Allergie bétalactamine

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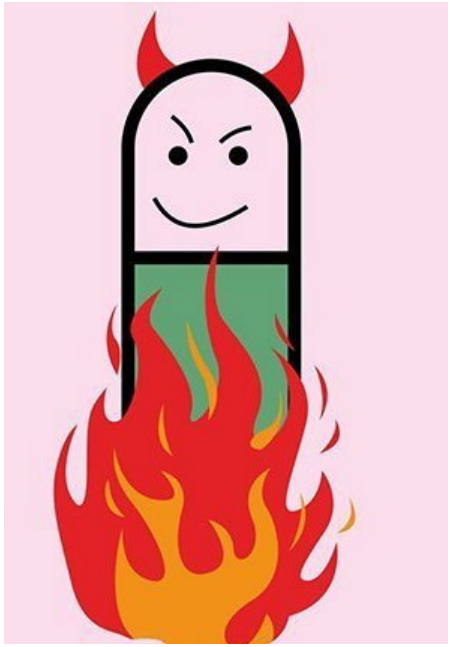
Pôle des Voies Respiratoires

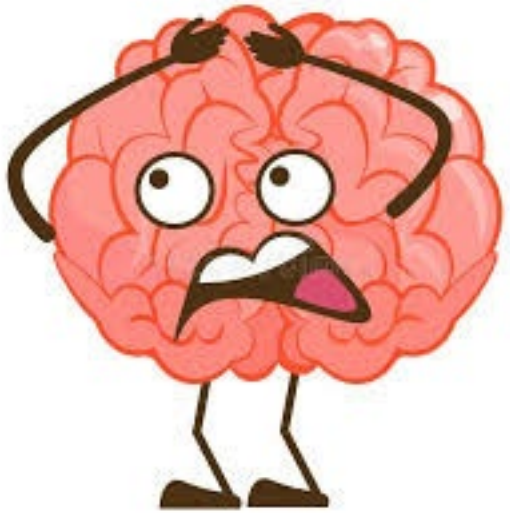
CHU de Toulouse

Liens d’intérêts

- Pas de liens d’intérêts pour cette présentation

« Allergie » aux pénicillines





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Guidelines

ESCMID clinical guidelines on the evaluation and management of a reported antibiotic allergy

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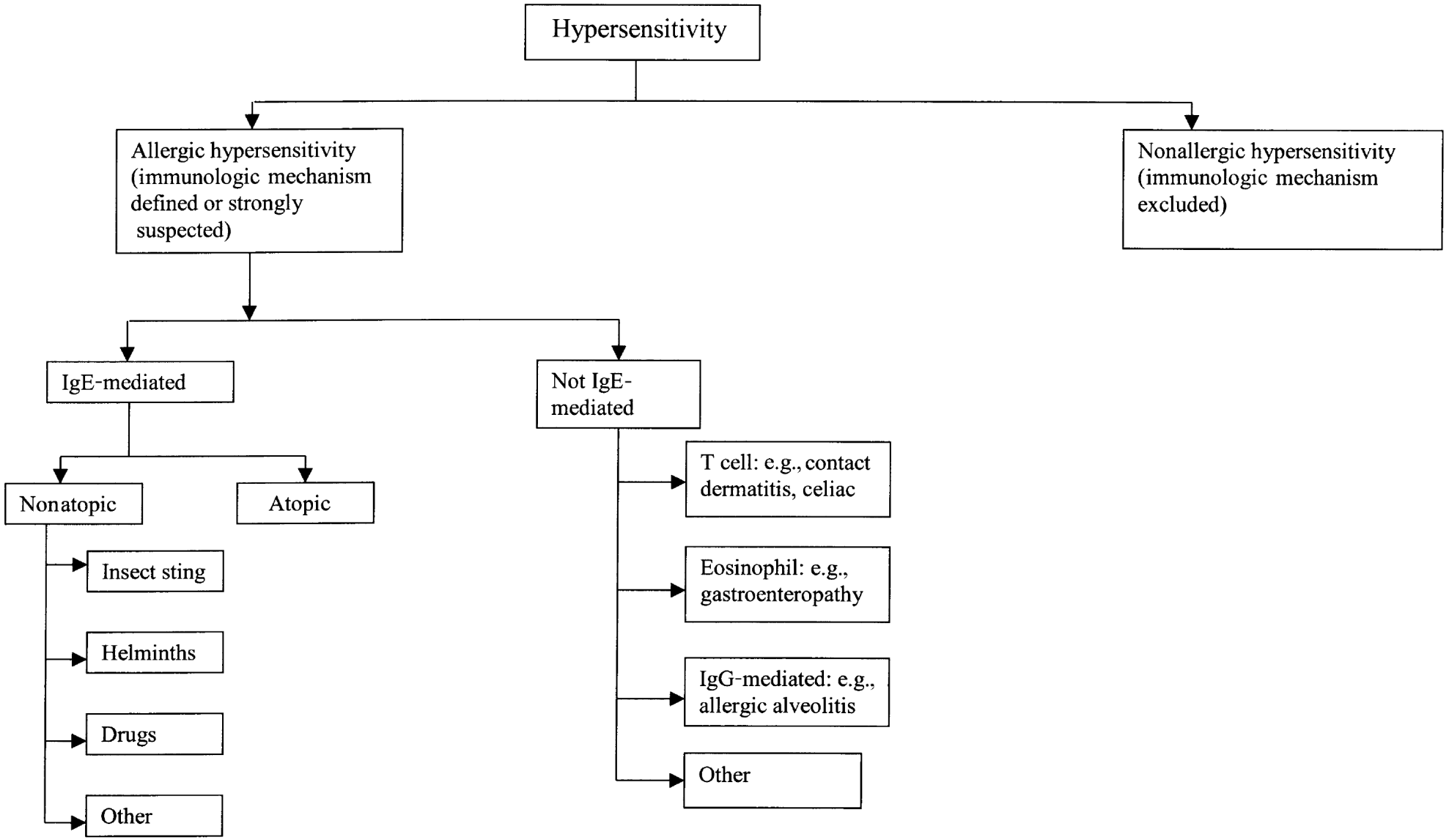
Joean O et al. ESCMID clinical guidelines on the evaluation and management of a reported antibiotic allergy. Clin Microbiol Infect. 2026 Feb 16:S1198-743X(26)00069-8.

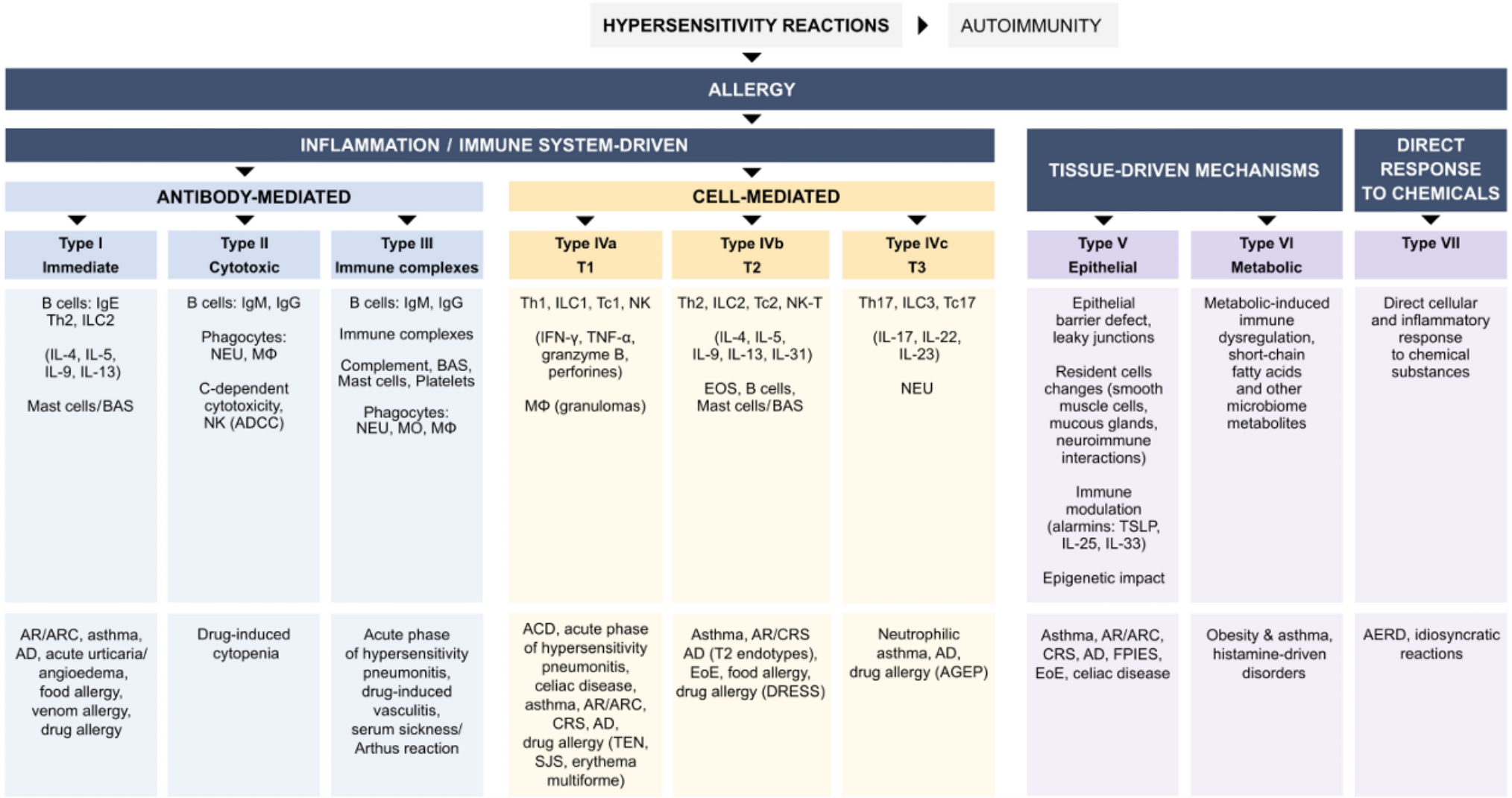
Définition



Johansson SG et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy. 2001 Sep;56(9):813-24.

Définition

- Allergie=mécanisme immunologique



Jutel M et al. Nomenclature of allergic diseases and hypersensitivity reactions: Adapted to modern needs: An EAACI position paper. Allergy. 2023 Nov;78(11):2851-2874

Définition

Subjective reaction

Itch, dizziness/light-headedness, nausea, chest discomfort *but without any objective skin features, physical signs or physiological compromise*.

Skin only reaction

Generalized erythema, urticaria or angioedema without any sentinel features (see below) of other organ involvement

Anaphylaxis

Typical anaphylaxis: Any skin feature listed above *plus* at least one sentinel feature from either the respiratory *or* cardiovascular system:

- *Respiratory*; dyspnoea, wheeze, stridor, hypoxaemia (cyanosis or $SpO_2 \leq 92\%$)
- *Cardiovascular*; hypotension (SBP < 90 mmHg in an adult), collapse, altered conscious state, incontinence

Atypical anaphylaxis: Severe gastrointestinal features are commonly associated with, or may precede, anaphylactic shock. Also, skin features may be absent in up to 20% of anaphylaxis cases. Therefore, a sudden onset of symptoms affecting skin plus gastrointestinal tract (cramping abdominal pain, vomiting), or features affecting two or more organ systems (any two of gastrointestinal, respiratory, cardiovascular) or even severe bronchospasm or hypotension alone without any other features may justify a provisional diagnosis of anaphylaxis in the right context (see text).

