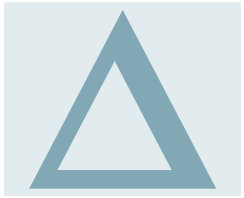
Antibiotikaallergi

≈ betalaktamallergi

≈ penicillinallergi



CHANGE PAGE

In patients allergic to penicillin, consider second and third generation cephalosporins for life threatening infections

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Contributors: The original concept for the article came from SP. SP and BH researched and wrote the article, and are guarantors.

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The clinical problem

Many patients claim to be allergic to penicillin. For those confirmed as being truly allergic (type 1 allergy, with features of urticaria, pruritic rash, etc), the cited overall rate of 10% cross reactivity between penicillin and cephalosporins is an overestimate.[1] For life threatening infections in which a non-cephalosporin antibiotic would be suboptimal, consider giving a second or third generation cephalosporin: ceftriaxone, cefotaxime, cefuroxime, ceftazidime, as clinically appropriate.

The evidence for change

The term "allergy" is often applied incorrectly by both

penicillin allergy and 44 897 with no such history and showed the risk of cross reactivity was related to cephalosporin generation.[11] It found an odds ratio of 4.79 (95% confidence interval 3.71 to 6.17) for an allergic reaction to a first generation cephalosporin or cefamandole in patients allergic to penicillin and odds ratios of 1.13 (0.61 to 2.12) and 0.45 (0.18 to 1.13) for second and third generation cephalosporins, respectively.

Thus, first generation cephalosporins with a chemical side chain similar to penicillin have the potential for cross reactivity, but the attributable risk is closer to 0.5% than 10%. Second and third generation cephalosporins, such as ceftriaxone, cefotaxime, cefuroxime, and ceftazidime,

rate of cross-reactivity between penicillins and meropenem has not been prospectively determined.

Objective: To assess the tolerability of meropenem in patients with documented penicillin allergy.

Design: Prospective skin testing and antibiotic challenge.

Setting: Allergy units of 2 Italian medical centers.

Patients: 104 consecutive participants with immediate hypersensitivity reactions to penicillins and positive skin test results to at least 1 penicillin reagent.

Measurements: Skin tests to meropenem and, if results were negative, challenges with escalating doses of meropenem.

ARTICLE

eropenem in Patients with illins

MD; Francesco Gaeta, MD; Rocco Valluzzi, MD; and

sults: One participant (0.9% [95% CI, 0.02% to 5.2%]) had a sitive intradermal test result to meropenem. The remaining 103 participants with negative skin test results to meropenem tolerated escalating dose challenges.

Limitation: Challenges were not followed by therapeutic courses.

Conclusions: These data indicate a low rate of cross-reactivity between penicillins and meropenem. Therefore, the practice of avoiding meropenem therapy in penicillin-allergic patients should be reconsidered. In patients who especially require meropenem treatment, the authors recommend pretreatment skin tests because negative results indicate tolerability.

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For author affiliations, see end of text.

Läkartidningen

KLINIK & VETENSKAP ÖVERSIKT

Citera som: Läkartidningen. 2015;112:C9A4

Korsallergi mellan penicilliner och övriga betalaktamantibiotika

Risken är betydligt mindre än man tidigare trott

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»Resultat av studier som har publicerats under senare år talar för att risken för korsallergi mellan olika klasser av betalaktamantibiotika länge överskattats.«

Betalaktamantibiotika (penicilliner, cefalosporiner, karbapenemer och monobaktamer [Tabell I]) har snabb baktericid effekt och relativt låg risk för allvarliga biverkningar. De är förstahandsalternativ vid luftvägsinfektioner, urinvägsinfektioner, hud- och mjukdelsinfektioner, bukinfektioner och CNS-infektioner. Användningen av dessa preparat begränsas inte i första hand av gastrointestinala biverkningar, som är

de till behandlingen. Särskilt vid allvarliga reaktioner ska patienten förses med skriftlig information.

