Safety Outcomes of a Hospital-Wide β-Lactam Graded Challenge Allergy Protocol

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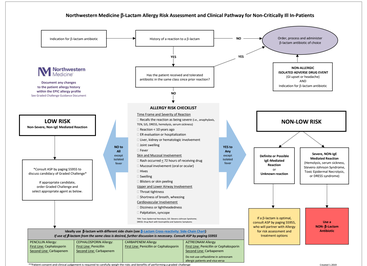
Background

Up to 15% of hospitalized patients report a penicillin allergy, but most can tolerate a β-lactam (BL). Use of second-line, alternative, non-BL antibiotics poses untoward health consequences. Assessing for true penicillin allergies includes penicillin skin testing (PST) and a direct amoxicillin challenge, each with their own limitations when applied to vulnerable hospitalized patients. For inpatients, a graded challenge (GC) with the desired BL offers a streamlined short-term approach for many who could benefit from a first-line BL agent.

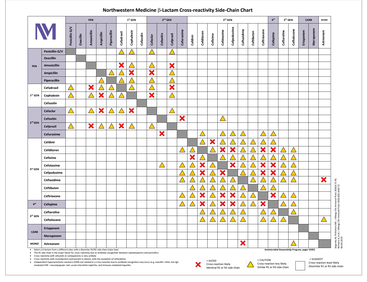
In 2019, a hospital-wide BL Allergy Assessment and Clinical Pathway was implemented at Northwestern Memorial Hospital (NMH) in Chicago, Illinois, which included a BL GC procedure managed by the antimicrobial stewardship program (ASP) for low-risk patients (Figure 1 & 2).

Figure 1



NMH Allergy Toolkit

Figure 2



The aim of this study was to assess the safety outcomes of the GC procedure in hospitalized patients. A retrospective, observational cohort study was conducted in adult inpatients who completed a GC procedure between 9/2019 - 9/2021 at NMH, an 894-bed tertiary academic medical center.

Methods

Primary objective:
To determine the incidence of a hypersensitivity reaction* post administration of a β-lactam GC dose or completed GC procedure, with or without a preceding PST.

**Hypersensitivity reactions: non-severe cutaneous reactions including itching, flushing, rash, tingling, and urticarial (hives); severe IgE reactions include shortness of breath, angioedema, swelling, bronchospasm, wheezing, hypotension, syncope, dizziness, arrhythmia, anaphylaxis, or a positive PST; and severe delayed immunologic reactions include organ-specific reactions and severe cutaneous adverse reactions occurring anytime post administration of a β-lactam GC dose until hospital discharge.*

Secondary objectives:
1) To determine the incidence of a non-hypersensitivity reaction or intolerance post administration of a β-lactam GC dose or completed GC procedure, with or without a preceding PST.
2) To identify successful antimicrobial stewardship interventions** in subjects tolerant to a β-lactam GC assessment procedure in efforts to improve antibiotic use.

***Interventions include: timely antibiotic switch to an appropriate and preferred β-lactam antibiotic with completion of treatment course and updating or de-labeling of penicillin allergy profile in the electronic medical chart.*

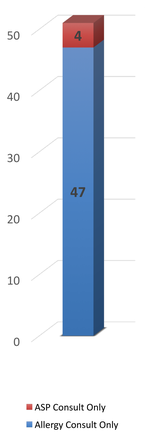
Inclusion Criteria
- ≥18 years of age
- In-patients at Northwestern Memorial Hospital, Chicago, Illinois.
- Completed a β-lactam GC between 9/2019-9/2021 as instructed in the 2019 NMH GC guidance document. Partial IV graded challenge doses were included if Allergy and Immunology approved.