Severe anaphylaxis: Anaphylaxis as defined above is classified as '**severe**' if there is hypoxaemia, hypotension, collapse, altered consciousness or incontinence.

Stone SF et al. Immediate-type hypersensitivity drug reactions. Br J Clin Pharmacol. 2014 Jul; 78(1): 1–13.

Définition

Note: We are not “hypersensitivitists” but “allergists.”

We spend a lot of time to exclude half of our patients from our specialty trying to explain them that they are not “allergic” but only “hypersensitive.”

Ring J et al. Provocative proposal for a revised nomenclature for allergy and other hypersensitivity diseases. Allergy. 2018 Oct;73(10):1939-1940

Epidémiologie « allergie » pénicilline

- Méta-analyse sur 53 études:
- patient étiqueté allergique à la pénicilline: 8-12%

	No. of participants, (%) of women [mean age]	Participants self-reporting drug allergy, n (%)	
		Total	Female
Total	37,459 (55.5) [41.4]	3,585 (9.6)	1,706 (17.0)
Total studies	126,306 (52.8)	10,437 (8.3)	4,185 (11.4)

Sousa-Pinto B et al. Frequency of self-reported drug allergy: A systematic review and meta-analysis with meta-regression. *Annals of allergy, asthma & immunology.* 2017;119(4):362-73.e2.

Proportion de vrai allergie à la pénicilline

- >90% des patients étiquetés « allergiques » à la pénicilline ne sont pas allergiques

Table 1.—Distribution of Penicillin Skin Test Results According to History of Penicillin Reaction*

	History of Penicillin Reaction, No. (%)		
	Positive	Unknown	Negative
Skin testing performed			
Total (N = 1539)	**825**	**104**	**610**
Skin test negative	656 (80)	100 (96)	578 (95)
Skin test positive	146 (18)	4 (4)	25 (4)
Skin test uninterpretable	23 (3)	0 (0)	7 (1)
Completed protocol			
Total (n = 1422)	**726**	**96**	**600**
Skin test negative	566 (78)	93 (97)	568 (95)
Skin test positive	139 (19)	3 (3)	25 (4)
Skin test uninterpretable	21 (3)	0 (0)	7 (2)

Table 4.—Results of Therapeutic Administration With Penicillin Agent*

	History of Penicillin Reaction, No.		
	Positive	Negative	Unknown
Skin test positive (9 challenged)			
Reaction	2	0	0
No reaction	6	1	0
Skin test negative (1227 challenged)			
Reaction	7	0	0
No reaction	559	568	93

Sogn DD et al. Results of the National Institute of Allergy and Infectious Diseases Collaborative Clinical Trial to test the predictive value of skin testing with major and minor penicillin derivatives in hospitalized adults. *JAMA* 1992;152(5):1025-32.

Allergie Amoxicilline

- La réalité: Allergie ≈ 4% des hypersensibiltiés aux pénicillines[1]

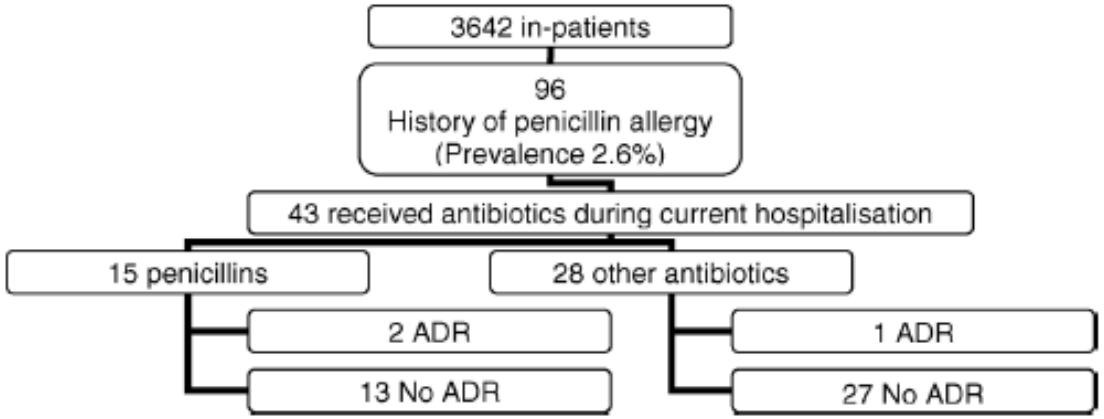
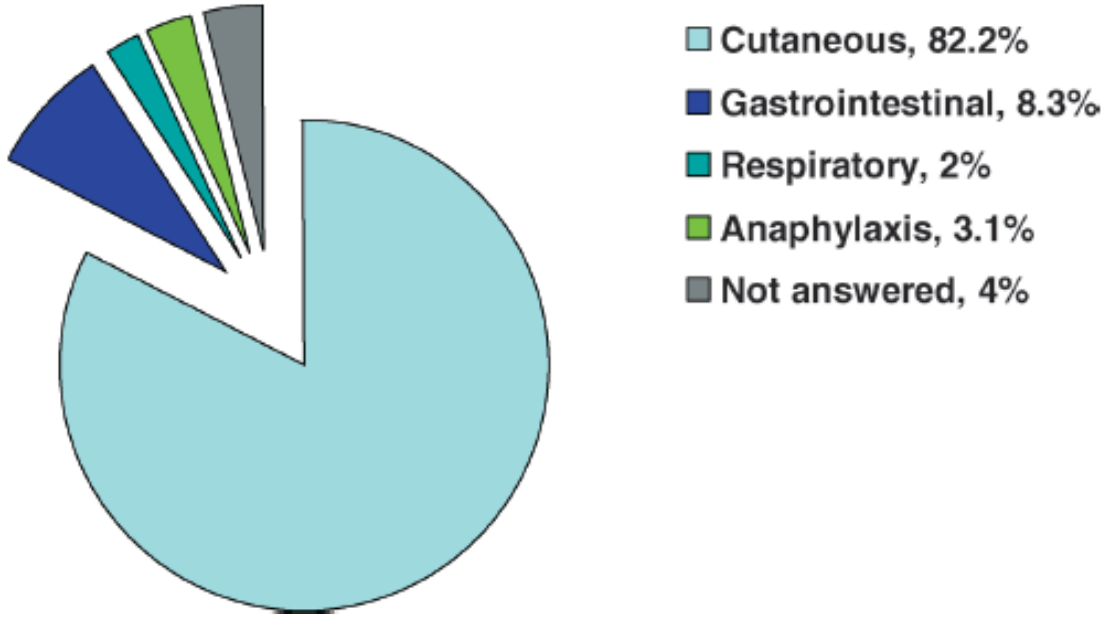


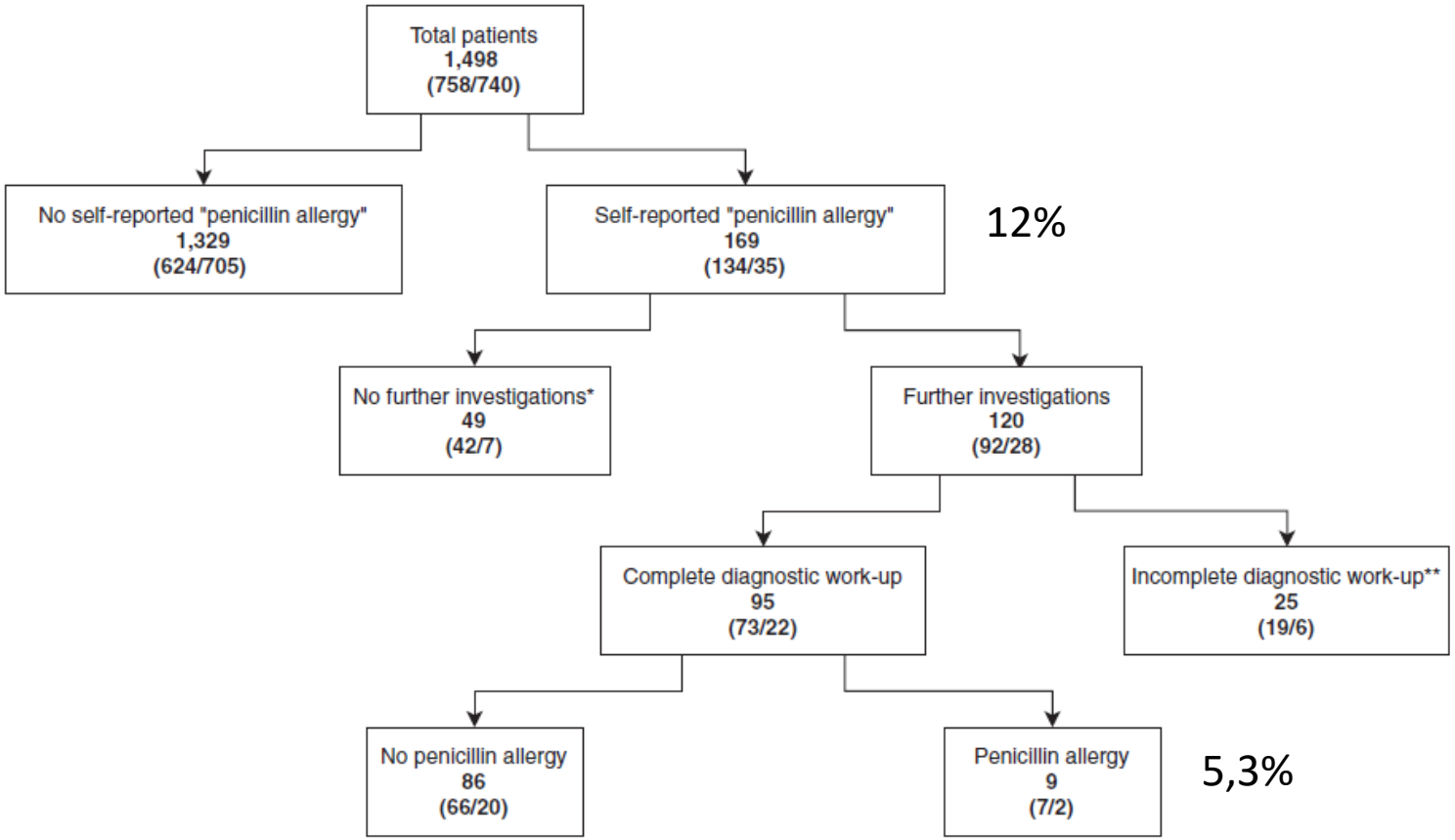
Fig. 1. Patients in the study.



1. Stone Jr CA. The challenge of de-labeling penicillin allergy. Allergy. 2020 Feb;75(2):273-288.
2. Borck JE et al. The prevalence of suspected and challenge-verified penicillin allergy in a university hospital population. Basic Clin Pharmacol Toxicol. 2006 Apr;98(4):357-62.

