack sufficient priority (n = 45) or the allergist decided, based on a thorough history, that the index reaction was not compatible with a DHR (n = 4). **Investigations had to be postponed for various reasons (eg, pregnancy and intake of antihistamines). In 2 out of these 25 participants, the DC resulted in only subjective symptoms (itch, epigastric pain, shortness of breath). As both were unwilling to repeat the DC, they were included in the group of the patients with incomplete diagnostic work-up.

Diagnosis of DHR

- Misdiagnosis = problem
 - Underdiagnosis = risk for life-threatening re-exposure
 - Overdiagnosis = epidemic of 'false allergies' (penicillin!!)
 - Inferior antibiotics, longer hospital stays, societal costs, microbial resistance , ...
 - Often starts at childhood -> adulthood
 - Referral!!

Diagnosis of drug hypersensitivity

SIGNS & SYMPTOMS

Immediate drug hypersensitivity

Tryptase

Skin testing immediate readings
(15 min)

sIgE antibody quantification

Basophil activation test
Mast cell activation test

Drug challenge

Non-immediate drug hypersensitivity

Patch test
Skin testing delayed readings
(48-72h)

Lymphocyte transformation
test

Drug challenge

Diagnosis of DHR

- KEY MESSAGE = CORRECT DESCRIPTION



“RASH”



Diagnosis of DHR

- KEY MESSAGE = CORRECT DESCRIPTION



Diagnosis of DHR

- History
 - Index drug (s)
 - Signs (pictures!), symptoms
 - Timing
 - Treatment
 - Indication for the drug/type of infection
 - cave EBV + amoxi does not exclude amoxi allergy!!
 - Other medication used
 - ...

Diagnosis of drug hypersensitivity

SIGNS & SYMPTOMS

Immediate drug hypersensitivity

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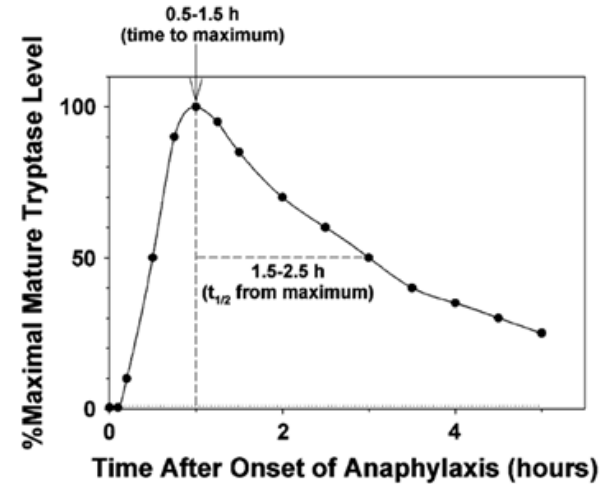
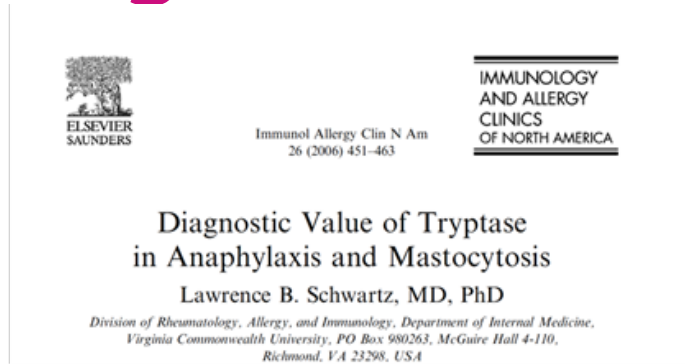
Non-immediate drug hypersensitivity

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(48-72h)

Lymphocyte transformation
test

Drug challenge

Diagnosis of DHR



Mast cell activation = acute tryptase > 1.2 (baseline tryptase) + 2

Diagnosis of

SIGNS & SYMPTOMS

Immediate drug hypersensitivity

Tryptase

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(15 min)

sIgE antibody quantification

Basophil activation test
Lymphocyte transformation
test

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test

Drug challenge

Diagnosis of DHR

Skin prick test



Intradermal test



Diagnosis of ALLERGY

SIGNS & SYMPTOMS

Immediate drug hypersensitivity

Tryptase

Skin testing immediate readings
(15 min)

sIgE antibody quantification

Basophil activation test
Lymphocyte transformation
test

Drug challenge

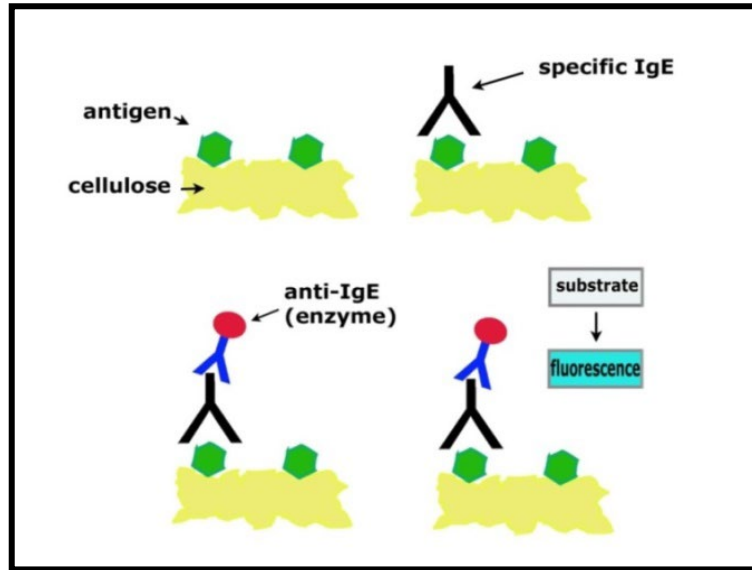
Non-immediate drug hypersensitivity

Patch test
Skin testing delayed readings
(48-72h)

Lymphocyte transformation
test

Drug challenge

Diagnosis of DHR



- Problems

- Sensitivity and specificity vary significantly
- Aspecific binding to solid phase (high total IgE)
 - $\text{Ratio sIgE/total IgE} \geq 0,002^* = \text{positive}$
- Negative over time (while still allergic!)

Diagnosis of

SIGNS & SYMPTOMS

Immediate drug hypersensitivity

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Diagnosis of DHR



Contraindications

- Anaphylaxis

Diagnosis of

SIGNS & SYMPTOMS

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Non-immediate drug hypersensitivity

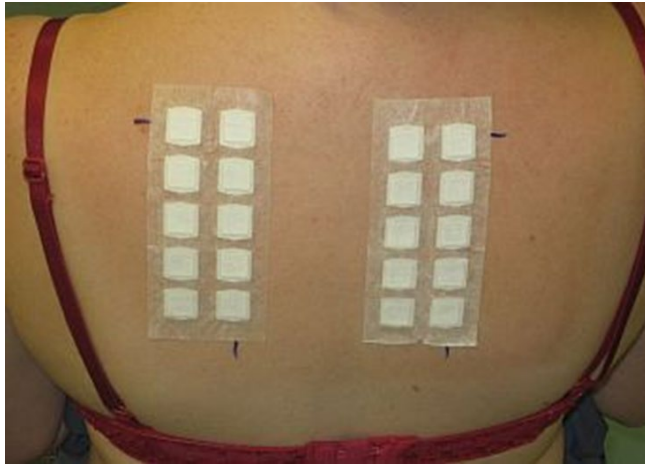
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Drug challenge

Diagnosis of DHR

Patch test



Intradermal test



Diagnosis of drug hypersensitivity

SIGNS & SYMPTOMS

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test

Drug challenge

Diagnosis of DHR



Contraindications

- SCAR
- Hematologic reactions e.g. vasculitis

Prolonged challenges extending over several consecutive days = **limited use** *

Diagnosis of DHR

Can we perform direct challenges in low risk patients?

Diagnosis of DHR

Can we perform direct challenges in **low risk patients?**

Authors	Definition of uncomplicated exanthema/benign rash	N	Age Median (range)	Protocol	Outcome
Caubet et al, JACI 2011	Small erythematous maculae/papulae >24 hours, also disseminated over different parts of the body Mean appearance after the last dose 4.9 days; mean duration 3.8 days	41 Total 88	Children 3.5 y (0.5-14.5)	Viral tests ENDA protocol Challenge: single 150% if ST negative, 50-150% if ST positive (immediate retests)	Patch test and delayed readings negative in all patients; including 6 OCT positive Immediate readings positive in MPE SS 50%, SP 86.7%
Vyles et al, Pediatrics 2017	Non-hive rash (73%) Hive rash (13%) Itching (63%) No bullous, no diffuse erythema No info about spreading and resolution time	100	Children Testing: 9y (5-12) Event: 1y (0.75-3)	SPT en IDT BPO-PLL and PCN-G (immediate reading) 3 positive in medical record; 0 positive before the challenge Single dose graded challenge (500/520 mg AX)	None positive
Confino-Cohen et al, JAIP 2017	NIDHR Rash, itching, 31% no recollection No SCAR Time between last dose and symptoms unknown in 55% No info about spreading and resolution time	642	Children and adults 8y (0.1-83) 435 children	SPT and IDT PPL, MD, PCN G and culprit BL Immediate readings, 34 positive 5 consecutive days (1st dose fractioned in clinic)	IDHR 9 (1 pos ST) NIDHR 54 (1 pos ST) 29 ST pos, challenge negative No severe reaction

Authors	Definition of uncomplicated exanthema/benign rash	N	Age Median (range)	Protocol	Outcome
Ibanez et al ANAI, 2018	Exanthema without systemic symptoms or signs No info about spreading Info about duration and treatment	411 Total 732	Children 5.5 y (SD 3.87)	ST and DPT according to ENDA guidelines	30/33 positive challenge, skin test negative. Symptoms mainly non-immediate 12 false positive ST Duration >3 day and steroid use associated with positive challenge
Vezir et al PAI, 2016	MPE, without systemic symptoms and signs Median onset: 2nd day, 6 hr from last dose No info about spreading and resolution time	74 (Total 119)	Children 4.3 y (2-7.5)	No ST Most of the case Aminopenicillins 5 consecutive days (1st dose fractioned in clinic)	4 positive challenge (urticaria)
Kuruvilla et al, AAP 2019	Benign delayed rash No info about spreading and onset and resolution time	20 In total 50 patients	Adults 59y (18-81)	No ST Single dose 500 mg	3 subjective symptoms considered negative challenges

Authors	Definition of uncomplicated exanthema/benign rash	N	Age Median (range)	Protocol	Outcome
Iammatteo, JAIP 2018	Urticaria, rash, unknown reaction as child No other info	155	Children and adults >7 y 51.8 y	Direct challenge placebo controlled Single fractioned, max 500 mg	16 placebo reactions 19 challenge reactions, 15 judged «non-allergic» 4 judged «allergic»
Mill, JAMA pediatrics 2016	Definition of NIDHR: skin rash, > 1 hr, arthritis and arthralgia Mild: limited to the oral mucosa or the skin; severe cardiovascular or respiratory symptoms or of any 4 systems; and all other moderate SJS and TEN excluded Different rash duration	818	Children 1.7 y (1.0-3.9)	Graded challenge single dose (max 1.5g) ST BPO-PLL immediate readings Retrospective and prospectiva arm	31 non immediate reactions
Mustafa, JAIP 2019	Skin rash without fever, blistering, involvement of mucous membrane) Cutaneous-only or unknown (>1 year ago) 5-17 years, >10 years ago for those 18 years or older) No info about time onset or duration	159 Total 363	Children and adults 35y (1-90)	Randomized study: ST->2step single dose challenge vs 2step single dose challenge (400 mg) ST: BPO-PLL, PCN G. Immediate readings	ST negative in 70 of 80 (87.5%) patients. All 70 patients had a negative challenge. Direct challenge was negative in 76 of 79 (96.2%) patients .