Patienter med misstänkt IgE-medierad allergi bör remitteras för allergiutredning med hudtest (pricktest och intrakutantest), specifik IgE-analys (RAST) och eventuell provokation (Fakta 3). Specifik IgE-analys kan också ordineras av inremitterande läkare. I utvalda fall kan de patienter med IgE-medierad allergi som bedöms ha stort framtida behov av

Historiska felkällor

Risken för korsallergi kan ha överskattats i publicerade studier på grund av:

- Spår av penicilliner i de tidiga beredningarna av cefalosporiner
- Oklara definitioner av allergi
- Att studierna huvudsakligen inkluderade första generationens cefalosporiner
- Att patienter med penicillinallergi generellt har ökad risk för allergi mot alla typer av läkemedel

Consequences of avoiding β-lactams in patients with β-lactam allergies

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Garrett E. Schramm, PharmD, BCPS[b] *Aurora, Colo, Rochester, Minn, and St Louis, Mo*

Background: The choice of empiric antibiotics for the treatment of gram-negative bacilli (GNB) bloodstream infections (BSIs) in patients presenting with a β-lactam (BL) allergy is often a difficult decision given that these agents are first-line treatment in many guidelines.
Objective: We sought to compare rates of clinical failure between patients with a history of BL allerg
either a BL or a non–β-lactam (NBL).
Methods: Adult patients with a past medical
allergy and receipt of antibiotics for treatme
were included from 3 academic medical cent
groups were classified as BL or NBL groups
empiric antibiotics received. Clinical failure
96 hours after initiation of empiric antibiotic
reactions during receipt of antibiotic therapy
were recorded.
Results: A total of 552 patients were include
patients in the BL group and 119 patients in
Clinical failure was higher in the NBL group
BL group (38.7% vs 27.4%, $P = .030$). The m
of clinical failure was a temperature of greate
96 hours after receipt of empiric antibiotics (
vs BL group: 13.9%, $P = .016$). Hypersensiti
(2.9%) of 552 patients. Thirteen (2.5%) of 5
experiencing hypersensitivity reactions were
during treatment for GNB BSI.
Conclusion: Among patients with a BL aller
antibiotics is associated with a lower rate of c
low rate of hypersensitivity provides further
risk of cross-reactivity between BL classes. T
support the practice of using a BL from an a
patients in need of gram-negative antibiotic c
Clin Immunol 2015;■■:■■-■■.)

Abbreviations used
APACHE: Acute Physiology and Chronic Health
BL: β-Lactam
BSI: Bloodstream infection
GNB: Gram-negative bacilli
NBL: Non–β-lactam

Clinical Infectious Diseases
MAJOR ARTICLE

Impact of Reported Beta-Lactam
Outcomes: A Multicenter Prospe

**Derek R. MacFadden,[1] Anthony LaDelfa,[2] Jessica Leen,[2] Wayne L. Gold,[1] Nick Daner
Ilana Saltzman,[1] Megan Devlin,[1] Nisha Andany,[1] and Jerome A. Leis[1,3]**

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Health Sciences Centre, Canada

(See the Editorial Commentary by Blumenthal and Shenoy on pages 911–3.

Background. Reported allergy to beta-lactam antibiotics is common
could tolerate these antibiotics. We prospectively evaluated the impact
Methods. We conducted a trainee-led prospective cohort study to dete
allergy on patients seen by infectious diseases consultation services at 3 acade
of readmission for the same infection, acute kidney injury, *Clostridium diff*
continuation. Predictors of interest were history of beta-lactam allergy and
Results. Among 507 patients, 95 (19%) reported beta-lactam allergy; p
lactam therapy was preferred, 25 (35%) did not receive preferred therapy
non-severe prior reactions. After adjustment for confounders, patients who
risk of adverse events (adjusted odds ratio [aOR], 3.1; 95% confidence interval [CI], 1.28–7.89) compared with those without reported allergy. In contrast, patients who received preferred beta-lactam therapy had a similar risk of adverse events compared with patients not reporting allergy (aOR, 1.33; 95% CI, .62–2.87).
Conclusions. Avoidance of preferred beta-lactam therapy in patients who report allergy is associated with an increased risk of adverse events. Development of inpatient programs aimed at accurately identifying beta-lactam allergies to safely promote beta-lactam administration among these patients is warranted.