Allergie Amoxicilline

- Prévalence



Van Gasse AL. Prevalence of self-reported and confirmed penicillin allergy in a Belgian outpatient population. Allergy. 2020 Aug;75(8):2111-2115

Risque si étiqueté « allergique » à la pénicilline

- Etude chez 51 807 patients hospitalisés avec étiquette d'allergiques à la pénicilline. Plus de traitement IV, à large spectre, allongement durée hospitalisation

TABLE III. Case and control demographics, health care use, and outcomes

	Female subjects		Male subjects		
	Cases with history of penicillin "allergy," n = 36,583	Control subjects with no history of penicillin "allergy," n = 73,166	Cases with history of penicillin "allergy," n = 14,999	Control subjects with no history of penicillin "allergy," n = 29,998	*P* values between cases and control subjects
Total hospital days per unique subject (d), mean ± SD	6.3 ± 12.4	5.6 ± 10.1	7.1 ± 13.4	6.8 ± 12.2	Female subjects: $P < .0001$ Male subjects: $P = .0076$
Unique patients exposed to ≥1 antibiotic during the index hospitalization, no. (%)	20,471 (56.0)	39,622 (54.2)	8,332 (55.6)	16,562 (55.2)	Female subjects: $P < .0001$ Male subjects: $P = .4940$
Unique patients exposed to ≥1 antibiotic during any hospitalization, no. (%)	24,351 (66.6)	46,645 (63.8)	9,930 (66.2)	19,660 (65.5)	Female subjects: $P < .0001$ Male subjects: $P = .1600$
Courses of parenteral antibiotics used per unique subject, mean ± SD	1.8 ± 3.0	1.6 ± 2.7	2.1 ± 3.5	2.0 ± 3.3	Female subjects: $P < .0001$ Male subjects: $P = .0011$
Courses of oral antibiotics used per unique subject, mean ± SD	0.5 ± 1.2	0.4 ± 1.0	0.5 ± 1.3	0.4 ± 1.2	Female subjects: $P < .0001$ Male subjects: $P < .0001$

Macy E. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study. *JACI.* 2014;133(3):790-6.

Risque si étiqueté « allergique » à la pénicilline

- Etude chez 51 807 patients hospitalisés avec étiquette d'allergiques à la pénicilline. Plus de SARM, plus de clostridium difficile

TABLE III. Case and control demographics, health care use, and outcomes

	Female subjects		Male subjects		
	Cases with history of penicillin "allergy," n = 36,583	Control subjects with no history of penicillin "allergy," n = 73,166	Cases with history of penicillin "allergy," n = 14,999	Control subjects with no history of penicillin "allergy," n = 29,998	*P* values between cases and control subjects
C difficile prevalence, no. (%)	1,071 (2.9)	1,686 (2.3)	427 (2.9)	755 (2.5)	Female subjects: $P < .0001$ Male subjects: $P = .0561$
MRSA prevalence, no. (%)	960 (2.6)	1,631 (2.2)	566 (3.8)	1,053 (3.5)	Female subjects: $P < .0001$ Male subjects: $P = .1574$
VRE prevalence, no. (%)	234 (0.6)	337 (0.5)	68 (0.5)	128 (0.4)	Female subjects: $P = .0001$ Male subjects: $P = .6855$

Macy E. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study. *JACI.* 2014;133(3):790-6.

Risque si étiqueté « allergique » à la pénicilline

- Evaluation de la mortalité des patients « allergiques » à la pénicilline à partir d'une base de donnée Américaine

Table 2 Association of a Recorded Penicillin Allergy on All-Cause Mortality

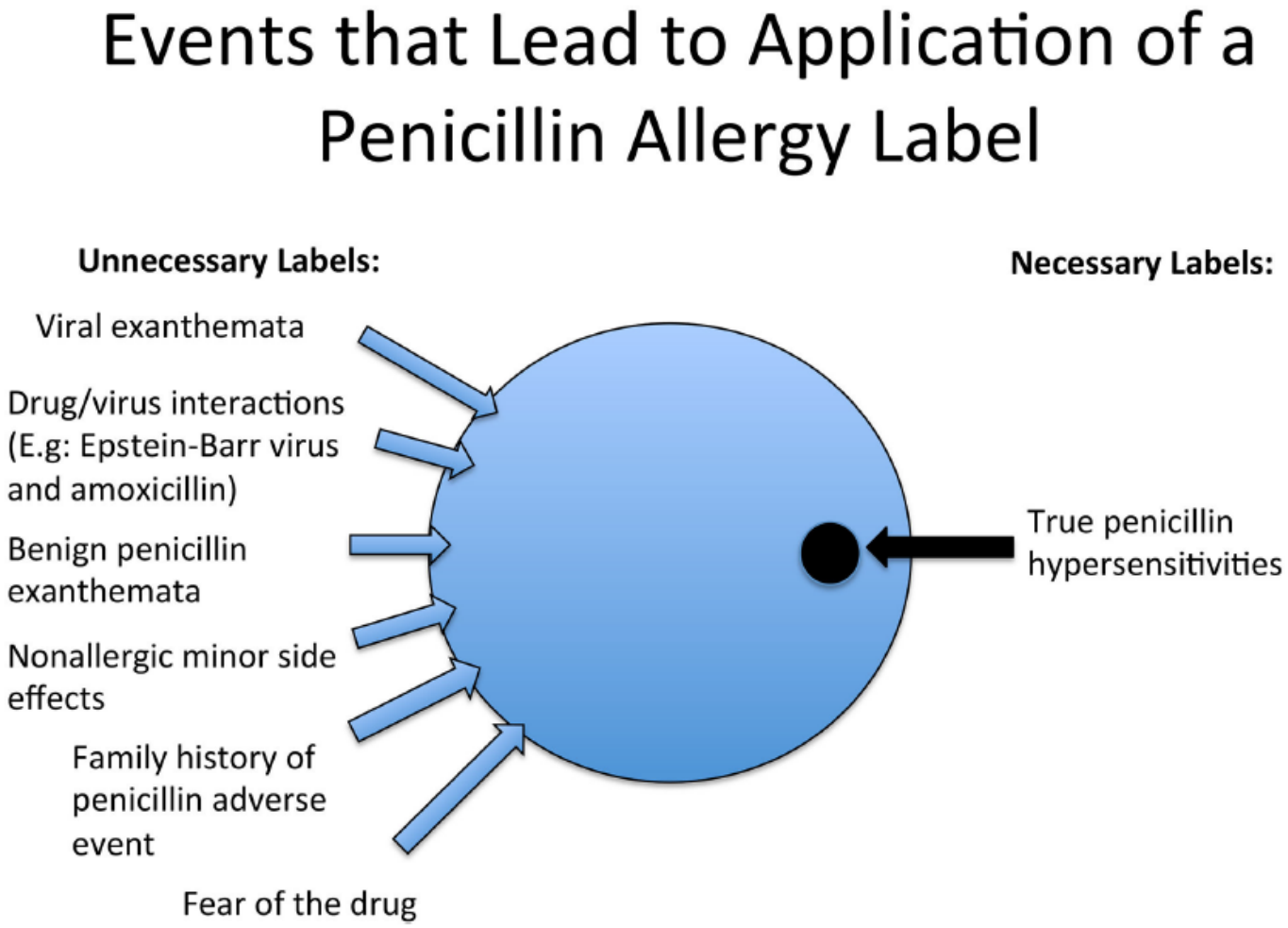
	Recorded penicillin allergy	
	Yes	No
Number of patients	63,690	237,167
Follow-up time in years (mean ± SD)	6.0 ± 4.28	6.1 ± 4.26
Number of person-years	379,369	1,441,303
All-cause mortality		
Number of deaths	8773	28,793
Age-, sex-, and entry time-matched HR (95% CI)	1.18 (1.15 to 1.21)	1.0 (reference)
Multivariable adjusted HR (95% CI)*	1.14 (1.12 to 1.17)	1.0 (reference)

Risque de mortalité augmenté de 14%

Blumenthal KG et al. Recorded Penicillin Allergy and Risk of Mortality: a Population-Based Matched Cohort Study. *Journal of general internal medicine* 2019;34(9):1685-7.

Allergie Amoxicilline

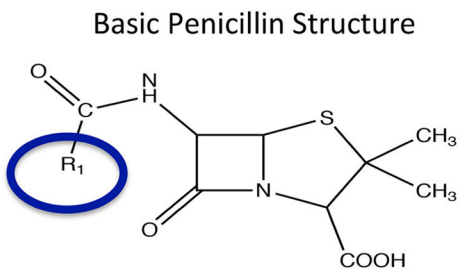
- La réalité

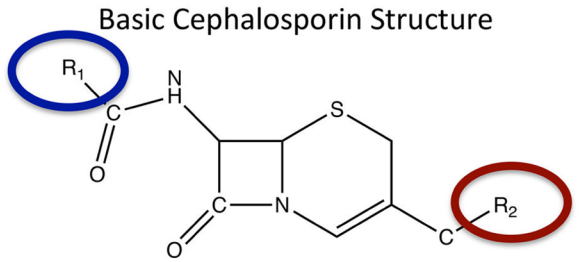


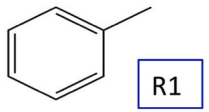
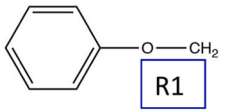
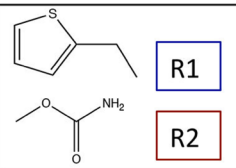
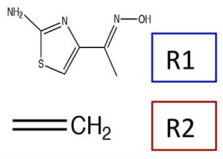
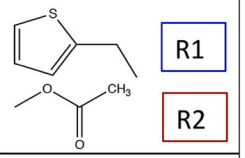
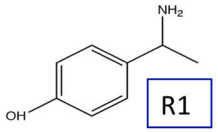
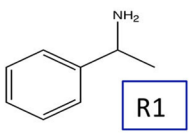
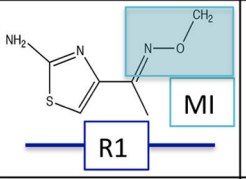
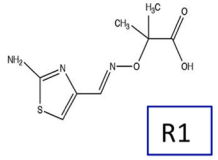
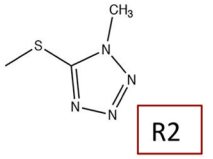
Stone Jr CA. The challenge of de-labeling penicillin allergy. Allergy. 2020 Feb;75(2):273-288.

Molécule chimique

- Bétalactamine





				
Penicillin G	**Penicillin VK**	**Cefoxitin** Cephalothin (R1) Cefuroxime (R2)	**Cefdinir** Cefixime (R1 similar, R2 identical)	**Cephalothin** Cefoxitin (R1) Cefotaxime (R2)
				
Amoxicillin Cefadroxil, Cefprozil, Ampicillin*, Cefaclor* Cephalexin*	**Ampicillin** Cefaclor, Cephalexin, Amoxicillin*,Cefadroxil* Cefprozil*	**Ceftriaxone** Cefotaxime, Cefpodoxime, Cefepime **Ceftriaxone** Cefuroxime, Cefepime Cefotaxime	**Ceftazidime** Aztreonam	**Cefotetan** Cefamandole (R2)

Stone Jr CA. The challenge of de-labeling penicillin allergy. Allergy. 2020 Feb;75(2):273-288.

Qui autoriser?