Study (First Author, Year)	Children (n)	Positive Challenge (%)	Severe Reactions	Low-Risk Definition Used	Direct Challenge Protocol
Chow, 2025	95	5%	None	Not specified in available data	Not specified in available data
Blumenthal, 2024	9225	3.5%	5 (0.05%)	Mild, non-immediate reactions (e.g., benign rash, GI symptoms); excludes anaphylaxis, severe cutaneous, or organ involvement	Protocols varied: single or multiple doses, observation 1–2 hours, some with extended home dosing
Krusenstjerna-Hafstrøm, 2020	141	2.8%	None	Rash-only history, no anaphylaxis or severe symptoms	Not specified in available data
Rathkopf, 2021	54	0%	None	Nonspecific rash or urticaria; excludes severe symptoms (respiratory distress, angioedema, mucosal involvement, etc.)	Single oral amoxicillin dose (20 mg/kg, max 500 mg), 60 min observation
Atakul, 2022	72	4.2%	None	Not specified in available data	3-day challenge: two divided doses on day 1, then home dosing for 3 days, 4-hour initial observation
Petersen, 2020	305	7%	None	Not specified in available data	Two-step titrated DPT: initial dose in clinic, then 5-day home challenge; some reactions after 2nd dose or days 3–6

Study (First Author, Year)	Children (n)	Positive Challenge (%)	Severe Reactions	Low-Risk Definition Used	Direct Challenge Protocol
Gervais, 2025	100	2%	1 anaphylaxis	Judged low risk for anaphylaxis by clinician; details not fully specified	Not specified in available data
Pachasidchai, 2023	154	1.9%	None	Not specified in available data	Day 1: two divided doses (10% then 90% of therapeutic dose, 30 min apart), then home dosing twice daily for 5 days, phone follow-up
Patel, 2022	12	0% (1 late rash)	None	Not specified in available data	Two-step amoxicillin challenge (total 250 mg), 60 min observation, phone follow-up at 7–10 days
Searns, 2020	47	2%	None	Used a risk assessment tool: low risk = no increased risk, mild symptoms only	Single, non-graded amoxicillin dose (45 mg/kg, max 1000 mg), 60 min observation
Kelso, 2022	64	0% (3 late rashes)	None	Side effects, family history, remote (>5 years) history without IgE features, or unknown reaction not requiring hospitalization; excludes anaphylaxis, urticaria within 2 hours, angioedema, severe cutaneous/systemic reactions	Single oral amoxicillin dose (age/weight-based), 2-hour observation

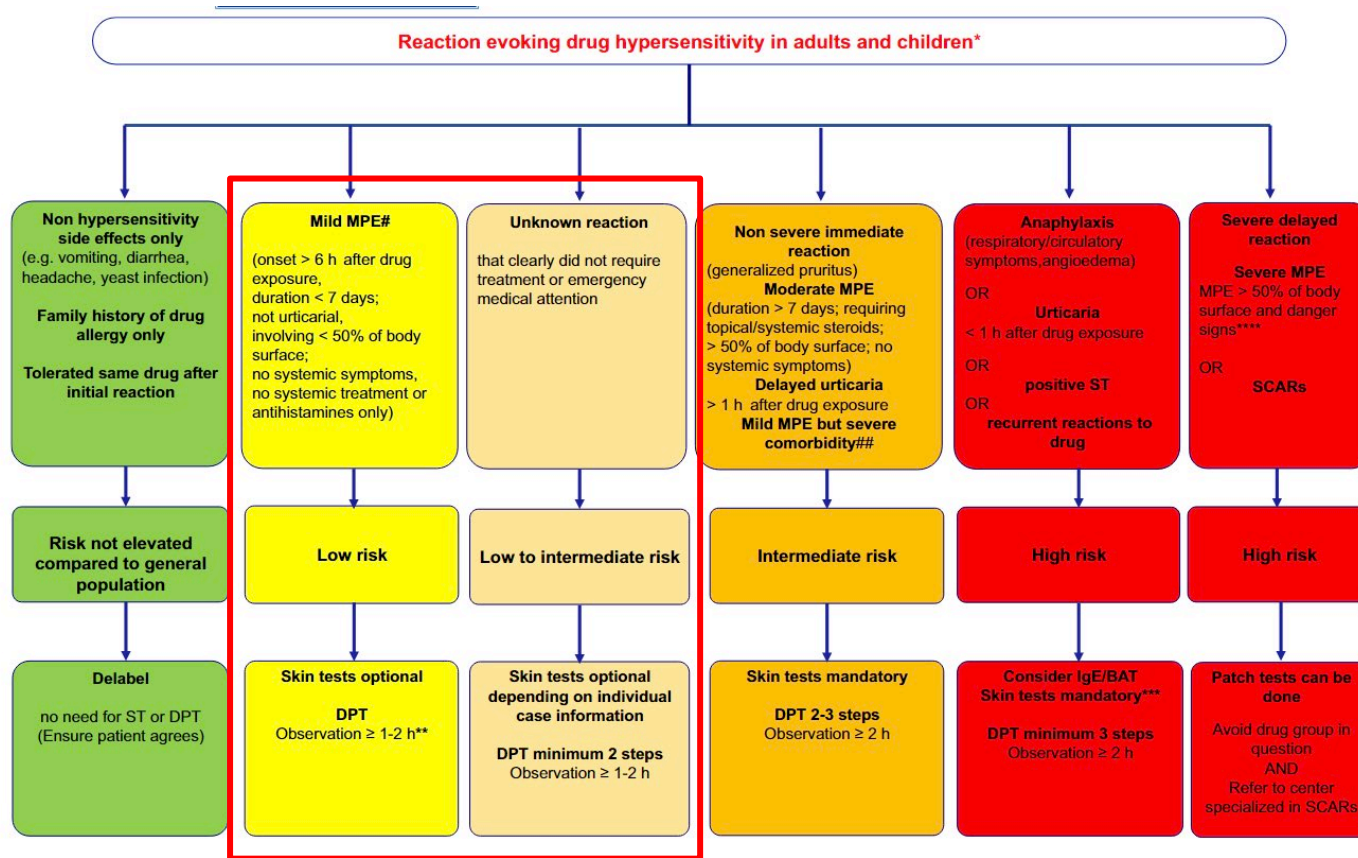
Diagnosis of DHR

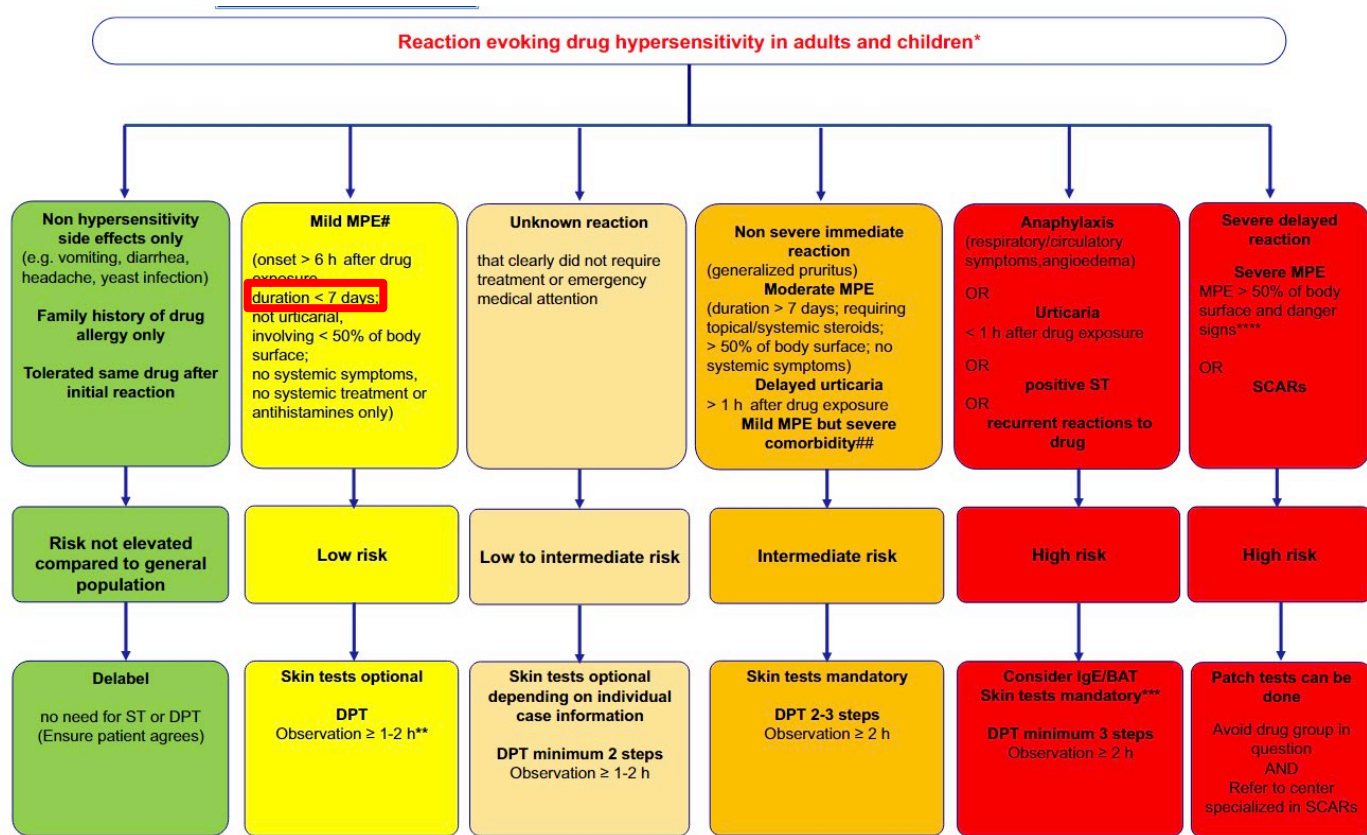
- Penfast

PEN	Penicillin allergy reported by patient	☐ If yes, proceed with assessment										
F	Five years or less since reaction ^a	☐ 2 points										
A	Anaphylaxis or angioedema	☐ 2 points										
	OR											
S	Severe cutaneous adverse reaction ^b											
T	Treatment required for reaction ^a	☐ 1 point										
		☐ Total points										
Interpretation												
<table border="1"> <thead> <tr> <th>Points</th> <th></th> </tr> </thead> <tbody> <tr> <td>☐ 0</td> <td>Very low risk of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)</td> </tr> <tr> <td>☐ 1-2</td> <td>Low risk of positive penicillin allergy test 5% (1 in 20 patients)</td> </tr> <tr> <td>☐ 3</td> <td>Moderate risk of positive penicillin allergy test 20% (1 in 5 patients)</td> </tr> <tr> <td>☐ 4-5</td> <td>High risk of positive penicillin allergy test 50% (1 in 2 patients)</td> </tr> </tbody> </table>			Points		☐ 0	Very low risk of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)	☐ 1-2	Low risk of positive penicillin allergy test 5% (1 in 20 patients)	☐ 3	Moderate risk of positive penicillin allergy test 20% (1 in 5 patients)	☐ 4-5	High risk of positive penicillin allergy test 50% (1 in 2 patients)
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Diagnosis of DHR

- **Penfast** in children: Copaescu et al studie
 - Cohort: 2,028 children (median age 4.3 y) referred for suspected penicillin allergy
 - Prevalence of confirmed allergy = 5%
 - AUC = 0,528 – almost no better dan chance
 - Cut off ≥ 3 (as in adults):
 - Sensitivity: ~57%
 - Specificity: ~46%
 - Negative predictive value (NPV): ~95%
 - Positive predictive value (PPV): low (~6%)
 - Interpretation: Almost all children with a low score were indeed not allergic, but the model could hardly distinguish between allergic vs. non-allergic.