Keywords. beta-lactam allergy; penicillin allergy; clinical outcome; quality improvement; antimicrobial stewardship.

Clinical Infectious Diseases
MAJOR ARTICLE

The Impact of Reported Beta-Lactam Allergy in Hospitalized Patients With Hematologic Malignancies Requiring Antibiotics

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Background. Patients hospitalized with hematologic malignancy are particularly vulnerable to infection. The impact of reported beta-lactam (BL) allergy in this population remains unknown.
Methods. This was a retrospective cohort study of adult inpatients with hematologic malignancy admitted at 2 tertiary care hospitals from 2010 through 2015. The primary outcome was hospital length of stay (LOS) after administration of the first antibiotic. Secondary outcomes included readmission, mortality, complications, hospital charges, and antibiotic usage. Our goal was to define the impact of BL-only allergy (BLOA) label on clinical outcomes compared to those with no BL allergy (NBLA) in hematologic malignancy inpatients who required systemic antibiotics.
Results. In our cohort (n = 4671), 38.3% had leukemia, 4.9% had Hodgkin lymphoma, 36.1% had non-Hodgkin lymphoma, and 20.7% had multiple myeloma. Among patients, 35.1% reported antibiotic allergy, and 14.1% (n = 660) had BLOA (including 9.3% with penicillin-only allergy and 3.3% cephalosporin-only allergy). Patients with BLOA had longer median LOS compared to patients with NBLA (11.3 vs 7.6 days, $P < .001$), which remained significant after multivariable adjustment. Patients with BLOA also had significantly worse outcomes in terms of mortality rate at 30 days (7.6% vs 5.3%, $P = .017$) and 180 days (15.8% vs 12.2%, $P = .013$), 30-day readmission rate, *Clostridium difficile* rate, hospital charges ($223 046 vs $173 256, $P < .001$), antibiotic classes used, and antibiotic duration.
Conclusions. In hospitalized patients with hematologic malignancy, patients with reported BL allergy had worse clinical outcomes and higher healthcare cost than those without BL allergy label.

Keywords. allergy; penicillin; beta-lactam; hematologic malignancy.

Undvikande av betalaktamer på felaktiga grunder

- Sämre effekt
  - Högre mortalitet
  - Längre vårdtid
  - Fler återinläggningar
- Fler/värre biverkningar
  - C. difficile
- Högre kostnader

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Guidelines

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

Roos Wijnakker [1, 15, *], Maurits S. van Maaren [2], Lonneke G.M. Bode [3], Maja Bulatovic [4], Bart J.C. Hendriks [5], Masja C.M. Loogman [6], Suzanne P.M. Lutgens [7], Ananja Middel [8], Chris M.G. Nieuwhof [9], Eveline E. Roelofsen [10], Jan W. Schoones [11], Kim C.E. Sigaloff [12], Aline B. Sprikkelman [13], Lieke M.M. de Vrankrijker [14], Mark G.J. de Boer [15]

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ARTICLE INFO

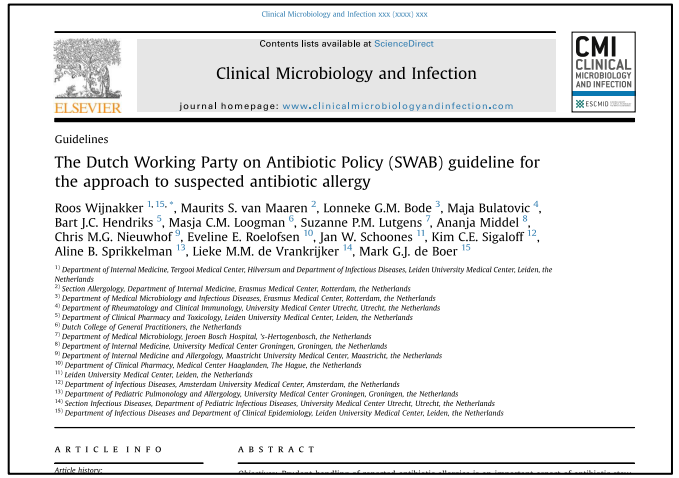
Article history:

ABSTRACT

Objectives: Prudent handling of reported antibiotic allergies is an important aspect of antibiotic stew-

Bakgrund

- SWAB - Nederländska specialistföreningarna för
  - Infektion
  - Mikrobiologi
  - Sjukhusfarmakologi
- 12 PICO questions
- Systematisk litteratursökning
- Evidensvärdering enl GRADE



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ARTICLE INFO

ABSTRACT

Table 1
Definitions of the severity of an allergic reaction

Definitions used in this guideline	By symptoms of a reaction; World allergy organization and the European academy of allergy and clinical immunology criteria	OR
Severe	1. Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both (e.g. generalized hives, pruritus or flushing, swollen lips-tongue-uvula) AND at least one of the following: a. Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxaemia) b. Reduced blood pressure or associated symptoms of end-organ dysfunction (e.g. hypotonia (collapse), syncope, incontinence) c. Severe gastrointestinal symptoms (e.g. severe crampy abdominal pain, repetitive vomiting), OR 2. Acute onset of hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement. OR 3. Danger signs for severe cutaneous adverse reactions: a. Tiny vesicles or crusts, the grey-violaceous or dusky colour of lesions, painful or burning skin and/or mucosa in addition to fever and malaise, haemorrhagic erosions of mucous membranes, and skin detachment (Stevens-Johnson Syndrome/toxic epidermal necrolysis) b. Exanthema with pustules (acute generalized exanthematous pustulosis) c. Purpura (vasculitis) d. Macules/papules together with non—cutaneous organ involvement; progression to more than 50% of the body surface area, deviating laboratory values (differential blood count, liver and kidney parameters)(drug reaction with eosinophilia and systemic symptoms). e. Facial oedema, oedematous, and infiltrated skin inflammation. Acute fever of 38.5 °C and higher. (acute generalized exanthematous pustulosis/drug reaction with eosinophilia and systemic symptoms) *Note:* if maculopapular exanthema meets the symptom or CIOMS criteria for a severe reaction, it should be considered as such.	
Non-severe	1. Symptom(s)/sign(s) from 1 organ system present: a. Cutaneous: urticaria, erythema-warmth, pruritus, tingling, and itching of the lips. b. Upper respiratory: Nasal symptoms (e.g. sneezing, rhinorrhoea, nasal pruritus, and/or nasal congestion), Throat-clearing (itchy throat), Cough not related to bronchospasm. c. Conjunctival: erythema, pruritus, or tearing. OR 2. Maculopapular exanthema without organ involvement. OR 3. Other: nausea, metallic taste	

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

Oana Joean [1, †], Kevin Sermet [2, †], Liat Ashkenazi-Hoffnung [3], Yasemin Cakir Kiymaz [4], Kimberly Blumenthal [5], Cecilia Bonazzetti [6], Anca Mirela Chiriac [7], Silvia Gomez-Zorrilla [8, 9], Eleni Karakike [10], Elham Khatamzas [11], Neil Powell [12], Jason A. Trubiano [13], Roos Wijnakker [14], Jonathan Sandoe [15], Blin Nagavci [16, 17], Mark G.J. De Boer [18, *]

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Table 2
Definitions of severe and nonsevere manifestations of a suspected antibiotic allergic reaction