- Peuvent être d’emblée autorisés :

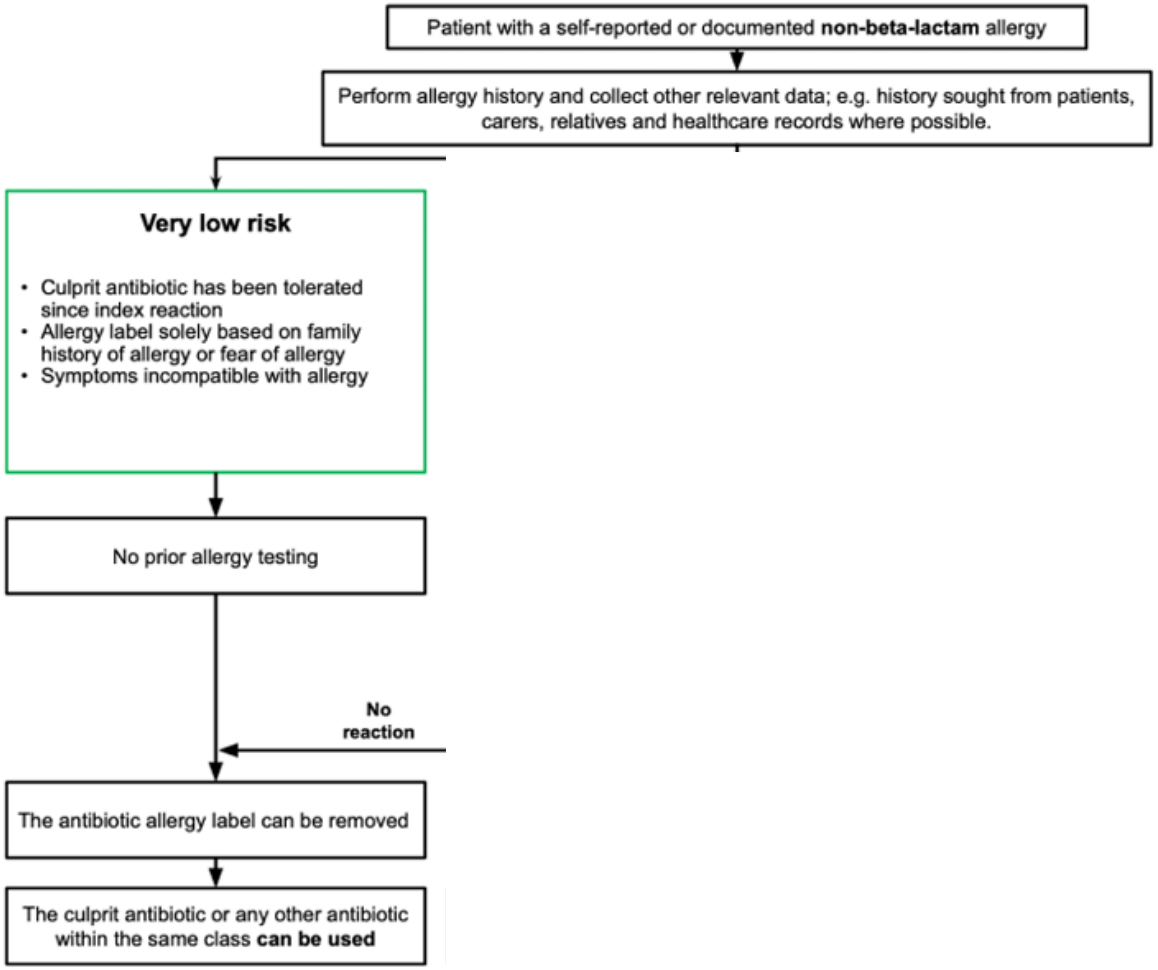
- Reprise de la pénicilline sans réaction depuis la réaction
- Antécédent familial d’ « allergie » à la pénicilline
- Réaction non évocatrice d’allergie (mycose…)

Table 1
Summary of recommendations

Topic	Recommendation	Source guideline/ adolopment status	Strength	Evidence grading (method)	Important remarks
1. General recommendations on the approach and work-up of suspected penicillin- or other β-lactam allergy					
Can nonspecialist healthcare professionals identify low-risk patients and safely perform controlled drug challenge test?	1.1. All patients labelled as 'penicillin allergic' should have a penicillin-allergy assessment using needs-based prioritization.	British (BSACI)/ adapted	Strong	Grade E (SIGN)	Dutch (SWAB) has a similar recommendation, and separately recommends performing an antibiotic allergy anamnesis.
	1.2. Nonallergists should perform controlled drug challenge test in low-risk patients in a setting where allergic reactions including anaphylaxis can be treated.	British (BSACI)/ adopted	Strong	Grade E (SIGN)	See recommendation 3.1 for further details
2. Recommendations on direct removal of the allergy label and on performing a controlled drug challenge					
When is, based on patient-derived information, a reaction not allergic and can the allergy label be removed?	2.1. We recommend that an antibiotic allergy label can be removed directly without previous allergy testing when one of the following criteria applies (very low* risk of antibiotic allergy): > The culprit drug has been used since the index reaction without occurrence of an allergic reaction. > The allergy label was solely based on positive family history of allergy or on fear of allergy. > The reported signs and symptoms are not compatible with an allergic reaction (i.e. GI complaints only, palpitations, blurred vision, headache, candidiasis).	Dutch (SWAB)/ adapted	Strong	Moderate (GRADE)	*Very low risk was further defined by the guideline panel. The recommendation extents to all settings otherwise defined in this guideline as very low risk (of developing an allergic reaction upon exposure)

Et les autres?

Joean O et al. ESCMID clinical guidelines on the evaluation and management of a reported antibiotic allergy. Clin Microbiol Infect. 2026 Feb 16:S1198-743X(26)00069-8.



* For certain agents, such as vancomycin, teicoplanin, quinolones, and amphotericin B, adverse reactions often result from non–IgE-mediated mast cell degranulation, which is typically infusion rate–dependent

** **Patients unsuitable for challenge test:** Severe or uncontrolled airways disease, Severe cardiac disease including aortic stenosis, Pregnancy, Acutely unwell or clinically unstable, Unable to provide informed consent, Currently taking high-dose corticosteroids or antihistamines

***Acute urticaria typically appear <1 hour after exposure to the culprit, and disappear again < 1 day: Some guidelines and clinical rules may classify isolated urticaria (no other symptoms) and/or focal (not generalized) urticaria as non-severe or benign, i.e. as low risk. The guideline panel decided to classify urticaria as high risk based on adoption from the BSACI guideline, but acknowledges limited evidence. In case of clinical need to use a specific antibiotic, a controlled drug challenge test can be considered and discussed in a multidisciplinary team.

Fig. 2. Flow diagram for the approach towards non−β-lactam antibiotics. Legend: ßL, β-lactam; CDCT, controlled drug challenge test; SCAR, severe cutaneous adverse reaction.

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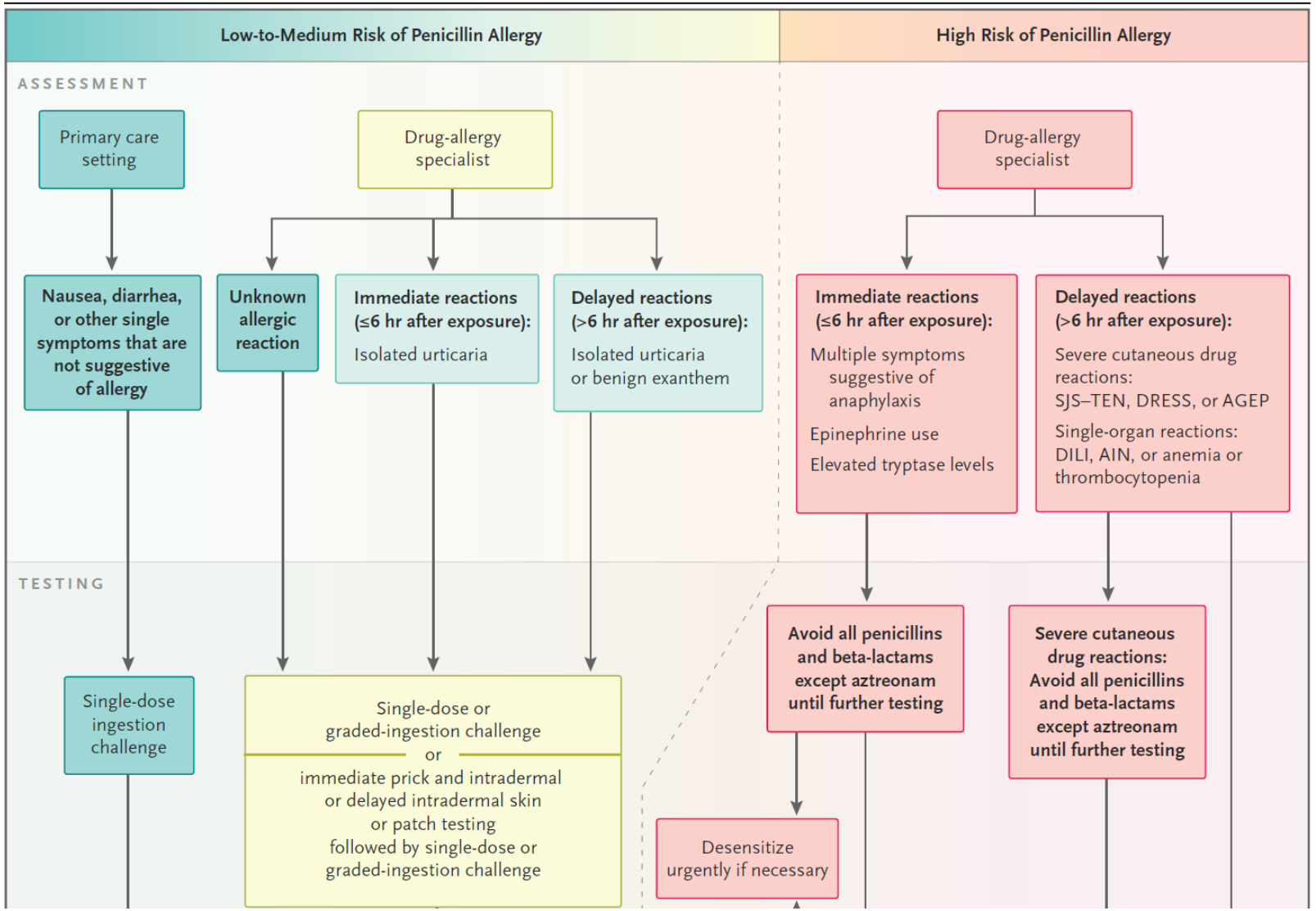
La prise en charge en allergologie