Diagnosis of DHR

Progressively Simplified Testing in the Evaluation of Nonimmediate Reactions to Penicillins



Antonino Romano, MD^{a,b,*}, Rocco Luigi Valluzzi, MD^{c,*}, Francesco Gaeta, MD, PhD^{d,*}, Cristiano Caruso, MD, PhD^e, Alessandra Zaffiro, MD^f, Donato Quaratino, MD^f, Alessandro Toscano, MD^g, Athina Van Gasse, MD, PhD^g, Didier G. Ebo, MD, PhD^g, and Vito Sabato, MD, PhD^g *Troina, Rome, and Sondrio, Italy; and Antwerp, Belgium*

What is already known about this topic? Morbilliform drug eruptions (MDEs) and delayed-appearing urticaria are the most frequently reported nonimmediate reactions to penicillins. Direct challenges have been proposed for adults reporting distant MDEs lasting fewer than 7 days or isolated urticaria.

What does this article add to our knowledge? Results of delayed-reading intradermal tests with the responsible penicillins were positive in almost 70% of adults, with well-characterized MDEs lasting more than 4 days, whereas they were negative in all those reporting urticarial and/or angioedematous reactions lasting more than 1 day.

How does this study impact current management guidelines? Delayed-reading intradermal tests are particularly useful in patients with well-characterized MDEs lasting more than 4 days. Direct challenges are advisable in patients reporting nonimmediate urticarial and/or angioedematous reactions lasting more than 1 day or other cutaneous reactions lasting 4 or fewer days, even well-characterized MDEs.

Diagnosis of DHR

- Direct challenges
 - Good option in low risk children
 - Delabelling initiatives
- Unmet needs
 - Unanimous definition of uncomplicated/mild exanthema
 - Optimal and standardized protocols for challenges

Child, 2d after treatment with m



Diarrhea



Maculopapular exanthema



Urticaria

Child, 2d after treatment with m



Diarrhea



Maculopapular exanthema



Urticaria

Take home message

“post hoc est not propter hoc”

- History = crucial
- ABC of correct referral – as soon as possible!

A -> drug(s)

B -> timing

C -> signs and symptoms (+photos)

- Direct challenge in *low risk* patients
- Delabelling + avoidance of false labels



Overzicht Programma

1. Introductie

Dr. Pieter Goeminne | Longziekten en allergieën Vitaz

2. Antibiotica-allergie bij kinderen

Prof. dr. Van Gasse Athina | Kinderallergoloog ZAS

3. Antibiotica-allergie bij volwassenen

Prof. dr. Schrijvers Rik | Internist | Allergoloog UZ Leuven

4. Masterproefonderzoek: Bètalactam-allergie labeling en delabeling binnen Vitaz

Apr. Vanderper Vanessa | Antibioticabeleid & HOST Vitaz

5. Vragenronde & receptie



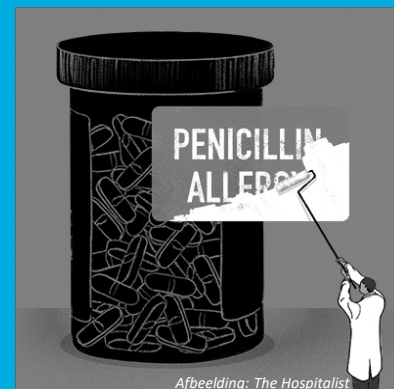
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LEUVEN



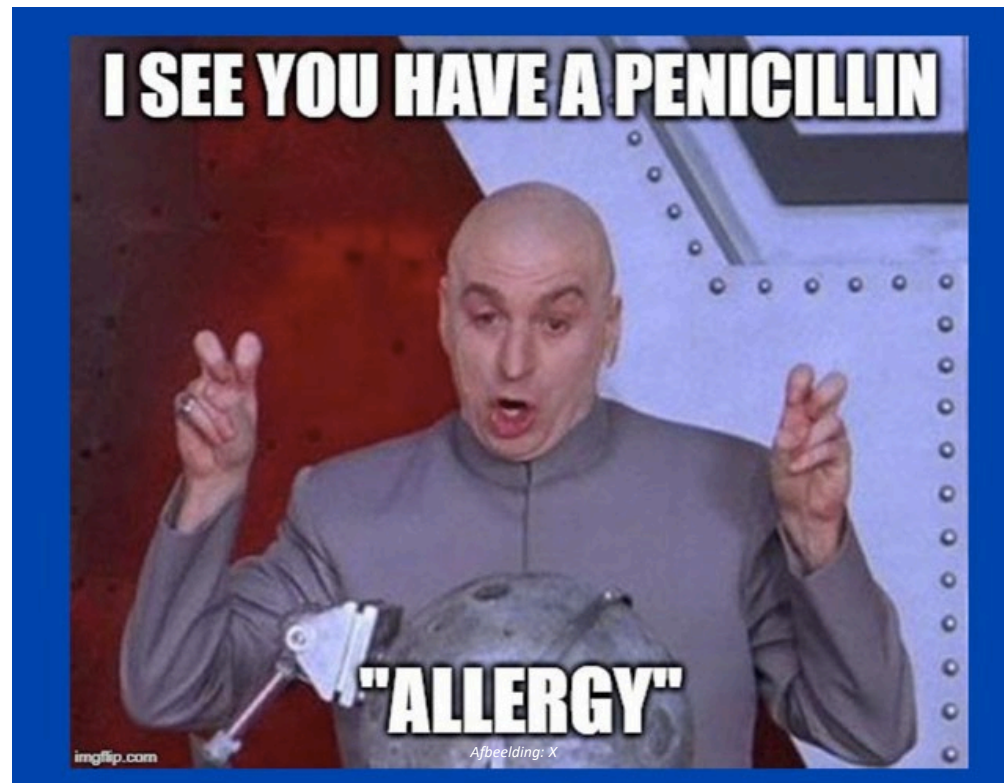
Antibiotica allergie labeling en delabeling

Rik Schrijvers MD PhD

General internal medicine, allergy and clinical immunology, UZ Leuven
Allergy and Clinical Immunology research group, KU Leuven



18 September 2025



Drug allergy prototypes and allergy workup

Type I (IgE-mediated)



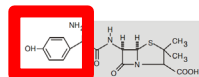
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High-risk cases:
diagnostic
confirmation and
label refinement

RULE

Skin testing:

- allergy for **chain in amoxicillin**
- negative for flucloxacillin, piperacillin



Challenge test:

- tolerance for flucloxacillin (and all non-RI-containing betalactams)

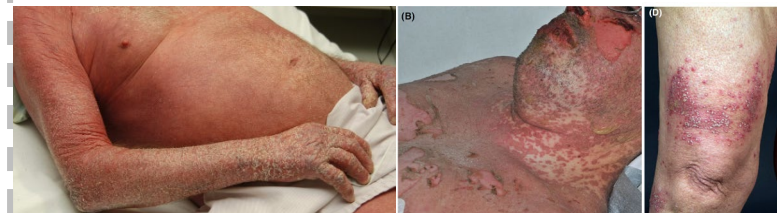
Type IV (T-cell-mediated)

- I-I-I rule does not apply
- Usually mild (maculopapulous exanthema)



Low-risk cases:
safe delabeling

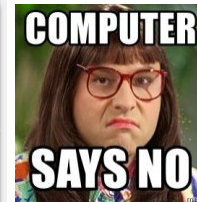
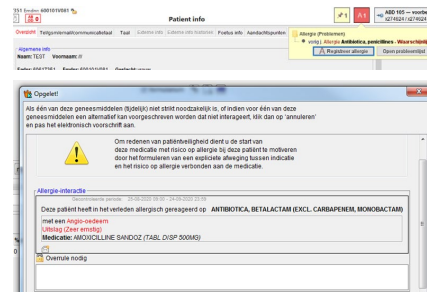
- Rare, severe manifestations (SCARs: DRESS, AGEP, SJS/TEN)



Antibiotic allergy labels

Case

- F58, admission because of backpain, fever
- CRP 250
- CT negative
- Blood cultures: MSSA
- Penicillin allergy label



- Vancomycine of flucloxacilline or cefazoline?

Antibiotic allergy *label* prevalence

- **7% of hospitalized** patients has ‘an’ antibiotic allergy label
- **5% for penicillines** (class), representing 75% of all antibiotic allergy labels
- “**Anaphylaxis or SCAR**” in **5%**, angio-oedema in **12%**, **rash** in **54%**, **various** in **22%**

Prevalence of Antibiotic Allergy Labels in a Tertiary Referral Center in Belgium

Liesbeth Gilissen, MPharm^{a,b}, Isabel Spriet, PharmD, PhD^{c,d}, Karin Gilis, BSc^e, Willy E. Peetermans, MD, PhD^{f,g}, and Rik Schrijvers, MD, PhD^h *Leuven, Belgium*
 Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2021;■:■-■)

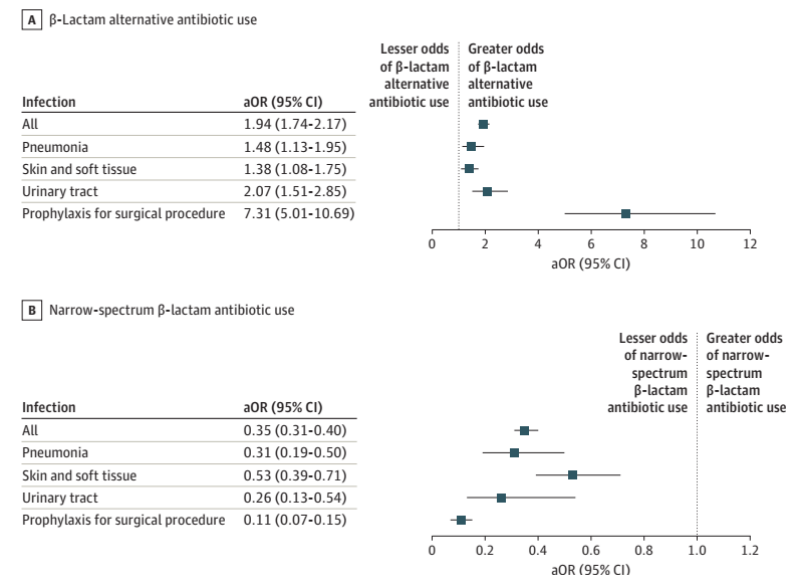
Antibiotic allergy label	Inpatients (% of total, n= 273 129)	Total (% of total, n= 1 009 598)	
Betalactams (BL)(any label)	16 415 (6.01)	25 062 (2.48)	89% BL label
Penicillins general label (unspecified)	13 910 (5.09)	21 277 (2.11)	
Cephalosporins	957 (0.35)	1 357 (0.13)	
Carbapenems	23 (0.01)	23 (<0.01)	
Monobactams	3 (<0.01)	4 (<0.01)	7% Quinolone label
Quinolones	1 301 (0.48)	1 836 (0.18)	
Sulfonamides/Trimethoprim	701 (0.26)	1 008 (0.10)	
Macrolides	522 (0.19)	821 (0.08)	
Nitrofurantoin derivatives	275 (0.10)	378 (0.04)	
Tetracyclines	174 (0.06)	228 (0.02)	
Glycopeptides	155 (0.06)	166 (0.02)	
Lincosamides	96 (0.04)	118 (0.01)	
Aminoglycosides	55 (0.02)	71 (0.01)	
Imidazole derivatives	32 (0.01)	38 (<0.01)	
At least one antibiotic allergy label	18 585 (6.80)	28 147 (2.79)	