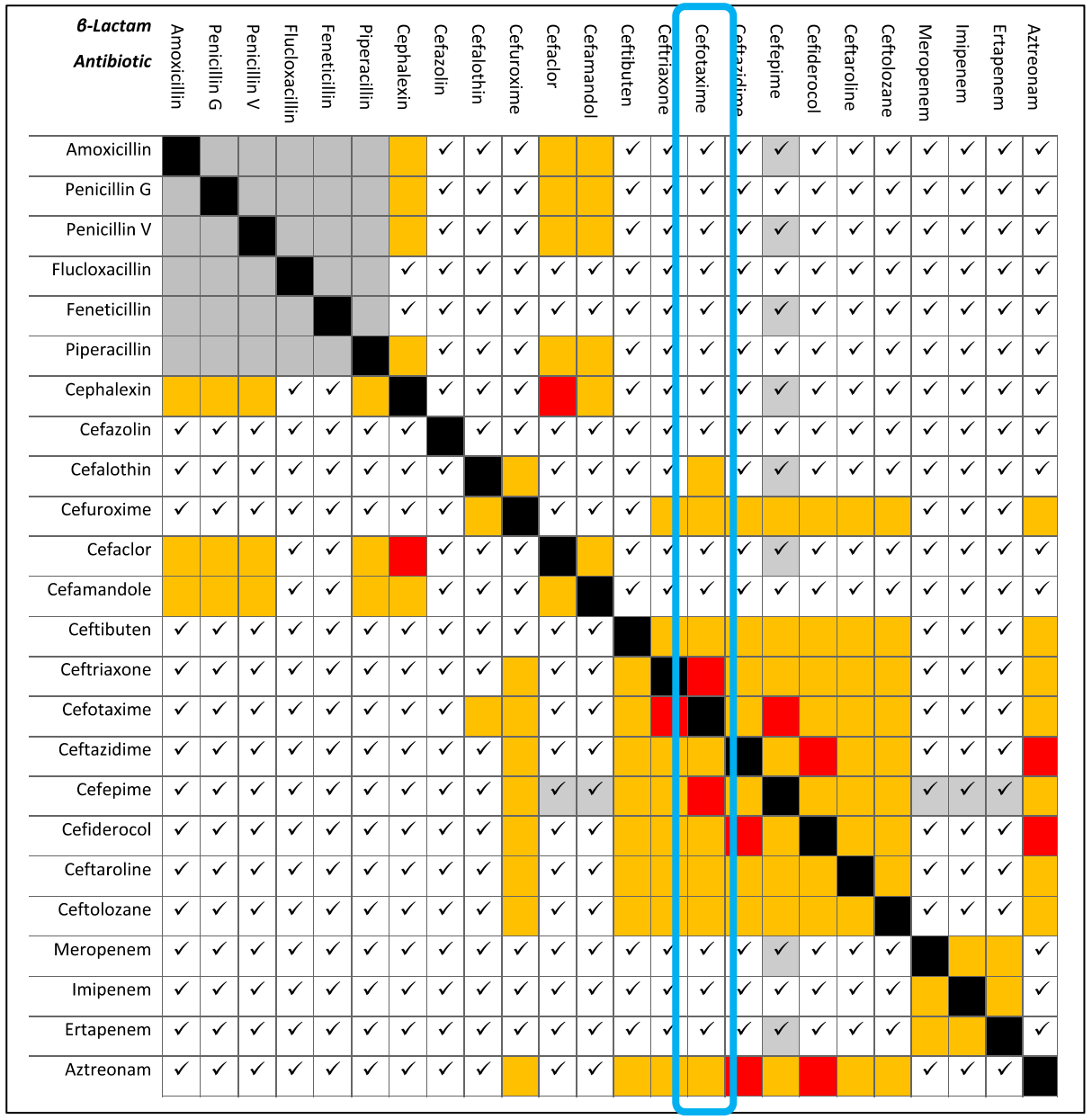
Definitions	By symptoms of reaction (WAO/EAACI criteria [18,19])	OR	By consequences of reaction (CIOMS criteria [20])
Severe	1. Acute onset of an illness (minutes to several hours) with involvement of the skin OR/AND mucosal tissue (e.g. generalized urticaria[a], pruritus or flushing, swollen lips-tongue-uvula) AND at least one of the following: a Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia) b. Reduced BP or associated symptoms of end-organ dysfunction (e.g. hypotonia [collapse], syncope, incontinence) 2. Acute onset of hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement. 3 Danger signs for severe cutaneous adverse reactions: a Tiny vesicles or crusts, grey-violaceous or dusky colour of lesions, painful or burning skin and/or mucosa in addition to fever and malaise, haemorrhagic erosions of mucous membranes and skin detachment (SJS/TEN) b. Exanthema with pustules (AGEP) c. Purpura (vasculitis) d. Macules/papules together with noncutaneous organ involvement; progression to more than 50% of the body surface area, deviating laboratory values (differential blood count, liver and kidney parameters) (DRESS). e. Facial oedema, oedematose and infiltrated skin inflammation. Acute fever of 38.5°C and higher. (AGEP/DRESS)	OR	Those reactions that are fatal, life threatening, cause hospitalization, result in persistent or significant disability or incapacity, require intervention to prevent permanent damage, or cause congenital anomalies
Nonsevere	1. Symptom(s)/sign(s) from one organ system present: a. Cutaneous: urticaria[a] (localized), erythema-warmth, pruritus, tingling, itching of the lips, OR b. Upper respiratory: nasal symptoms (e.g. sneezing, rhinorrhoea, nasal pruritus, and/or nasal congestion), throat-clearing (itchy throat), cough not related to bronchospasm. OR c. Conjunctival: erythema, pruritus, or tearing 2. Maculopapular exanthema without organ involvement. OR 3. Other: nausea, metallic taste, gastrointestinal symptoms (e.g. cramping abdominal pain, repetitive vomiting)	OR	All other consequences