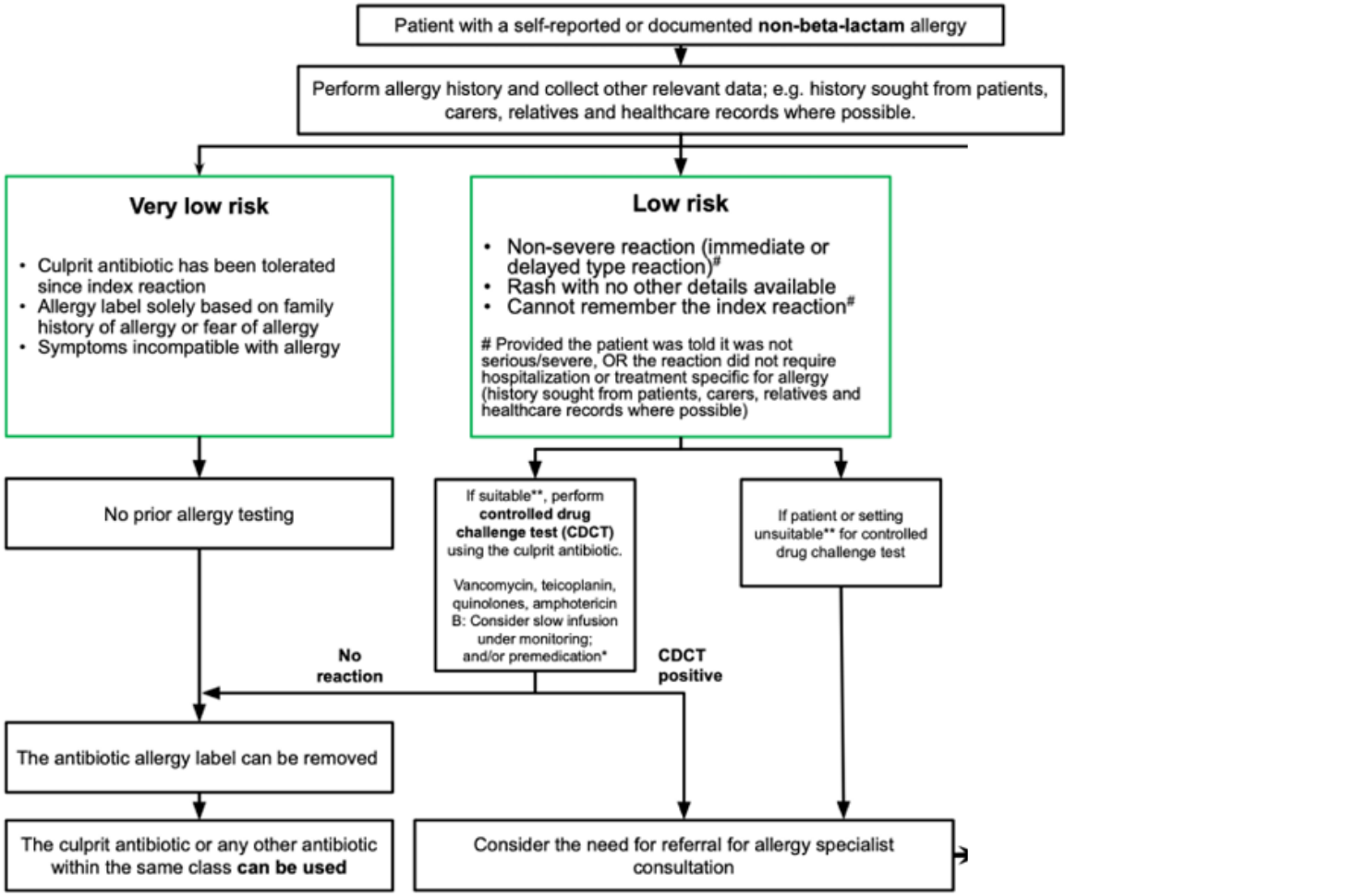
Castells M, Khan DA, Phillips EJ. Penicillin Allergy. *The New England journal of medicine* 2019;381(24):2338-51

Et les autres?

- Réaction inconnue
- Prurit
- Urticaire
- Œdème
- Eczéma
- Nausée/vomissement
- Diarrhée
- Réaction retardée sans argument pour toxidermie sévère

Which patients with a reported ß-lactam antibiotic allergy have a low risk of an actual allergy and can therefore be re-exposed to the culprit antibiotic?	2.2.a We recommend that patients with a history of a 'low-risk' index reaction can receive a controlled drug challenge of the culprit ß-lactam antibiotic in an appropriate clinical setting: > Patients with a history of a nonsevere cutaneous reaction >5 years ago (independent of the type—immediate or delayed—of the reaction) > The patient reports only a rash with no other history available[#] > The patient cannot remember the index reaction symptoms[#] [#]Under the condition that the patient was either told it was not serious/severe AND/OR the reaction did not require hospitalization or treatment specific for allergy	Dutch (SWAB) and British (BSACI)/ adapted	Strong	Low (GRADE)	This recommendation was the result of a fused adaptation of three recommendations: (I) Dutch (SWAB): we suggest that patients with suspected nonsevere, immediate-type index reactions that occurred >5 years ago, can receive a therapeutic dose of the culprit ß-lactam antibiotic in a controlled setting. (II) Dutch (SWAB): we suggest that patients with suspected nonsevere, delayed-type index reactions that occurred >1 year ago can receive the culprit β-lactam antibiotic without formal allergy testing. (III) British (BSACI) GL: all patients identified as low risk for true penicillin allergy should be offered direct drug provocation testing (controlled drug challenge test), providing no exclusion criteria are met
	Recommendation 2.2.b We suggest that hospitalized patients with a suspected nonsevere, delayed-type index reaction that occurred >5 years ago (low-risk category) can receive the culprit β-lactam antibiotic without controlled drug challenge testing.* *Follow-up is warranted; if no reaction occurs during treatment, the label should be removed	Dutch (SWAB), British (BSACI) and supported by USA (AAAAI-ACAAI)/ adapted	Weak	Low (GRADE)	This recommendation is aimed at—and can be applied to—a subpopulation of the patient population captured in recommendation 2.2.a. Importantly, both recommendations must not be read as contradictory guidance. Rather, recommendation 2.2.b must be read as a specific additional recommendation in this section, that

Joean O et al. ESCMID clinical guidelines on the evaluation and management of a reported antibiotic allergy. Clin Microbiol Infect. 2026 Feb 16:S1198-743X(26)00069-8.



* For certain agents, such as vancomycin, teicoplanin, quinolones, and amphotericin B, adverse reactions often result from non–IgE-mediated mast cell degranulation, which is typically infusion rate–dependent

**** Patients unsuitable for challenge test:** Severe or uncontrolled airways disease, Severe cardiac disease including aortic stenosis, Pregnancy, Acutely unwell or clinically unstable, Unable to provide informed consent, Currently taking high-dose corticosteroids or antihistamines

*****Acute urticaria typically appear <1 hour after exposure to the culprit, and disappear again < 1 day:** Some guidelines and clinical rules may classify isolated urticaria (no other symptoms) and/or focal (not generalized) urticaria as non-severe or benign, i.e. as low risk. The guideline panel decided to classify urticaria as high risk based on adoption from the BSACI guideline, but acknowledges limited evidence. In case of clinical need to use a specific antibiotic, a controlled drug challenge test can be considered and discussed in a multidisciplinary team.

Fig. 2. Flow diagram for the approach towards non–β-lactam antibiotics. Legend: ßL, β-lactam; CDCT, controlled drug challenge test; SCAR, severe cutaneous adverse reaction.

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Allergie Amoxicilline

- Le « single challenge »

Figure. CONSORT Diagram

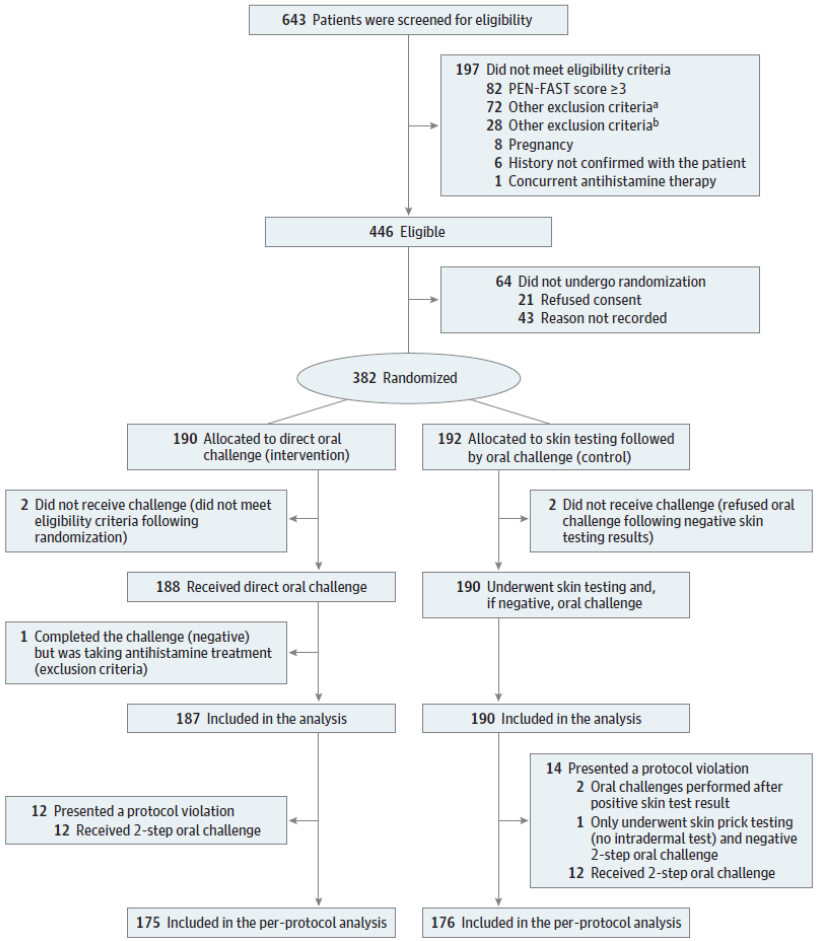


Table 1 PEN-FAST, penicillin allergy clinical decision rule

PEN	Penicillin allergy reported by patient	
F	Reaction ≤5 years	2 points
A	Anaphylaxis/or angioedema	2 points
S	Severe cutaneous adverse reaction	
T	Treatment required for reaction	1 points
	Total points	

Points	Interpretation
0	Very low risk (<1%)
1–2	Low risk (5%)
3	Moderate risk (20%)
4–5	High risk (50%)

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
Timing		
<1 h	6 (27)	5 (21)
1-12 h	9 (41)	9 (38)
13-24 h	3 (14)	2 (8)
25-48 h	2 (9)	4 (17)
2-5 d	2 (9)	4 (17)
Time since oral challenge, median (IQR), h	4.1 (0.7-16.7)	6.9 (2.1-35.1)
Severity[a]		
Grade 1	17 (77)	16 (67)
Grade 2	5 (23)	8 (33)
Degree of causality[b]		
Certain	2 (9)	1 (4)
Probable/likely	6 (27)	4 (17)
Possible	7 (32)	5 (21)
Unlikely	6 (27)	14 (58)
Unassessable/unclassifiable	1 (5)	0
Management		
None	13 (59)	16 (67)
Rechallenge	0	1 (4)
Withdrew from study	0	0
Other[c]	0	2 (8)
Drug therapy		
Oral antihistamine	9 (41)	6 (25)
Other[d]	2 (9)	5 (21)
Emergency department referral	0	0
Intensive care unit referral	0	0
Calculated duration of adverse event, median (IQR), h	11 (1.2-48.3)	60 (2-76)
Recovered/resolved	22 (100)	20 (83)[e]

Copaescu AM et al. Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy: The PALACE Randomized Clinical Trial. JAMA Intern Med. 2023 Sep 1;183(9):944-952

Etude prospective Toulousaine

- 1047 patients avec réintroduction dose unique en cas de réaction médicamenteuse

Critères d'inclusion :