Penicillin AB allergy *label* is not benign US/Aus

- *Penicillin allergy label* is associated with
 - ↑ Broad spectrum AB
 - ↑ Non-BL AB (FQ, Vanco, Clinda)
 - ↓ First-choice treatment (-30%)
 - ↑ Time to first dose (236 vs 186 min)
 - ↑ Risk of treatment failure, toxicity
 - ↑ Clostridium, MRSA, VRE (+23/14/30%)
 - ↑ *all-cause* mortality (+14% in outpatients)
 - ↑ Cost 30-40%

- *High* penicillin allergy label prevalence
- *High proportion* delabeled patients

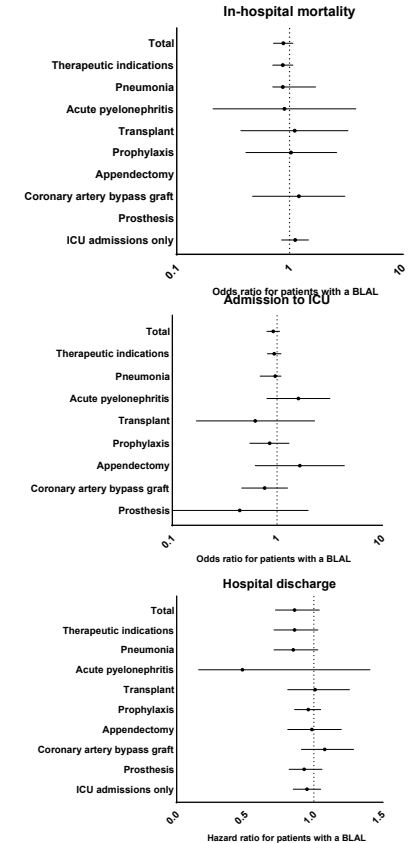
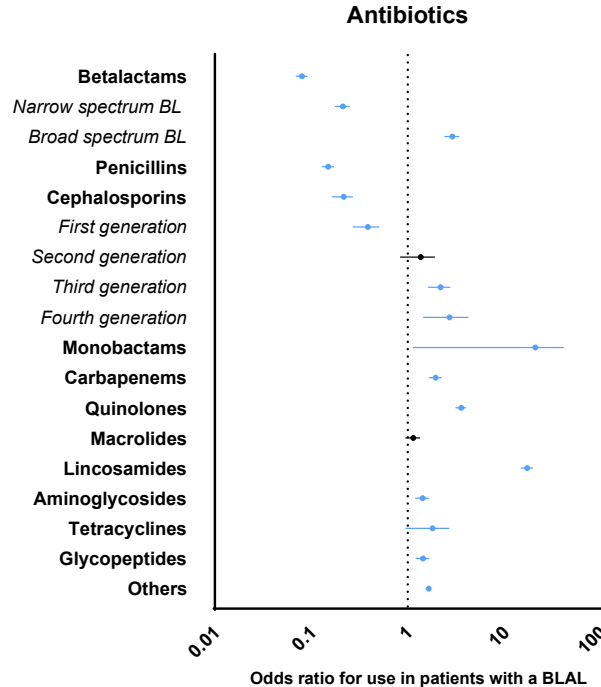
Figure. Association of Documented Penicillin Allergies With Inpatient Antibiotic Use Among US Inpatients



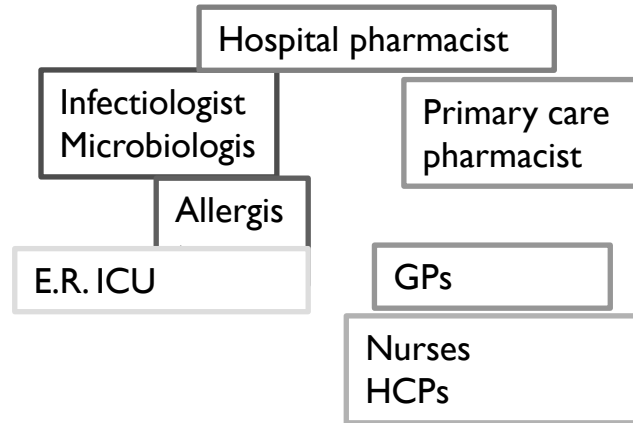
Penicillin AB allergy associations Belgium

- *Betalactam/Penicillin allergy label was associated with*
 - Altered antibiotic use
 - No increased mortality, hosp. duration, ICU admission

Diagnose	Patients	BLAL (%)
Antibiotic therapy	15 274	932 (6.10)
Pneumonia	13 385	805 (6.00)
Pyelonephritis	1 134	77 (6.79)
Transplantation	1 112	93 (8.36)
Heart transplantation	111	6 (5.41)
Kidney transplantation	414	30 (7.25)
Liver transplantation	333	18 (5.41)
Lung transplantation	293	43 (14.7)
Antibiotic prophylaxis	7203	549 (7.62)
Appendectomy	1 895	107 (5.65)
Coronary artery bypass graft	2 433	146 (6.00)
Prosthesis	2 905	239 (8.23)
Hip prosthesis	1 357	113 (8.33)
Knee prosthesis	1 578	127 (8.05)
ICU admissions	7 174	438 (6.10)
Total	21 999	1 394 (6.30)



Clinical decision support tools for delabeling



US initiative 2017

Special Article
Addressing Inpatient Beta-Lactam Allergies: A Multihospital Implementation
Kimberly G. Blumenthal, MD, MS^{a,b,c,d}, Erica S. Sherry, MD, PhD^{a,b,c,d}, Anna R. Wolfson, MD^{a,d}, David N. Berkowitz, PharmD^a, Victoria A. Carballo, MPH^a, Diana S. Baklan, MD, MPH^a, Kathleen A. Morais, PhD, PharmD^a, Romy Elshaboury, PharmD, BCPS, AGCP^a, Rosa G. Gaudin, PharmD, BCPS^a, Frances Blake, MD, MBA^a, David W. Kohn, PharmD, BCPS, AGCP^a, Jennifer Gattell, PharmD, BCPS^a, Barbara B. Landt, MD, MPH^a, Joyce T. Hsu, MD^a, Manique M. Freiley, RPh^a, Alana Shvachkin, PharmD, RPh, BCPS^a, and Paige G. Wickner, MD, MPH^a ^a Boston, Mass

JACI Pract 2017

Revised EU (Allergy) guidelines

Received: 31 July 2019 | revised 8 October 2019 | Accepted: 23 October 2019
DOI: 10.1111/ALL.14122
EAACI POSITION PAPER
Towards a more precise diagnosis of hypersensitivity to beta-lactams – an EAACI position paper
Antonino Romano¹ | Marina Atanaskovic-Markovic² | Annick Barbaud³ | Andreas J. Bircher⁴ | Knut Brockow⁵ | Jean-Christophe Caubet⁶ | Gulem Celik⁷ | Josefina Cernadas⁸ | Anca-Mirela Chiriac⁹ | Pascal Demoly¹⁰ | Lene H. Garvey^{11,12} | Cristobalina Mayorga^{13,14} | Alla Nakonechna^{15,16} | Paul Whitaker¹⁷ | Maria José Torres¹⁸

Allergy 2019

Revised US (Allergy) guidelines

Practice parameter
Drug allergy: A 2022 practice parameter update
David A. Khan, MD,¹ Alberto Barreij, MD,² Kimberly G. Blumenthal, MD, MS,³ Elizabeth J. Phillips, MD,^{4a} Roland Solensky, MD,⁵ Andrew A. White, MD,⁶ Jonathan A. Bernstein, MD,⁷ Derek K. Chu, MD, PhD,^{8a} Anna K. Ellis, MD,⁹ David B. K. Golden, MD,¹⁰ Matthew J. Greenhawt, MD,¹¹ Caroline C. Horner, MD,¹² Dennis Ledford, MD,¹³ Jay A. Lieberman, MD,¹⁴ John Oppenheimer, MD,¹⁵ Matthew A. Rank, MD,¹⁶ Marcus S. Shaker, MD, MS,¹⁷ David R. Shukus, MD,¹⁸ Dana Wallace, MD,¹⁹ and Julia Wang, MD²⁰
^a Boston, Mass; ¹ Murdoch, Australia; ² Nashville and Memphis, Tenn; ³ Cornell, NYC; ⁴ San Diego, Calif; ⁵ Cincinnati and Columbus, Ohio; ⁶ Hamilton and Kingston, Ontario, Canada; ⁷ Baltimore, Md; ⁸ Aurora, Colo; ⁹ Leuven, Belgium; ¹⁰ Tampa and Fort Lauderdale, Fla; ¹¹ Bergen, NJ; ¹² Scotland, Ariz; ¹³ Leuven, Belgium; ¹⁴ New York, NY

Chief Editor(s): David A. Khan, MD, David B. K. Golden, MD, Marcus Shaker, MD, MS, and David R. Shukus, MD

JACI 2022

Dutch (SWAB) guidelines

Contents lists available at ScienceDirect
Clinical Microbiology and Infection
Journal homepage: www.elsevier.com/locate/cmi
Guidelines
The Dutch Working Party on Antibiotic Policy (SWAB) guideline for the approach to suspected antibiotic allergy
Roos Wijnacker^{1,2,3}, Maurits S. van Maaren⁴, Lonneke G.M. Bode⁵, Maja Bulatovic⁶, Bart J.C. Hendriks⁷, Manja C.M. Logman⁸, Suzanne P.M. Ligtgens⁹, Annelia Middel¹⁰, Chris M.G. Nieuwhof¹¹, Eveline E. Roelofsen¹², Jan W. Schoones¹³, Kim C.E. Sigaloff¹⁴, Aline B. Sprickelman¹⁵, Lieke M.M. de Vrieskrijger¹⁶, Mark G.J. de Boer¹⁷

Clin Mic Inf 2023

How to identify *low risk* patients?