Rekommendationer (NL)

- We suggest that patients with suspected **non-severe, immediate-type** index reactions that occurred >5 years ago, can receive a therapeutic dose of the culprit ß-lactam antibiotic in a controlled setting
- We recommend that patients with suspected non-severe, 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

Rekommendationer (NL)

- We recommend that patients with a suspected **immediate-type** allergy to penicillins can receive cephalosporins, but only those with dissimilar side chains, **irrespective of severity and time since the index reaction**

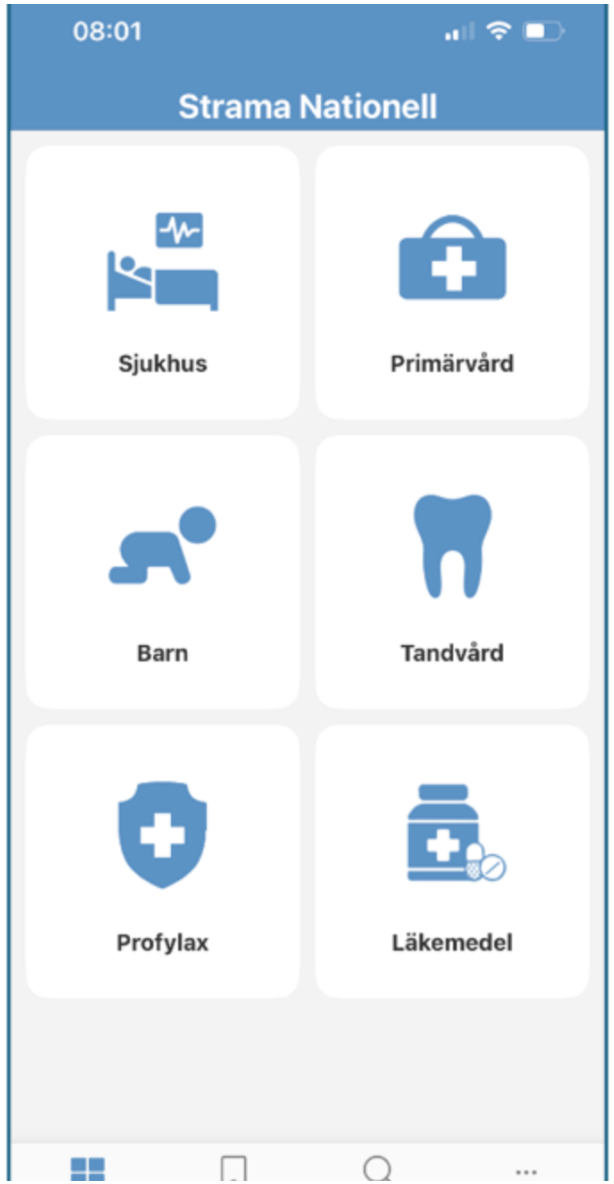


	Cross-tabulation was similar
	Allergy possible based on the formation of PPL
	Potential cross-allergy based on an identical R1 side chain
	Potential cross-allergy based on similarity in R1 or R2 side chains or clinical studies
✓	No risk of a cross-allergic reaction