-âge > 14 ans

-antécédent d'une réaction compatible avec une allergie

-faible risque d'allergie vraie = réaction de grade I

-risque élevé d'allergie pour la réintroduction d'alternative = réaction grade II ou III

-tests cutanés négatifs

Critères d'exclusion:

-tests cutanés positifs

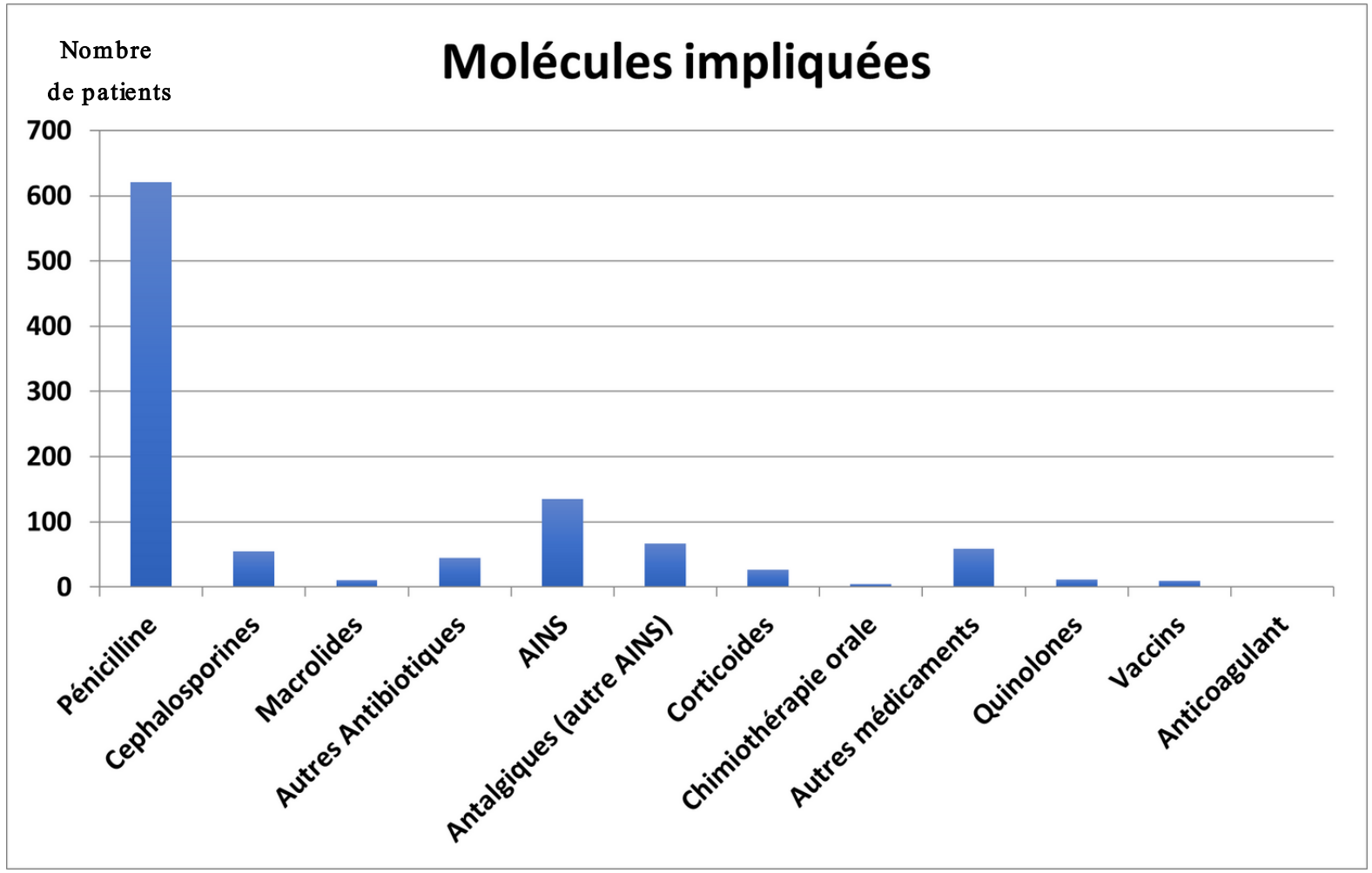
-toxidermie sévère

-asthme non contrôlé

-infection sévère en cours

-grossesse

Etude prospective Toulousaine

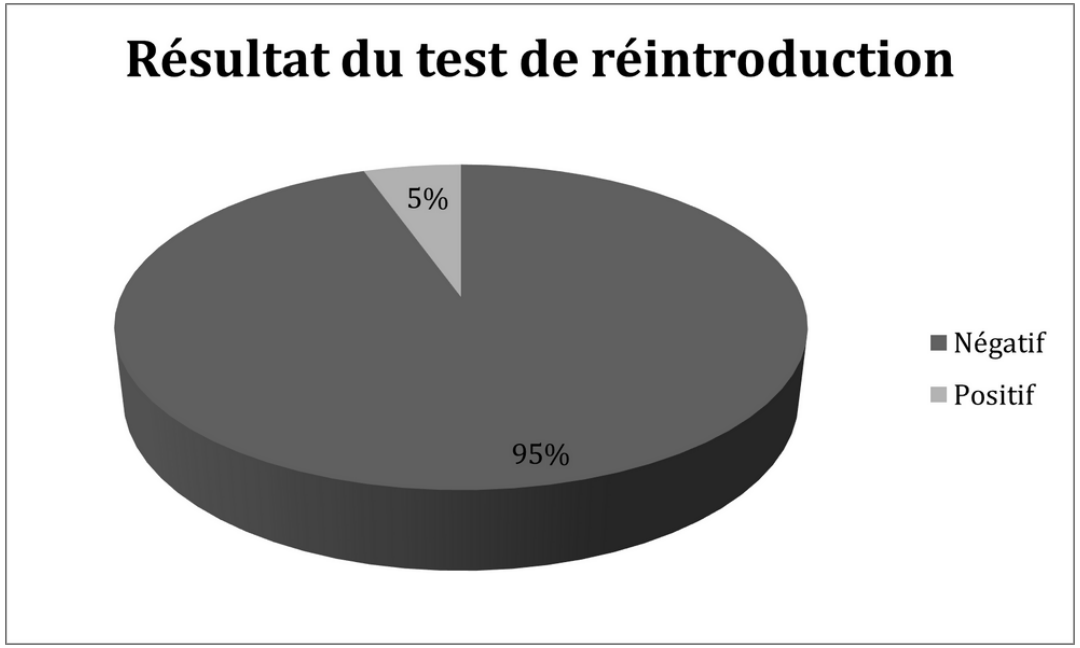


Etude prospective Toulousaine

Chronologie- Réaction index (m/a)	
Récent (<12 m)	168 (16)
Intermédiaire (1-5 a)	155 (14,8)
Ancien (>5 a)	458 (43,7)
Inconnu	266 (25,4)
Délai de survenue en heure	
<1h	163 (15,6)
1-6h	132 (12,6)
6-24h	132 (12,6)
>24h	157 (14,9)
Inconnu	463 (44,2)

Tests cutanés	
Non réalisés	246 (23,5)
Réalisés	801 (76,5)
Négatif	796 (99,4)
Positif	5 (0,62)

Etude prospective Toulousaine



	Réactions immédiates (N = 32)	*Réactions retardées (N = 25)*
Signes cutanés		
Léger	12 (21)	7 (12,3)
Modéré	15 (26,3)	16 (28,1)
Sévère	0	1 (1,7)
Signes respiratoires		
Léger	2 (3,5)	0
Modéré	5 (8,8)	1 (1,7)
Sévère	0	0
Signes digestifs		
Léger	2 (3,5)	1 (1,7)
Modéré	0	3 (5,3)
Sévère	0	1 (1,7)
Signes neurologiques		
Léger	3 (5,3)	1 (1,7)
Modéré	1 (1,7)	2 (3,5)
Sévère	0	1 (1,7)

considered. (high risk for an antibiotic allergy)					
3. Details of performing a controlled drug challenge					
What are the minimum safety requirements for direct controlled drug challenge test?	3.1. We recommend that the principles for the conduct of a drug provocation test (controlled drug challenge test) be applied as follows in patients identified as low-risk for penicillin allergy: - Inform the patient and obtain consent - CDCT should be performed in a setting where vital signs can be measured, and allergic reactions can be treated. - Single-dose or graded-dose CDCT can be used depending on local preference o Single-dose CDCT: Administer 100% of a full dose of the index antibiotic, preferably orally, or via an alternative route if necessary. If the index drug is unknown but probably a penicillin, amoxicillin (500 mg for adults) should be used ○ Graded-dose CDCT according to local protocol* - Should symptoms consistent with anaphylaxis develop during the test, treat the patient in accordance with local protocol or national guidelines for the management of anaphylaxis - The patient should be observed for 1 h after the last dose. - The patient should be provided with clear written instructions about what to do if symptoms develop after leaving the hospital. - A system should be in place to inform the GP and other relevant healthcare professionals about the result of the CDCT. The patient should receive clear (preferably) written information about the test result and its implications	British (BSACI)/ adapted	Strong	Grade E (SIGN)	Amoxicillin 500 mg dose taken from another PICO/key question and incorporated here. In the text, brief note on absence of evidence for either graded or full dose challenge. *Graded-dose CDCT suggested by the BSACI 2022 Guideline [8]: Administer 10% of a full dose of the index antibiotic (i.e. 50 mg amoxicillin for adults); observe for 30 min; administer 50% of a full dose of the index antibiotic (i.e. 250 mg amoxicillin for adults); observe for 30 min; administer remainder of a full dose of the index antibiotic (i.e. 200 mg amoxicillin for adults); observe for 60 min.

Joean O et al. ESCMID clinical guidelines on the evaluation and management of a reported antibiotic allergy. Clin Microbiol Infect. 2026 Feb 16:S1198-743X(26)00069-8.

Qui ne pas réintroduire?

Which patients with a reported ß-lactam antibiotic allergy have a low risk of an actual allergy and can therefore be re-exposed to the culprit antibiotic?	2.3. We recommend against re-exposure to the culprit drug class in patients with severe delayed-type index reactions (high risk for an antibiotic allergy).	Dutch (SWAB)/ adapted	Strong	GPS	The sentence 'In the absence of acceptable alternative antimicrobial treatment, the use of the culprit should be discussed in a multidisciplinary team' will be added as a separate statement in the text of the GL-document.
	2.4. We recommend that patients with suspected nonsevere, immediate-type index reactions that occurred ≤5 years ago OR a suspected severe immediate-type index reaction irrespective of time elapsed, should be referred for formal allergy work up before re-exposure can be considered. (high risk for an antibiotic allergy)	Dutch (SWAB)/ adapted	Strong	Low (GRADE)	

Joean O et al. ESCMID clinical guidelines on the evaluation and management of a reported antibiotic allergy. Clin Microbiol Infect. 2026 Feb 16:S1198-743X(26)00069-8.