- Was there anaphylaxis?
- Do you recall the name of the drug?
- Was the reaction >1 year ago?
- If no to all 3 questions: 98.4% have NO allergy

PEN-F₂(AS)₂T₁ ≤ 2

- **PEN** Penicillin allergy label (0 pt)
 - **F** Five years or less since reaction (2 pt)
 - **A** Anaphylaxis or angioedema (2pt)
 - **S** Severe cutaneous adverse reaction (2pt)
 - **T** Treatment required for the reaction (1pt)
- Score 0 (<1%), 1-2 (5%), 3 (20%), 4-5 (50% test positivity)**

- **111 criterion:** An urticarial eruption <1h (OR 17, 95%CI 9-31), after the first dose (OR 11, 95%CI 6-20)), regressed <24h (OR 48, 95% CI 14-157).
- Sensitivity (85%), specificity (85%), NPV (80%), PPV (90%)
- **Urticaria meeting the 1-1-1 criterion : referral**

Original Article

Identifying Low-Risk Beta-Lactam Allergy Patients in a UK Tertiary Centre



Leonard Quok Chean Siew, MBChB, MSc, PhD, MRCP^{a,b,c}, Philip Hai Li, MBBS, MRes (Med), MRCP^{a,c}, Timothy J. Watts, MBBS, MRCP^a, Iason Thomas, MD, MSc, MRCP^{a,b}, Kok Loong Ue, MBChB, MRCP^{a,b}, M. Rosario Caballero, MD, PhD^a, Krzysztof Rutkowski, MD, MRCP^a, Stephen J. Tili, MBBS, PhD, FRCP^{a,b}, Prathap Pillai, MBBS, PhD, MRCP^{a,b}, and Rubaiyat Haque, MBBS, FRCP^{a,b} London, UK; and Hong Kong, China

Retrospective, 1092 patients

Table 4. Validation of PEN-FAST in Predicting a Positive Penicillin Allergy Test Result in All Derivation and Validation Cohorts

Cohort	No. of patients	No. (%) with positive finding ^a	Validation ^a			
			AUC (95% CI)	Sensitivity (95% CI, %)	Specificity (95% CI, %)	NPV (95% CI, %)
Melbourne, Australia	622	58 (9.3)	0.75 (0.68-0.81)	70.7 (57.3-81.9)	78.5 (74.9-81.9)	25.3 (18.8-32.7)
Perth, Australia	334	48 (14.4)	0.73 (0.66-0.81)	87.5 (74.8-95.3)	39.9 (34.1-45.8)	19.6 (14.5-25.6)
Sydney, Australia	80	27 (33.8)	0.78 (0.68-0.88)	70.4 (49.8-86.2)	84.9 (72.4-93.3)	70.4 (49.8-86.2)
Nashville, Tennessee	531	19 (3.6)	0.74 (0.62-0.86)	73.7 (4.8-90.9)	59.8 (55.4-64.0)	6.4 (3.5-10.4)

Abbreviations: AUC, area under the receiver operating characteristics curve; ^aBased on a PEN-FAST score of at least 1.

NPV, negative predictive value; PPV, positive predictive value.

^aIndicates any penicillin allergy test with a positive finding.

Prospective, 1567 patients

Prospective, 382 patients



The Journal of Allergy and Clinical Immunology:
In Practice

Volume 9, Issue 10, October 2021, Pages 3697-3704



Original Article

Urticaria: The 1-1-1 Criterion for Optimized Risk Stratification in β -Lactam Allergy Delabeling

Vito Sabato MD, PhD^{a,b,c,d,e}, Francesco Gaeta MD, PhD^{a,c}, Rocco Luigi Valluzzi MD^a, Athina Van Gasse MD, PhD^a, Didier Gaston Ebo MD, PhD^{a,b,c,d,e}, Antonino Romano MD^f

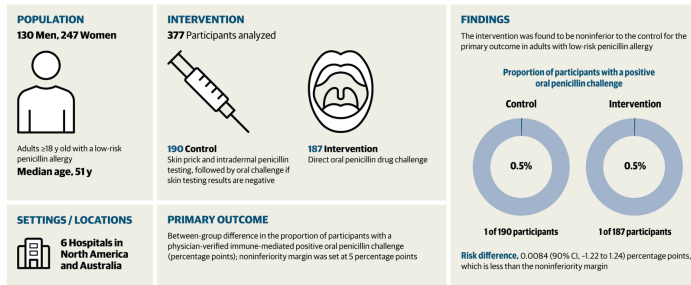
Quok et al. JACI Pract 2019
Trubiano et al. JAMA 2020, Copescu et al. JAMA 2023
Sabato et al. JACI Pract 2021

Can we safely delabel *low risk* patients?

JAMA Internal Medicine | [Original Investigation](#)

Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy The PALACE Randomized Clinical Trial

- Trial: Open label, randomized, multicentric (US/AUS)
- Population: Low-risk penicillin allergy labels : PEN F₂(AS)₂T₁ ≤2
- Result: No difference, safe



197 Did not meet eligibility criteria
82 PEN-FAST score ≥3
72 Other exclusion criteria^a
28 Other exclusion criteria^b
8 Pregnancy
6 History not confirmed with the patient
1 Concurrent antihistamine therapy

Table 2. Adverse Events Occurring Up to 5 Days After Oral Challenge

Variable	Adverse events, No. (%)	
	Intervention group (n = 22)	Control group (n = 24)
Type of adverse event		
An antibiotic-associated adverse event (any nonimmune mediated reaction)	6 (27)	2 (8)
Nausea/vomiting/diarrhea	2 (9)	0
Immediate diffuse rash/urticaria	2 (9)	1 (4)
Delayed diffuse rash/urticaria (>1 h)	6 (27)	3 (12)
Other nonsevere adverse events	6 (27)	18 (75)
Angioedema/laryngeal involvement/respiratory compromise	0	0
Anaphylaxis (or unexplained collapse)	0	0
Death	0	0

Can we safely delabel *low risk* patients?

- Lower NPV in EU context: 79-90% vs 96.3-98.7% in US/AUS

Comparative Performance of 4 Penicillin-Allergy Prediction Strategies in a Large Cohort

Beana Maria Ghiordanescu, MD^{1,2,3,4}, Juliana Ciocănea-Teodorescu, PhD^{1,2,3,4}, Nicolas Molinari, PhD^{1,2,3,4}, Anais Jelin, DPharm¹, Omar Al Ali, MD^{1,2}, Nik Schrijvers, PhD¹, Pascal Demoly, PhD^{1,2,3,4}, and Anca Mișela Chiriac, PhD^{1,2,3,4}
Bucharest, Romania; Montpellier and Nîmes, France; and Leuven, Belgium

Efficacy of the PEN-FAST score in a French cohort of patients with reported allergy to penicillins

Anatole Hanniet¹, Marc Puyraveau¹, Florence Castelain¹, Fabien Pelletier¹ and François Aubin^{1,2}

Strategy	AUC	Rationale for choosing threshold	Condition for negative test prediction	Sens	Spec	PPV	NPV
PEN-FAST	0.75 (0.72–0.78)		Score < 3	0.66 (0.62–0.71)	0.73 (0.71–0.75)	0.39 (0.36–0.41)	0.90 (0.88–0.91)

Missed positive high-risk cases

ANA, n (%) ¹	ANA with hypotension, n (%) ¹	SCAR, n (%) ¹	Other severe nonimmediate reactions, n (%) ¹
17 (17.9)	1 (1.1)	0 (0)	15 (62.5)

- Misclassification in all Penicillin-allergy prediction strategies

Strategy, class	Advise on betalactam use	Total number of patients (N=1884)	No Penicillin Allergy (N=1502, 79.7%)	Penicillin allergy (N=382, 20.3%)
PEN-FAST score				
≤ 2 (Very low/Low risk)	Low/no avoidance	1230 (65.3%)	1101 (73.3%)	129 (33.8%)
≥ 3 (Medium/High Risk)	<i>Not applicable</i>	654 (34.7%)	401 (26.7%)	253 (66.2%)

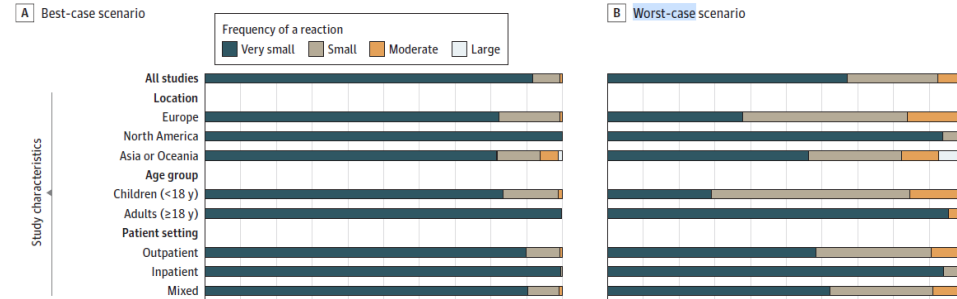
In red: unnecessary avoidance

In red: unwanted repeat iatrogenicity

Direct oral challenge in *low risk* patients

- Meta-analysis

- 56 studies (9225 participants, 1 RCT (n=159))
- No reaction in 96.5% of low risk labeled patients
- 3.5% had reactions but only 5/438 were severe, none fatal (3 anaphylaxis, 1 fever with rash, 1 acute kidney injury)



2418 STUL ET AL

J ALLERGY CLIN IMMUNOL PRACT
SEPTEMBER 2024

- Meta-analysis in *primary care*

- 12 studies (1070 participants, 3 primary care, 9 outpatient hospital setting)
- No reaction in 97.1%. Ten (<1%) developed immediate reactions

TABLE I. Study characteristics

Author	Year	Country	Study design	Setting	Sample size	Mean age (SD) (y)	Female (%)
Blumenthal	2019 ³⁹	USA	Retrospective	Outpatient allergy clinic	80	52 (18)	72.2
Copaescu	2023 ³⁶	Canada	Prospective	Outpatient allergy clinic (multicentric)	187	52 (N/A)	62
Gateman	2021 ⁴⁰	USA	Retrospective	Outpatient hospital setting and family medicine office	58	42.9 (15.5)	86.2
Iammatteo	2019 ⁴⁵	USA	Prospective	Outpatient allergy clinic	155	48.3-54.3 (1.85-13.3)	77.4
Kuruville	2019 ⁴²	USA	Retrospective	outpatient allergy clinic	38	59 (N/A)	80
Li	2021 ⁴⁴	Australia	Prospective	Outpatient hospital setting	64	50 (N/A)	85
Mak	2022 ⁴⁵	Canada	Prospective	Outpatient hospital setting	207	34.15 (3.99)	100
Savic	2019 ⁴¹	United Kingdom	Prospective	Outpatient allergy clinic	56	Adults (N/A)	N/A
Stevenson	2020 ⁴³	Australia	Retrospective	Outpatient immunology clinic (multicentric)	167	42.4 (19.5)	55.7
Waldron	2023 ³⁷	Australia	Prospective	Primary care	51	58 (N/A)	59.4
Wittmer	2023 ³⁴	Canada	Prospective	Primary care	26	30.2 (N/A)	4
Zhang	2021 ⁴⁶	Canada	Prospective	Multidisciplinary outpatient clinic	27	34.5 (5.1)	100

N/A, Not applicable; SD, standard deviation.