PPL, polyvalent penicilloyl polylysine (a major penicillin determinant)

Rekommendationer

- We recommend that patients with suspected **immediate-type** penicillin allergy, **irrespective of severity or time** since the index reaction, can receive **any monobactam or carbapenem**, without prior allergy testing
- We recommend that in patients with suspected **severe delayed type** allergy to penicillins, **all beta-lactam antibiotics should be avoided**, irrespective of time since the index reaction. In the absence of acceptable alternative antimicrobial treatment, the use of ß-lactam antibiotics should be discussed in a multidisciplinary team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Sjukhus
Primärvård
Barn
Tandvård
Profylax
Läkemedel

Tidigare reaktion vid penicillin	Antibiotikabehandling	Utredning och varningsmärkning
Icke-allvarlig **fördröjd** reaktion[1]	Penicilliner och övriga betalaktamantibiotika kan användas	Ta bort varningsmärkning.
Icke-allvarlig **snabb** reaktion (allergisk reaktion osannolik)[1]	Penicilliner och övriga betalaktamantibiotika kan användas	Ta bort varningsmärkning.
Icke-allvarlig **snabb** reaktion (allergisk reaktion möjlig)[1]	Cefalosporiner (förutom cefadroxil), karbapenemer och monobaktamer kan användas.	Provokation för penicilliner[4]. Om ingen reaktion och samma substans som vid tidigare reaktion användes, ta bort varningsmärkning.
Allvarlig **snabb** reaktion/anafylaxi[2]	Använd ej penicilliner. Cefalosporiner (förutom cefadroxil), karbapenemer och monobaktamer kan användas.	Varningsmärk journalen och ange substans, symtom och tidsförlopp. Remiss till allergolog för eventuell allergiutredning.
Allvarlig **fördröjd** reaktion[3]	Svåra makulopapulösa utslag[3]: Använd ej penicilliner. Cefalosporiner (förutom cefadroxil), karbapenemer och monobaktamer kan användas SCAR[3]: Ska INTE behandlas med något betalaktamantibiotika (varken penicilliner, cefalosporiner, karbapenemer eller monobaktamer)	Varningsmärk journalen och ange substans, symtom och tidsförlopp. Remiss till allergolog för eventuell allergiutredning.

1. Icke-allvarlig reaktion, snabb (≤6h) eller fördröjd
Möjlig allergisk reaktion:
Klåda inklusive på läpparna eller i halsen
Pirrande/stickande känsla
Lindrigt makulopapulöst exantem, utan eller med klåda (duration <7 d, <50% av hudkostym, ej krävt systemisk kortisonbehandling)
Begränsat erytem

Allergisk reaktion osannolik:
Milda GI-symtom (diarré, förstoppning, illamående)
Nysningar, svuva eller nästäppa
Milda ögonsymtom (rodnad, tårbildning, klåda)

2. Allvarlig snabb reaktion
Något av följande:
Urtikaria
Angioödem
Anafylaxi enligt kriterier nedan eller reaktion som krävt behandling med adrenalin.

Slutsatser

- Pressa anamnesen
- Värdera risken för suboptimal behandling
- Ordinera cefalosporin eller karbapenem till de patienter som har indikation (och inte har haft en svår fördröjd överkänslighetsreaktion)

På gång

Penicillinprovokation – AKUTEN

Förändringar sedan föregående version

Ny rutin.

Bakgrund och syfte

Felaktiga varningar för penicillinallergi är ett utbrett problem. Cirka 5–10 % av patienter som vårdas på sjukhus har en registrerad varning för penicillinallergi, men studier visar att upp till 95 % av dessa saknar en faktisk allergi vilket kan innebära att den enskilda patienten får sämre behandling och driver resistensutveckling på global nivå.

Denna rutin skall användas för säker penicillinprovokation inom akutsjukvård och slutenvård där patienter påbörjar behandling med penicillin.

Utförande