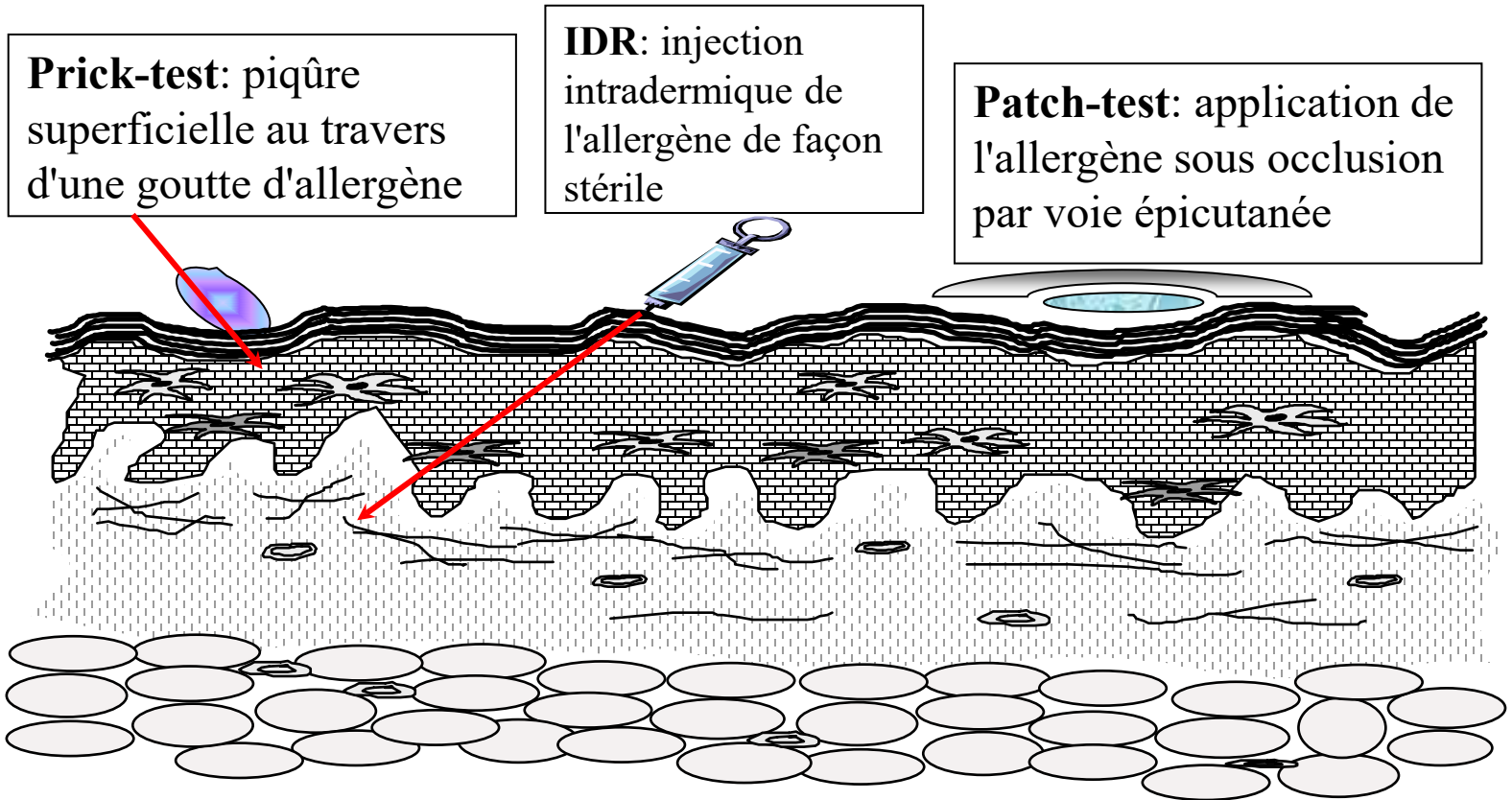
Qui explorer?

- Avis allergologique ou dermatologique impératif:

- Anaphylaxie sévère
- Syndrome de Stevens Johnson
- Syndrome de Lyell
- DRESS syndrome
- PEAG
- Atteinte systémique: cytolyse hépatique, néphropathie, cytopénie…

Si suspicion anaphylaxie ou toxidermie

- Tests cutanés
- Prick tests
- IDR



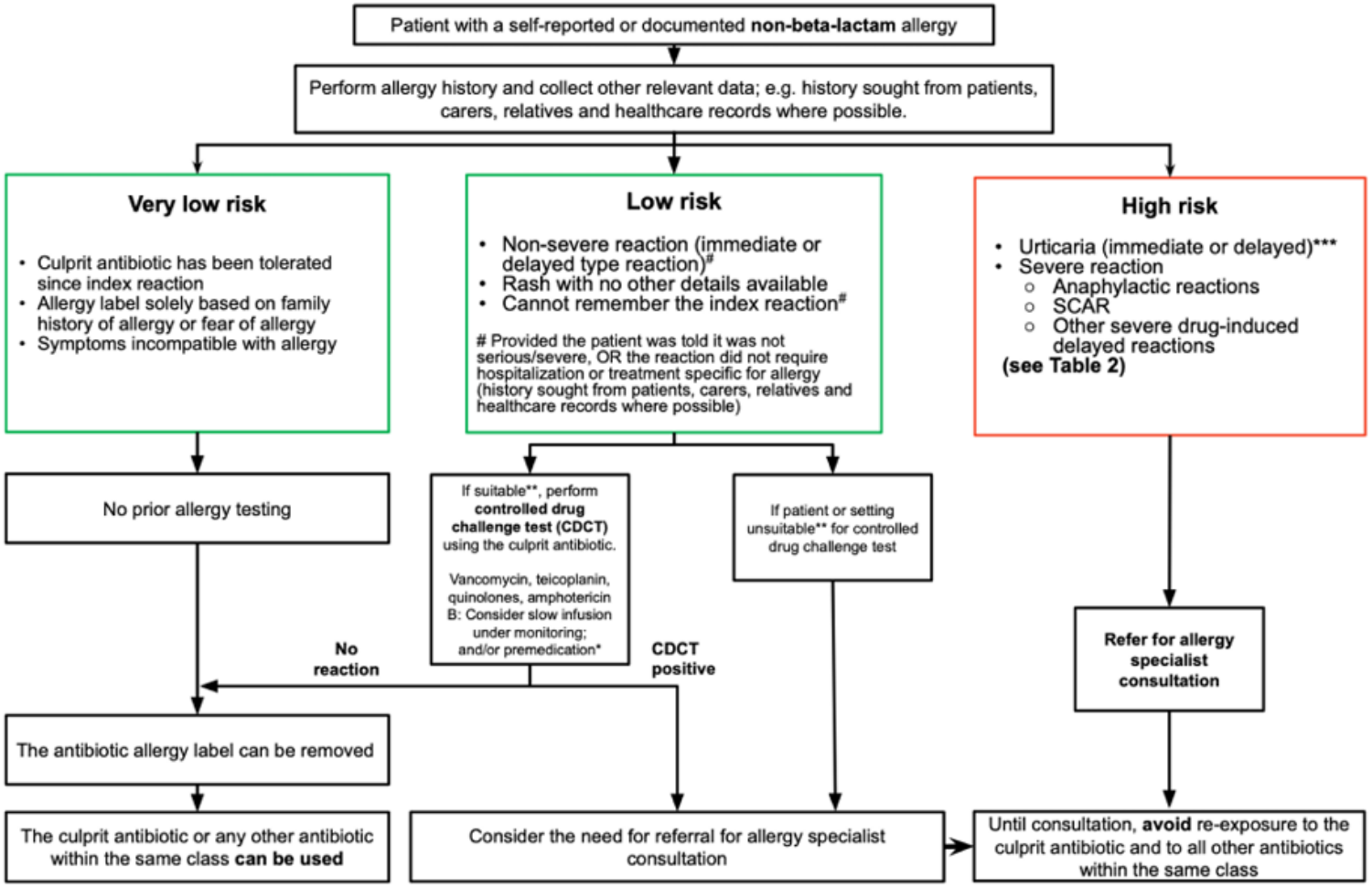
La prise en charge de l'allergologue

- Concentrations non-irritantes des IDR

TABLE 4 Highest nonirritating concentrations recommended for both prick and intradermal testing with beta-lactams

Hapten	Concentration
Benzylpenicilloyl-poly-L-lysine	6.0×10^{-5} mol/L
Benzylpenicilloyl-octa-L-lysine	8.64×10^{-5} mol/L
Sodium benzylpenilloate	1.5×10^{-3} mol/L
Benzylpenicillin	10 000 IU/mL
Amoxicillin and other semi-synthetic penicillins	20 mg/mL*
Cefepime	2 mg/mL
Other cephalosporins	20 mg/mL
Clavulanic acid	20 mg/mL
Aztreonam	2 mg/mL
Imipenem-cilastatin	0.5 mg/mL-0.5 mg/mL
Meropenem and ertapenem	1 mg/mL

Romano A et al. Towards a more precise diagnosis of hypersensitivity to beta-lactams - an EAACI position paper. *Allergy* 2020;75(6):1300-15.



* For certain agents, such as vancomycin, teicoplanin, quinolones, and amphotericin B, adverse reactions often result from non–IgE-mediated mast cell degranulation, which is typically infusion rate–dependent

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Et l’allergie croisée?

Should multiple-day challenges be performed in patients with reported penicillin allergy?	3.2. We recommend against the routine use of multiple-day drug challenge testing in the evaluation of penicillin allergy.	USA (AAAAI-ACAAI)	Strong	Not graded	
4. Cross-allergy between β-lactams Part I. Penicillins)					
In which patients with a reported allergy to a penicillin, a different penicillin can be administered with an acceptable low risk of an allergic reaction?	4.1. We recommend that in patients with a suspected immediate-type allergy to penicillins, irrespective of severity, that occurred ≤5 years ago, all other penicillins should be avoided	Dutch (Dutch (SWAB)/adopted	Strong	Low (GRADE)	
	4.2. We suggest that in patients with a suspected nonsevere immediate-type allergy to a certain penicillin, that occurred >5 years ago (low risk), a controlled drug challenge test with other penicillins can be performed based on indication.	Dutch (SWAB)/ adapted	Weak	Low (GRADE)	See corresponding recommendation 2.2a on using the culprit penicillin in case of low-risk allergy
	4.3. We suggest that in patients with a suspected nonsevere delayed-type allergy to penicillins that occurred >5 years ago (low risk), all other penicillins can be used in a controlled setting.	Dutch (SWAB)/ adapted	Weak	Low (GRADE)	If doubt between immediate-type or delayed-type use recommendation above, perform a controlled drug challenge/controlled drug challenge test

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		adolopment status		grading (method)	
Part II. Penicillins vs. cephalosporins or carbapenems					
In which patients with a reported immediate-type allergy to a penicillin, a cephalosporin can be administered with an acceptably low risk of an allergic reaction?	4.4. We recommend that patients with a suspected or proven immediate-type allergy to penicillins* can receive cephalosporins, but only those with dissimilar side chains.	Dutch (SWAB)/ adapted	Strong	Moderate (GRADE)	*With the exception of patients with severe anaphylaxis, in which case the panel recommends to seek expert evaluation first
In which patients with a reported delayed-type allergy for a penicillin, a cephalosporin can be administered with an acceptably low risk of an allergic reaction?	4.5. We suggest that patients with suspected or proven nonsevere, delayed-type allergy to penicillins, can receive cephalosporins with dissimilar side chains, irrespective of time elapsed since the index reaction.	Dutch (SWAB)/ adopted	Weak	Low (GRADE)	
In which patients with a reported immediate-type allergy to a penicillin, a cephalosporin can be administered with an acceptably low risk of an allergic reaction?	4.6. Cefazolin does not share any side chains with the currently available penicillins and can be used in cases of suspected or proven immediate-type allergy to a penicillin, irrespective of severity or time elapsed since the index reaction.	Dutch (SWAB)/ adapted	Strong	Moderate (GRADE)	*With the exception of patients with severe anaphylaxis, in which case the panel recommends to seek expert evaluation first
In which patients with a reported allergy to penicillin, a monobactam or carbapenem can be administered with an acceptable low risk of an allergic reaction?	4.7. We recommend that the following patients can receive any monobactam or carbapenem, without prior allergy testing: - patients with suspected or proven immediate-type penicillin allergy (low and high risk*) - nonsevere, delayed-type penicillin allergy (low risk)	Dutch (SWAB)/ adapted	Strong	Low (GRADE)	*With the exception of patients with severe anaphylaxis, in which case the panel recommends seeking expert evaluation first.