Blumenthal et al. JAMA internal medicine 2024

Cooper et al. JAC antimicrobi Resist 2021

Stul et al. J Allergy Clin Immunol Pract 2024

Non-invasive delabeling – Allergy fact checker



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Allergy EUROPEAN JOURNAL OF ALLERGY
AND CLINICAL IMMUNOLOGY

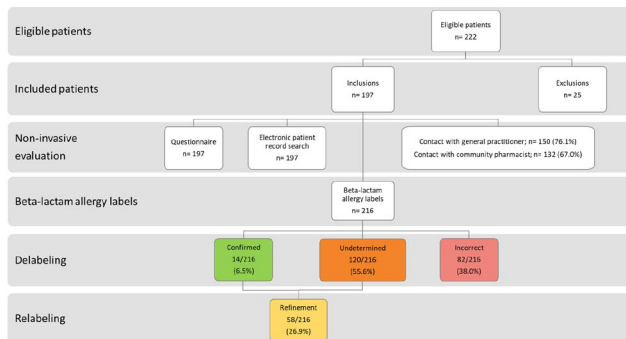


LETTER | [Full Access](#)

Non-invasive delabeling and refining of beta-lactam allergy labels in inpatients to optimize antimicrobial stewardship

Greet Van De Sijpe, Liesbeth Gilissen, Martijn Vandebotermiet, Willy E. Peetermans, Isabel Spriet, Rik Schrijvers

First published: 25 July 2022 | <https://doi.org/10.1111/all.15453>



Prospective study
Internal med. patients
BL AAL
N=197

38% delabeled
uneventful re-exposure
21% non-allergic mild ADR
16% info GP/Comm.Pharm.

27% refined
re-exposure to non-culprit
BL
6% correct (confirmed)



Multicentric, cluster randomized
controlled quality improvement
project (STAAL)

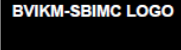
Evaluating impact of a non-invasive
semi-automated delabeling tool

KWS 64bit

Score: Allergy Fact Checker
Allergy Fact Checker



Nieuwe IGGI richtlijn delabeling penicilline-allergie

ADULTS	CHILDREN		
 	EMPIRICAL TREATMENT OF INFECTIOUS DISEASES / SYNDROMES	TARGETED TREATMENT OF BACTERIAL INFECTIONS	PROPHYLAXIS
	TARGETED TREATMENT OF FUNGAL INFECTIONS	TARGETED TREATMENT OF MYCOBACTERIAL INFECTIONS	ANTI-INFECTIVES
	TARGETED TREATMENT OF PARASITIC INFECTIONS	TARGETED TREATMENT OF VIRAL INFECTIONS	OVERVIEW TABLES
			OTHER INFORMATION

PENICILLIN ALLERGY

WORKING GROUP COMPOSITION

NAME	SPECIALTY	AFFILIATION
* BERGHMANS Mathilde.	Infectiologist.	CHU UCL Namur.
* COX Janneke.	Infectiologist.	Jessa hospital, Hasselt.
* DELAERE Bénédicte.	Infectiologist.	CHU UCL Namur.
* JACOBS Frédérique.	Infectiologist.	BVIKM-SBIMC.
* PIRSON Françoise.	Pneumologist - Allergologist.	Cliniques Universitaires Saint-Luc
* SCHRIJVERS Rik.	Internal medicine specialist.	UZ Leuven.
* TOSCANO Alessandro.	Immunologist - Allergologist.	UZ Antwerpen.
* VAN DE SIJPE Greet.	Clinical pharmacist.	UZ Leuven.
* VAN DER BREMPT Xavier.	Pneumologist - Allergologist.	Clinique Saint-Luc Bouge.

DID ANY OF THE FOLLOWING REACTIONS OCCUR?

- * Anaphylaxis, angio-oedema², hypotension, bronchospasm.
- * Urticaria occurring after < 1 hour, after the first dose and lasting < 24 hours (1-1-1 criterion).
- * Severe cutaneous adverse drug reaction [SCAR (**DRESS**, **SJS/TEN**, **AGEP**) or severe MPE.
- * Organ toxicity [hepatic, renal, haematological (cytopenia), other severe organ involvement].
- * Reaction requiring emergency treatment or emergency medical attention.

SEVERE REACTION → HIGH-RISK LABEL

How long after the exposure did the reaction occur?

Immediate onset (< 6 hours).

Penicillins must be avoided.

β-lactam antibiotics that can be used.

- * Cefazolin (refer to 8)
- * Second to fifth generation cephalosporins³ (refer to 8)
- * Carbapenems⁴
- * Monobactams⁵

The patient must be informed and observed during the administration of the first dose.

Delayed onset (≥ 6 hours up to several days).

All β-lactam antibiotics must be avoided.

Case-by-case decision.

- * In urgent need, a carbapenem⁴ or a monobactam⁵ can be used.
- * Some other β-lactam antibiotics can potentially be used (only after consultation with an infectiologist-allergologist).

NON-SEVERE REACTION → LOW-RISK LABEL

β-lactam antibiotics that can be used without additional challenge or precautions.

- * Carbapenems.
- * Cephalosporins with dissimilar⁶ side-chains (cefazolin and second to fifth generation cephalosporins³).
- * Monobactams.

Use of penicillins if recommended as first choice.

- * Not indicated in patients with risk factors (cardiopulmonary instability, pregnancy, ...).
- * If initial reaction occurred > 10 years ago or during childhood or adolescence: 1-step challenge procedure⁷.
- * If initial reaction occurred ≤ 10 years ago: 2-step challenge procedure⁸.

If the challenge procedures is negative: inform the patient and general practitioner and **delabel 1**

These patients must be referred for further validation/invalidation of the findings and for the identification of safe alternatives, especially if they:

- * experienced severe reactions in the past.
- * are labeled with allergy for multiple antibiotic classes.
- * are immunocompromised (or expected to be in the future) or female patient with childwish

FOOTNOTES

1. In case of an unspecified penicillin allergy label, **tolerated re-exposure** to amoxicillin or penicillin G/V allows for delabeling and for writing down in the file "no penicillin allergy".
2. **Angio-oedema.**
 - * Life threatening (orolaryngeal, ...) or generalised angio-oedema should be treated cautiously.
 - * Isolated, mild angio-oedema (extremities, ...) is less likely to be due to **IgE** mediated allergy.
3. **Cephalosporins.**
 - * Second generation: cefuroxime, cefuroxime axetil.
 - * Third generation: cefotaxime, ceftazidime, ceftazidime-avibactam, ceftriaxone.
 - * Fourth generation: cefepime.
 - * Fifth generation: ceftaroline, ceftolozane-tazobactam.
4. **Carbapenems:** meropenem, meropenem-vaborbactam.
5. **Monobactams:** aztreonam.
6. **Similar or identical side chains are present in:**
 - * amoxicillin, penicillin G, piperacillin, cefadroxil and cefalexine.
 - * aztreonam, ceftazidime and cefiderocol.
7. **1-step challenge procedure:** administration of a single dose of amoxicillin (500 mg to 1 g) followed by close patient observation for at least 30 minutes (up to 60 minutes). **Ensure emergency medical assistance is available.**
8. **2-step challenge procedure.**
 - * Not for patients with risk factors (cardiopulmonary instability, pregnancy). In hospital setting (medical supervision, **ensure emergency medications is standby**).
 - * Administration of a first dose of the antibiotic (10% of the therapeutic dose, liquid po formulation if available), followed 30 minutes later by a second dose (remaining 90% of the therapeutic dose)
 - * Vital parameters must be measured at the start and every 30 minutes until 1 hour after the administration of the entire second dose.
 - * In case of parenteral administration, the antibiotic must be injected slowly (bolus administration must be avoided).
 - * Depending on the urgency, this can be converted into a single step administration.
 - * A single-dose administration can be used for cefazolin for surgical prophylaxis, provided that is is done under careful anesthesiological supervision
 - * In case of true, confirmed, IgE mediated penicillin allergy: 2-4% risk of cross-reactivity, severe in only <1%.

Conclusions

- AB (mainly betalactam) allergy labels are **frequent**
- AB allergy labels are **not (necessarily) benign**
- Be **critical** for antibiotic allergy labels
- Value of **non-invasive EPR evaluation**
- Identify those with a **low risk** (vs high

		CEPH.												CARB.		MONOB.	PEN.											
		1 ST GEN.	2 ND GEN.	3 RD GEN.				4 TH GEN.	5 TH GEN.																			
		CEFDROXIL	CEFALEXIN	CEFAZOLIN	CEFUROXIME	CEFUROXIME AXETIL	CEFTAZIDIME	CEFTAZIDIME-AVIBACTAM	CEFTRIAXONE	CEFEPIME	CEFTADEROCOL	CEFTAROLINE	CEFTOLOZANE-TAZOBACTAM	MEROPENEM	MEROPENEM-VABORBACTAM	AZTREONAM	AMOXICILLIN	AMOXICILLIN-CLAVULANATE	BENZATHINE PENICILLIN G	FLUCLOXACILLIN	PENICILLIN G	PHENETICILLIN	PIPERACILLIN-TAZOBACTAM	TEMOCILLIN				

Overzicht Programma

1. Introductie

Dr. Pieter Goeminne | Longziekten en allergieën Vitaz

2. Antibiotica-allergie bij kinderen

Prof. dr. Van Gasse Athina | Kinderallergoloog ZAS

3. Antibiotica-allergie bij volwassenen

Prof. dr. Schrijvers Rik | Internist | Allergoloog UZ Leuven

4. Masterproefonderzoek: Bètalactam-allergie labeling en delabeling binnen Vitaz

Apr. Vanderper Vanessa | Antibioticabeleid & HOST Vitaz

5. Vragenronde & receptie

MASTERPROEF ZIEKENHUISFARMACIE

Ontwikkeling en implementatie van een bètalactam antibiotica allergie (de)labelingstrategie: optimaliseren van het antimicrobiële stewardship in een Belgisch perifeer ziekenhuis

Apr. Asa De Schepper

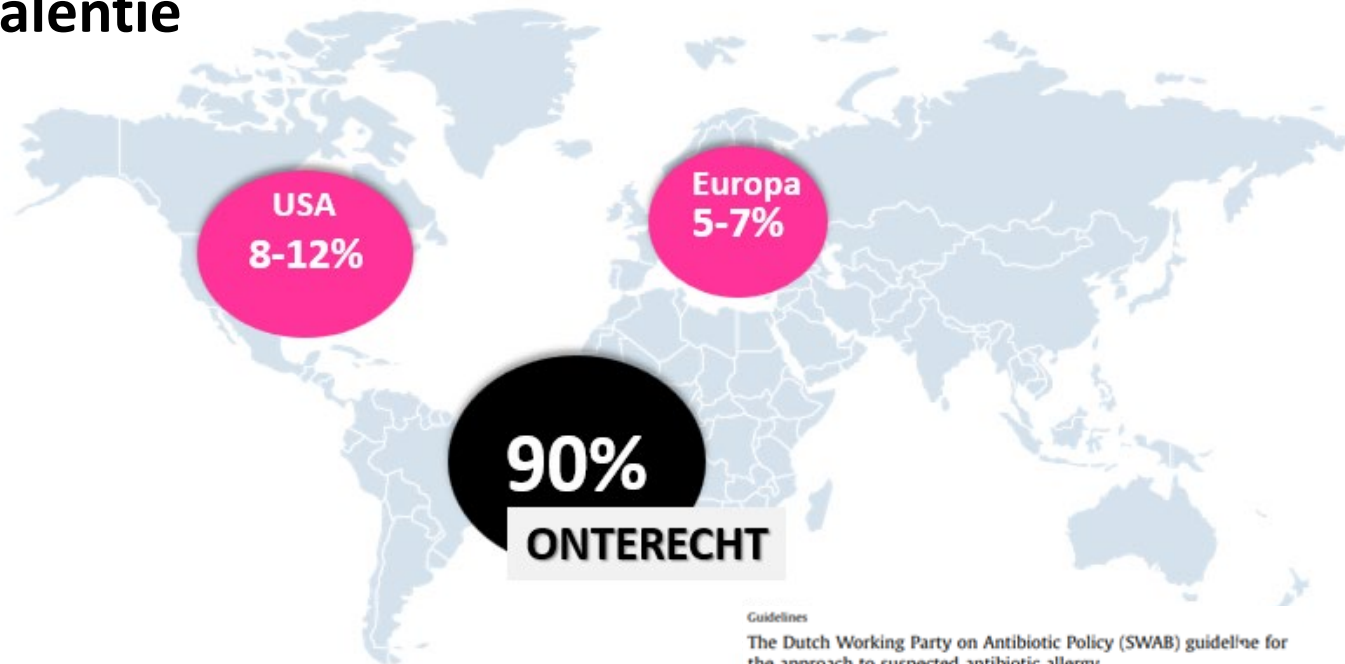
Promotoren: Apr. Ine De Kimpe, Apr. Cindy Miaolin Huang, Apr. Vanessa Vanderper

Academische promotor: Apr. Jens Van Krieken (UA)

INLEIDING, DOELSTELLINGEN EN ONDERZOEKSVRAGEN



Prevalentie



Guidelines

The Dutch Working Party on Antibiotic Policy (SWAB) guideline for the approach to suspected antibiotic allergy

Roos Wijnakker^{1,15,*}, Maurits S. van Maaren², Lonneke G.M. Bode³, Maja Bulatovic⁴, Bart J.C. Hendriks⁵, Masja C.M. Loogman⁶, Suzanne P.M. Lutgens⁷, Ananja Middel⁸, Chris M.G. Nieuwhof⁹, Eveline E. Roelofsen¹⁰, Jan W. Schoones¹¹, Kim C.E. Sigaloff¹², Aline B. Sprickelman¹³, Lieke M.M. de Vrankrijker¹⁴, Mark G.J. de Boer¹⁵

Implicaties

Onbeschikbaarheid
Bètalactam antibiotica
als eerste lijn AB



Suboptimale therapie

> Heropname

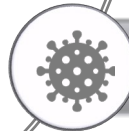
> Langere hospitalisatie



Ongewenste effecten



Hogere kostprijs



Resistentie ontwikkeling

Strategieën voor delabeling

Huidpriktest

Provocatietest

Non invasieve delabeling

(laag risico op allergie)

- Ontwikkelen en implementeren van een label- en delabelingsprotocol
- Identificeren en succesvol delabelen van patiënten met een incorrect bètalactam allergielabel binnen het ziekenhuis
 -  Alle B-lactam: penicillines, cefazolines, carbapenems en mono-bactamallergie
- Evaluatie van praktische toepasbaarheid van de opgestelde protocollen

- Wat is de **incidentie** van bètalactam antibiotica allergielabels binnen Vitaz?
- Wat is het **percentage succesvol gedelabelde** patiënten binnen de interventiegroep?
 - Via directe delabeling
 - Via delabeling na allergietesten

6%

Prevalence of Antibiotic Allergy Labels in a Tertiary Referral Center in Belgium

Liesbeth Gilissen, MPharm^{a,b}, Isabel Spriet, PharmD, PhD^{c,d}, Karin Gilis, BSc^e, Willy E. Peetermans, MD, PhD^{f,g}, and Rik Schrijvers, MD, PhD^{a,h} *Leuven, Belgium*

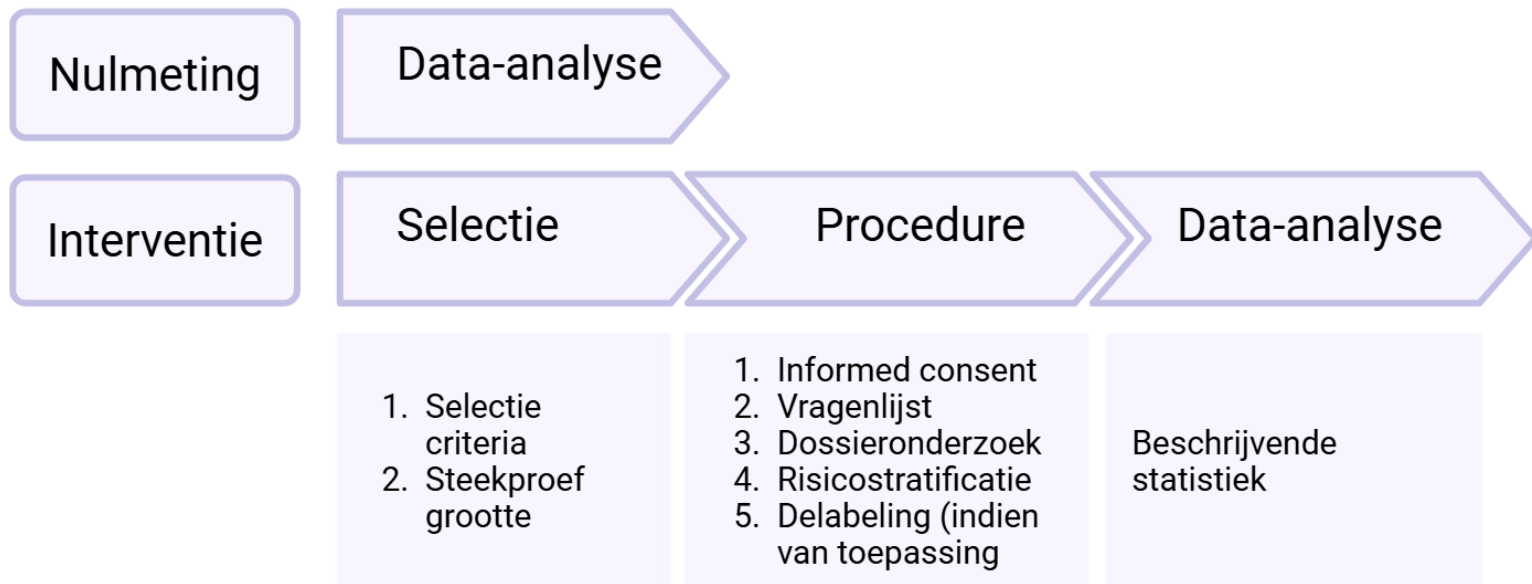
What is already known about this topic? Antibiotic allergy labels (AAL) appear in 10% to 15% of US patients' charts and subsequently affect future health care decisions. However, large-scale analyses of the prevalence and characteristics in European centers are scarce.

What does this article add to our knowledge? With an overall prevalence of 3% of patients who consulted our center, being 1% of outpatients and 7% of those hospitalized, AAL are reported less when compared with literature.

How does this study impact current management guidelines? Varying prevalences of AAL might impact the outcome of delabeling strategies that should be tailored to the local AAL "epidemic." Improved documentation of AAL can help minimizing the burden of incorrect AAL.

METHODE & DATA- ANALYSE

Methode

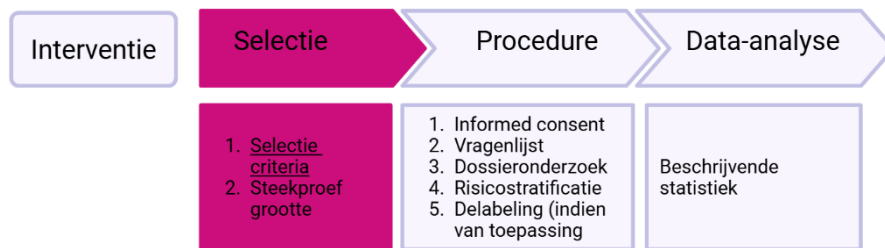


Methode

- Retrospectieve data via Beleidsinformatie:
 - **Aantal unieke gehospitaliseerde patiënten in 2024 met een bètalactam antibiotica allergielabel** in KWS + bijkomende gewenste data
 - ✓ pseudonimisatie
 - Aantal unieke gehospitaliseerde patiënten in 2024 (noemer)
- Data analyse
 - **Prevalentie** bètalactam allergielabels bepalen en **vergelijken** met de literatuur
 - Meest voorkomende **oorzaak** van labeling identificeren

Type allergielabel in KWS	☐ ...
Onderliggende ATC-code gekoppeld aan allergielabel (vul aan indien meer specifiek, bv. J01DE)	☐ J01C ☐ J01D
Reden van registratie	Zeer ernstige reacties ☐ Anafylactische shock ☐ Angio-oedeem ☐ Steven Johnson/Lyell ☐ Astma ☐ Urticaria ☐ HIT Ernstige reacties ☐ Uitslag ☐ Jeuk zonder uitslag Andere reacties
Datum van registratie allergielabel	
Informatiebron	☐ Gerapporteerd door patiënt/naaste ☐ Gedocumenteerd door externe arts ☐ Vastgesteld door Nexuz health arts
Wijze van objectivering (indien van toepassing)	☐ Niet van toepassing ☐ Allergietest ☐ Rechallenge ☐ Anafylactische shock of angio-oedeem geobserveerd
Graad van zekerheid	☐ Onduidelijk ☐ Waarschijnlijk ☐ Zeker

Methode



Inclusiecriteria

- Minstens **18 jaar** oud
- **Gehospitaliseerd**
- Beschikt over bètalactam antibiotica **allergielabel** in KWS

Exclusiecriteria

- Onbetrouwbare anamnese
- Klinische instabiliteit
- DNR3-code
- Wilsonbekwaamheid
- Zwangerschap
- Weigering tot deelname na geïnformeerd te worden

Methode

Interventie

Selectie

Procedure

Data-analyse

1. Selectie criteria
2. Steekproefgrootte

1. Informed consent
2. Vragenlijst
3. Dossieronderzoek
4. Risicostratificatie
5. Delabeling (indien van toepassing)

Beschrijvende statistiek

- Duur van **inclusieperiode**: oktober 2025 – februari 2026
- **Streefdoel** van het **aantal** patiënten:
 - Totaal patiënten in 2024: 1259
 - **Steekproefgrootte** berekend volgens Cochranes formule voor eindige populatie: **295 patiënten**



Methode



1. INFORMED CONSENT FORMULIER

✓ opgesteld volgens template van de universiteit Antwerpen

Methode



2. GESTRUCTUREERDE & UNIFORME ANAMNESE

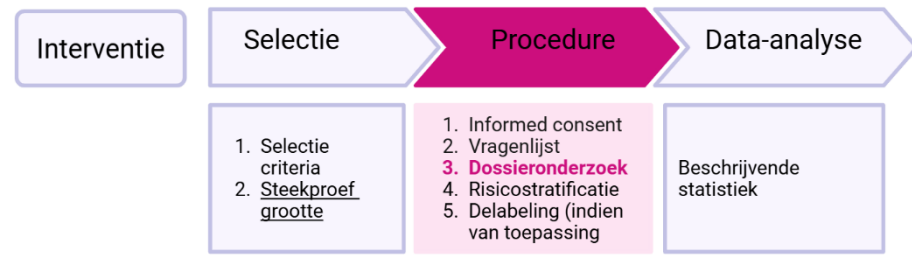
- ✓ Gebruik maken van **gestandaardiseerde vragenlijst**
 - Symptomen: welke, hoelang na toediening,...?
 - Wanneer?
 - Allergietest?
- ✓ Tijdsregistratie

Patiënten interview	Tijd start interview:
Tijd eind interview:	
Naam (wordt niet geregistreerd als data → transformeren i.k.v. pseudonimisatie)	
Geboortedatum (wordt niet geregistreerd als data)	
Klopt het dat u een penicilline allergie heeft?	☐ Ja ☐ Nee
Op welk antibioticum heeft u een reactie vertoond? Ging dit om een siroop, tablet, infuus?	☐ Bekend: ☐ Naam geneesmiddel: ☐ PO (tablet/siroop) ☐ Injectie (IV) ☐ Onbekend
Had u dit geneesmiddel al eerder gebruikt? Indien ja, wanneer?	☐ Ja (+ datum): ☐ Nee
Hoe lang geleden vond deze reactie plaats?	☐ <1 jaar geleden ☐ 1-10 jaar geleden ☐ >10 jaar geleden ☐ Onbekend
Hoe snel na de toediening begonnen de eerste klachten?	☐ <1 uur ☐ 1-6 uur ☐ >6 uur ☐ Onbekend
Hoeveel dosissen werden al toegediend voor de reactie begon?	
Welke symptomen gingen gepaard bij deze reactie?	☐ Diarree, nausea, braken ☐ Hoofdpijn ☐ Jeuk ☐ Huiduitslag ☐ Kortademigheid ☐ Angio-oedeem (zwellen van lippen, tong, ...) ☐ Lage bloeddruk ☐ Andere, nl: ...
Hoelang hielden de symptomen aan?	