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Table 3
Risk of cross-allergy between β-lactam antibiotics

Beta-lactam Antibiotic	Amoxicillin	Penicillin G	Penicillin V	Flucloxacillin	Feneticillin	Piperacillin	Cefalexin	Cefazolin	Cefalothin	Cefuroxime	Cefaclor	Cefamandole	Ceftibuten	Ceftriaxone	Cefotaxime	Ceftazidime	Cefepime	Cefiderocol	Ceftaroline	Ceftolozane	Meropenem	Imipenem	Ertapenem	Aztreonam
Amoxicillin	■	■	■	■	■	■	■	✓	✓	✓	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Penicillin G	■	■	■	■	■	■	■	✓	✓	✓	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Penicillin V	■	■	■	■	■	■	■	✓	✓	✓	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Flucloxacillin	■	■	■	■	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Feneticillin	■	■	■	■	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Piperacillin	■	■	■	■	■	■	■	✓	✓	✓	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cefalexin	■	■	■	✓	✓	■	■	✓	✓	✓	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cefazolin	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cefalothin	✓	✓	✓	✓	✓	✓	✓	✓	■	■	✓	✓	✓	✓	■	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cefuroxime	✓	✓	✓	✓	✓	✓	✓	✓	■	■	✓	✓	✓	■	■	■	■	■	■	■	✓	✓	✓	■
Cefaclor	■	■	■	✓	✓	■	■	✓	✓	✓	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cefamandole	■	■	■	✓	✓	■	■	✓	✓	✓	■	■	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Ceftibuten	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Ceftriaxone	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Cefotaxime	✓	✓	✓	✓	✓	✓	✓	✓	■	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Ceftazidime	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Cefepime	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Cefiderocol	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Ceftaroline	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Ceftolozane	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■
Meropenem	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	■	■	✓
Imipenem	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	■	■	✓
Ertapenem	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	■	■	✓
Aztreonam	✓	✓	✓	✓	✓	✓	✓	✓	✓	■	✓	✓	■	■	■	■	■	■	■	■	✓	✓	✓	■

■	Cross-tabulation similar
■	Allergy possible based on the formation of Penicilloyl-poly-L-lysine (PPL)
■	Potential cross allergy based on similarity in R1 or R2 side chain and/or clinical studies
■	Potential cross allergy based on identical in R1 or R2 side chain
✓	No risk of a cross allergic reaction

Réaction croisée Amoxicilline-C3G

- Prévalence

Table 1 Rate of Cephalosporin Positive Skin Tests in Patients with Confirmed IgE-Mediated Hypersensitivity to Penicillins and Rate of Cephalosporin Positive Graded Challenges in Those with Negative Skin Tests to the Cephalosporin Concerned

Study (Reference)	Patients, n	Skin Testing				Challenge		
		Penicillin Reagents	Tested Cephalosporin(s)	Positive Patients,* n (%)	Positive Cephalosporins,¶ (n Positivities)	Administered Cephalosporin(s)	Administration Route	Reactions, n/ Challenges, (%)
Audicana et al[27]	34	PPL, MDM, AM, AX	Cephalexin, ceftazidime	5 (14.7)	Cephalexin (5)	Cephalexin, ceftazidime	Oral, intravenous	0/29 0/30
Novalbos et al[28]	41	PPL, MDM, BP, AX	Cefazolin, cefuroxime, ceftriaxone	0	None	Cefazolin, cefuroxime, ceftriaxone	Intramuscular, intramuscular, intramuscular	0/41 0/41 0/41
Romano et al[29]	128	PPL, MDM, BP, AM, AX	Cephalothin, cefamandole, cefuroxime, ceftazidime, ceftriaxone, cefotaxime	14 (10.9)	Cefamandole (9), cephalothin (8), ceftriaxone (3), cefuroxime (2), ceftazidime (2), cefotaxime (2)	Cefuroxime axetil, ceftriaxone	Oral, intramuscular	0/101 0/101
Caimmi et al[30]	69	PPL, MDM, BP, AX	Cefuroxime	0	None	Cefuroxime axetil	Oral	2/69 (2.9)
Romano et al[31]	252	PPL/BP-OL, MDM/MD, BP, AM, AX, PP	Cephalexin, cefadroxil, cefaclor, cefamandole, cefuroxime, ceftazidime, ceftriaxone, cefotaxime, cefepime	84 (33.3)	Cefadroxil, (62) cefaclor (38), cephalexin (33), cefamandole (11), ceftriaxone (6), cefotaxime (3), cefuroxime (2)	Cefaclor, cefadroxil cefuroxime axetil, ceftriaxone	Oral, oral, oral, intramuscular	3/170 (1.8) 4/167 (2.4) 0/244 0/244
Rodriguez-Bouza[32]	29	PPL/BP-OL, MDM/MD, BP, AM, AX	Cefuroxime	1 (3.4)	Cefuroxime (1)	Cefuroxime	Intramuscular	2/28 (7.1)
Romano et al[33]	131	BP-OL, MD, BP, AM, AX, PP	Cefazolin, ceftibuten	1 (0.7)	Cefazolin (1), ceftibuten (1)	Cefazolin, ceftibuten	Intramuscular, oral	0/129 0/129
Sánchez de Vicente et al[34]	137	PPL, MDM, AX	Cefuroxime, ceftriaxone	2‡ (1.5)	Cefuroxime (1), ceftriaxone (1)	Cefuroxime, ceftriaxone	Oral, intravenous	0/136 0/125
Total	**821**			**107 (13)**				**11/1825 (0.6)**

Caruso C et al. β-Lactam Allergy and Cross-Reactivity: A Clinician's Guide to Selecting an Alternative Antibiotic. J Asthma Allergy. 2021 Jan 18;14:31-46

Réaction croisée Amoxicilline-C3G

- Prévalence

TABLE II. AR of cross-reactivity to cephalosporins in penicillin-allergic patients

Cephalosporin			Cross-reactivity		
Generation	Name	No. of studies	n/N	AR in % (95% CI)*	Proportion of patients tested with DPT
First	Cephalexin	8	97/693	14.00 (11.61-16.79)	288 of 693 (42%)
	Cefadroxil	6	95/557	12.65 (5.85-25.26)	392 of 557 (70%)
	Cephalothin	3	9/184	4.89 (2.56-9.13)	2 of 184 (1%)
	Cefazolin	3	1/75	1.33 (0.19-8.86)	41 of 75 (55%)
	Cefatrizine	2	1/56	1.79 (0.25-11.61)	12 of 56 (21%)
	Cephaloridine	1	0/17	0.0 (0.0-19.5)†	17 of 19 (89%)‡
Second	Cefamandole	6	23/474	4.85 (3.25-7.20)	43 of 474 (9%)
	Cefaclor	7	90/679	13.25 (10.91-16.02)	363 of 679 (53%)
	Cefuroxime	14	16/984	0.96 (0.26-3.51)	835 of 993 (84%)
	Cefprozil	1	3/39	7.69 (1.62-20.87)†	39 of 53 (74%)
Third	Cefpodoxime	1	1/71	1.4 (0.0-7.6)†	71 of 71 (100%)
	Ceftazidime	4	2/433	0.31 (0.02-4.72)	27 of 433 (6%)
	Cefotaxime	4	5/436	1.15 (0.48-2.72)	0 of 436 (0%)
	Cefixime	7	2/324	0.62 (0.15-2.43)	218 of 324 (67%)
	Ceftriaxone	9	13/843	0.99 (0.25-3.87)	659 of 843 (78%)
	Ceftibuten	3	0/153	0.0 (0.0-2.4)†	76 of 153 (50%)
Fourth	Cefepime	2	1/285	0.31 (0.01-10.32)	1 of 285 (0.4%)

Picard M et al. Cross-Reactivity to Cephalosporins and Carbapenems in Penicillin-Allergic Patients: Two Systematic Reviews and Meta-Analyses. JACI in Practice. Nov-Dec 2019;7(8):2722-2738.e5

Réaction croisée Amoxicilline-C3G

- Prévalence

TABLE III. Cross-reactivity to cephalosporins in penicillin-allergic subjects according to the type of penicillin allergy

Cephalosporin		Type of penicillin allergy			
		IgE		T-cell	
Generation	Name	n/N	AR in % (95% CI)	n/N	AR in % (95% CI)
First	Cephalexin	40/310	12.9 (9.6-17.1)	57/383	14.9 (11.7-18.8)
	Cefadroxil	75/287	26.1 (21.4-31.5)	20/270	7.4 (4.8-11.2)
	Cephalothin	8/128	6.3 (2.7-11.9)	1/56	1.8 (0.3-11.6)
	Cefazolin	0/47	0.0 (0.0-7.5)	1/26	3.8 (0.0-19.6)
	Cefatrizine	NA	NA	1/56	1.8 (0.3-11.6)
	Cephaloridine	0/17	0.0 (0.0-19.5)	NA	NA
Second	Cefamandole	22/418	5.3 (3.5-7.9)	1/56	1.8 (0.3-11.6)
	Cefaclor	41/282	14.5 (10.9-19.2)	49/397	12.3 (9.5-16.0)
	Cefuroxime	7/490	1.1 (0.2-5.8)	7/423	0.5 (0.0-8.0)
	Cefprozil	NA	NA	3/39	7.7 (1.6-20.9)
Third	Cefpodoxime	NA	NA	1/71	1.4 (0.0-7.6)
	Ceftazidime	2/433	0.3 (0.0-4.7)	NA	NA
	Cefotaxime	5/380	1.3 (0.6-3.1)	0/56	0.0 (0.0-6.4)
	Cefixime	0/39	0.0 (0.0-9.0)	2/285	0.7 (0.2-2.8)
	Ceftriaxone	12/474	2.5 (1.4-4.4)	1/367	0.2 (0.0-9.5)
	Ceftibuten	NA	NA	0/153	0.0 (0.0-2.4)
Fourth	Cefepime	1/285	0.3 (0.0-10.3)	NA	NA

Picard M et al. Cross-Reactivity to Cephalosporins and Carbapenems in Penicillin-Allergic Patients: Two Systematic Reviews and Meta-Analyses. JACI in Practice. Nov-Dec 2019;7(8):2722-2738.e5

Conclusion

- Bien interroger les patients étiquetés « allergiques » à la pénicilline
- Si pas d'arguments pour une allergie, réintroduire pénicilline
- Si faible risque, réintroduire pénicilline
- Si haut risque, ne pas donner la pénicilline et référer à l'allergo