Werd er ooit een allergietest uitgevoerd voor uw penicilline allergie?	☐ Ja (huidtest of provocatietest?): ☐ Nee ☐ Onbekend
Gebruikte u gelijktijdig andere nieuwe geneesmiddelen?	☐ Ja, nl: ... ☐ Nee
Welke acties zijn genomen na het ontstaan van de klachten (medicatie zoals antihistaminica, ziekenhuisopname, ...). Indien medicatie toegediend werd, welke medicatie en heeft deze naar uw aanvoelen geholpen?	☐ Geen acties, antibioticum werd verder gegeven ☐ Stoppen met het antibioticum ☐ Medicatie om de symptomen onder controle te houden (antihistaminicum, corticosteroïden, adrenaline, ...) ☐ Medicatie gekend, nl: ☐ Medicatie onbekend ☐ Effect bekomen? ☐ Consultatie huisarts ☐ Spoedopname ☐ Onbekend
Heeft u hierna ooit nog een penicilline gebruikt?	☐ Ja (welk AB en wanneer): ☐ Nee ☐ Onbekend
Weet u nog waarvoor u dit antibioticum destijds gebruikte?	☐ Ja, nl: ☐ Nee
Had u gelijkaardige klachten voor het innemen van de antibiotica, bijvoorbeeld door de infectie zelf?	☐ Ja ☐ Nee

Methode

3. DOSSIERONDERZOEK



- ✓ Indien nodig bijkomend dossieronderzoek
 - Eerdere toediening van penicillines?
- ✓ Indien nodig contact opnemen bij de huisarts of huisapotheker



4. RISICOSTRATIFICATIE

- ✓ Patiënten categoriseren in risicoklassen a.d.h.v. beslissingsboom

Bronnen: IGGI, SWAB, HOST, UZA, UZ Gent, UpToDate

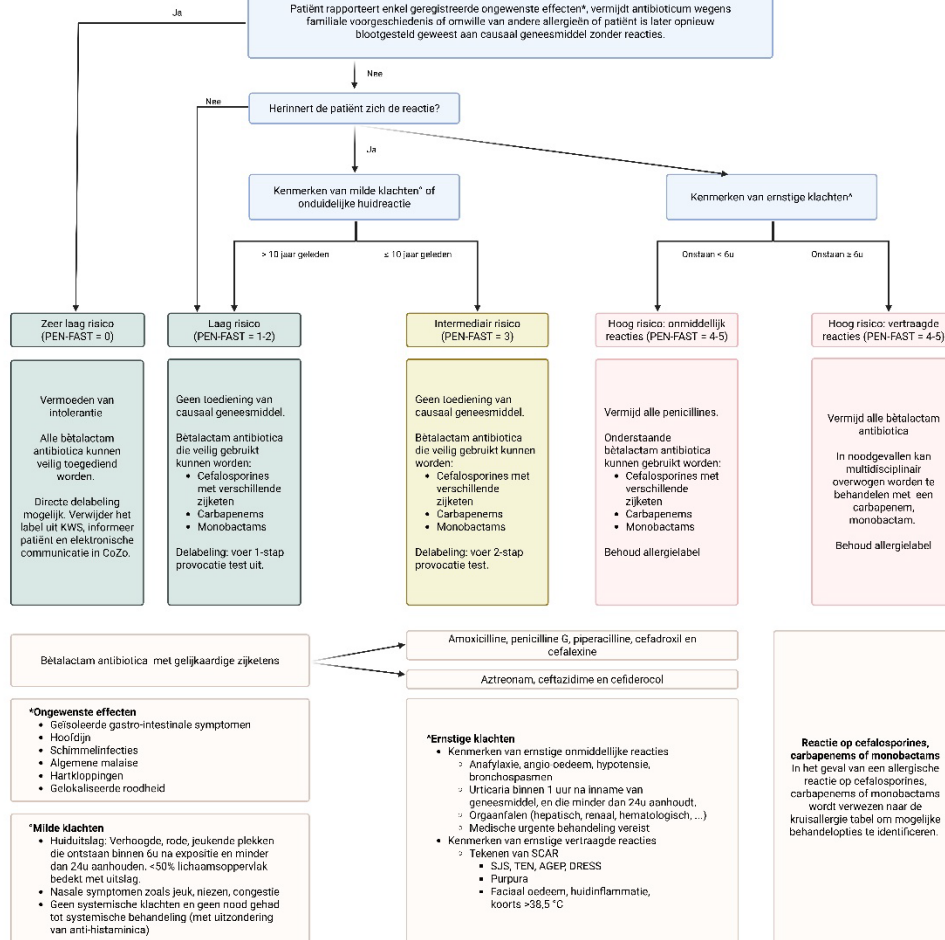
Link met PEN-FAST scores

ZEER LAAG risico PEN-FAST = 0	LAAG risico PEN-FAST = 1-2	INTERMEDIAR risico PEN-FAST = 3	HOOG risico PEN-FAST = 4-5
Ongewenste effecten Positieve familiale voorgeschiedenis	> 10 jaar geleden milde klachten of onduidelijke huidreactie	≤ 10 jaar geleden milde klachten of onduidelijke huidreactie	Voorgeschiedenis van ernstige klachten
Directe delabeling	1-stap provocatie	2-staps provocatietest	Label behouden

Penicilline allergie - Beslissingsboom

Allergie aan andere bètalactam antibiotica: Zie tabel kruisallergieën voor behandelopties

DRAFT



Methode



5. DELABELING (indien van toepassing)

✓ Directe delabeling

- Enkel mogelijk bij **zeer laag risico** patiënten
- Allergielabel verwijderen in KWS

✓ Communicatie

- In KWS via opvolgnota
- Naar de **eerste lijn** via CoZo
- Naar de **patiënt** + brochure meegeven

ZEER LAAG risico PEN-FAST = 0
Ongewenste effecten Positieve familiale voorgeschiedenis
Directe delabeling

Methode

5. DELABELING (indien van toepassing)



✓ 1-stap provocatietest

- Voorbereidende maatregelen (noodkoffer aanwezig, patiënt informeren, te staken GMen,...)
- 1 toediening van **causaal geneesmiddel** (per os) in de **therapeutische dosis**
 - ✓ indien onbekend: gebruik amoxicilline/clavulaanzuur
 - ✓ Observeer gedurende 1 uur + interpretatie
 - ✓ elke 30 minuten: controle vitale parameters
- Delabel indien mogelijk
- **Communicatie**
 - In KWS via opvolgnota
 - Naar de **eerste lijn** via CoZo
 - Naar de **patiënt** + brochure meegeven

LAAG risico
PEN-FAST = 1-2

> 10 jaar geleden
milde klachten of
onduidelijke
huidreactie

1-stap provocatie



Methode

5. DELABELING (indien van toepassing)

✓ 2-staps provocatietest

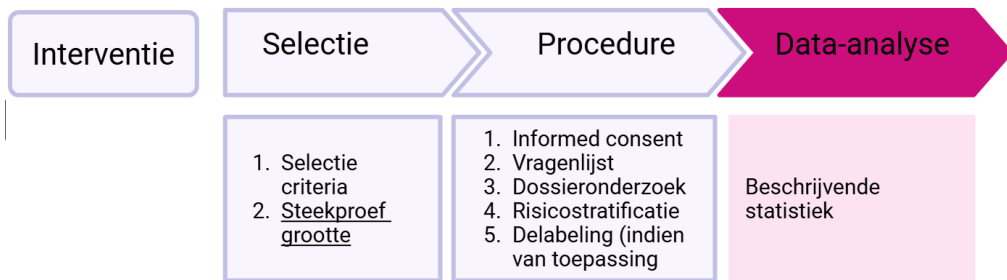
- Voorbereidende maatregelen (noodkoffer aanwezig, patiënt informeren, te staken GMen,...)
- Toediening van **causaal geneesmiddel** (per os)
 - ✓ indien onbekend: gebruik amoxicilline/clavulaanzuur
 - ✓ 1 toediening met **10% van de therapeutische dosis**
 - ✓ Observeer gedurende 1 uur
 - ✓ Controleer elke 30 min vitale parameters
 - ✓ Dien **2e dosis** toe van het geneesmiddel (resterende 90%)
 - ✓ Observeer gedurende 1 uur + interpreteer testresultaat
 - ✓ Controleer elke 30 min vitale parameters
- Delabel indien mogelijk
- **Communicatie**
 - In KWS via opvolgnota
 - Naar de **eerste lijn** via CoZo
 - Naar de **patiënt** + brochure meegeven

INTERMEDIAIR risico
PEN-FAST = 3

≤ 10 jaar geleden
milde klachten of
onduidelijke
huidreactie

2-staps provocatietest

Data-analyse



- Data van de nulmeting en de interventie wordt gedocumenteerd in Excel
- Beschrijvende statistiek toepassen
 - **Prevalentie** bètalactam antibiotica **allergielabel** binnen Vitaz
 - **Percentage gedelabelde** patiënten
 - % **Directe** delabeling
 - % Delabeling **na allergietesten**

Aan de hand van **tijdsregistratie** wordt de **praktische haalbaarheid** geëvalueerd.

Voorlopige tijdlijn

07/2025	Aanvraag indienen bij ethisch comité Opstellen label- en delabelingsprotocol
08/2025 – 09/2025	Opstellen label- en delabelingsprotocol, protocol voor provocatietesten en huidtesten ABTBG symposium september: presentatie Beoordeling voor ethisch comité Vitaz Verkrijgen data nulmeting
10/2025 – 02/2026	ABTBG 6/10: Finaliseren label- en delabelingsprotocol Metingen bij interventiegroep Simultane data-analyse
03/2026 – 05/2026	Data-analyse Evaluatie haalbaarheid protocol

TOEKOMST

- ✓ Implementatie in dagelijkse praktijk binnen VITAZ
- ✓ Aanbieden van flowcharts en documenten

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Bedankt!

GSK

VITAZ
STERK IN ZORG

 **Pfizer**