Exclusion Criteria
Pre-op surgical amoxicillin graded challenges

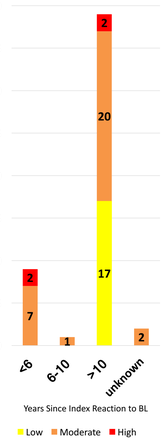
NM ADSP Antimicrobial And Diagnostic Stewardship Program

Results

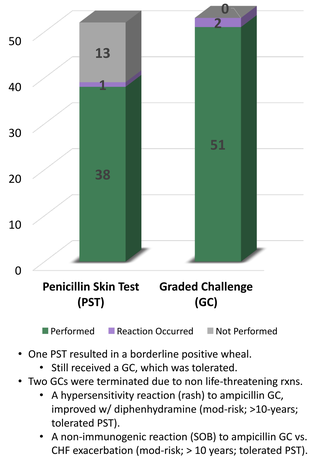
CONSULT SERVICE FOR GC (N)



RISK FOR SEVERE HYPERSENSITIVITY REACTION (N)

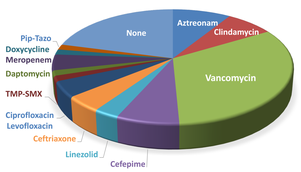


ALLERGY ASSESSMENT, PST vs. GC, (N)

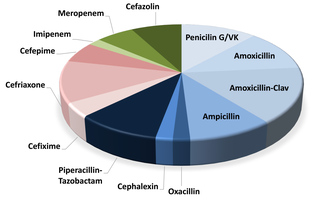


- One PST resulted in a borderline positive wheal.
  - Still received a GC, which was tolerated.
- Two GCs were terminated due to non life-threatening rxns.
  - A hypersensitivity reaction (rash) to ampicillin GC, improved w/ diphenhydramine (mod-risk; >10-years; tolerated PST).
  - A non-immunogenic reaction (SOB) to ampicillin GC vs. CHF exacerbation (mod-risk; > 10 years; tolerated PST).

EMPIRIC ANTIBIOTICS BEFORE GC

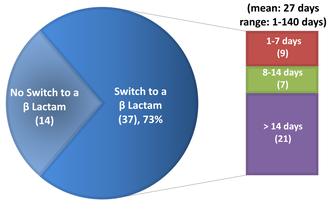


TOLERATED B-LACTAM WITH GC

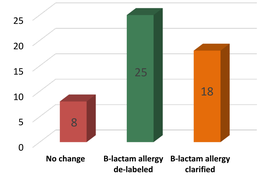


13 moderate-risk (> 10 years) and 5 high-risk (< 10 years) patients tolerated GC with a *penicillin* or cephalexin.

SWITCH TO A B-LACTAM AFTER GC AND DURATION OF THERAPY, DOT, (N)



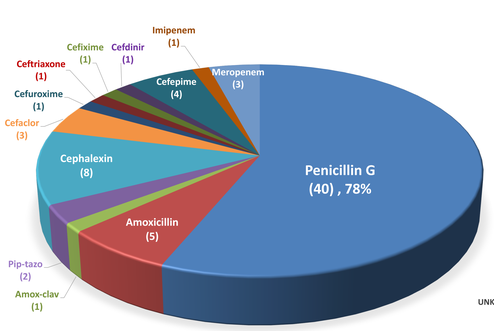
DOCUMENTATION TO ALLERGY PROFILE AS A RESULT OF GC, (N)



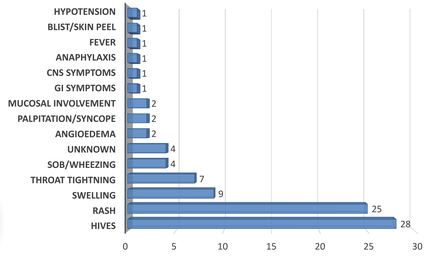
Baseline Characteristics

N= 51	N (%)
Female	26 (51)
Ethnicity	
White	34 (67)
Black	10 (19)
Hispanic	4 (8)
Asian	2 (4)
American Indian or Alaskan Native	1 (2)
Age (years)	58 (range: 20-87)
Mean Charleston Comorbidity Index (CCI)	3.8 (range: 0-11)
History of Immunosuppression	21 (41)
History of Psychiatric Condition	14 (27)

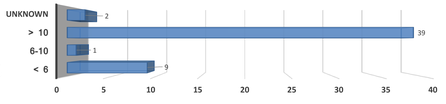
B-LACTAM ANTIBIOTIC ALLERGY LABEL (N)



Documented Reactions to β-Lactam



Years Since Index Reaction to β-Lactam



REFERENCES: Lee CE, Zembower TR, Fotis MA, et al. The Incidence of Antimicrobial Allergies in Hospitalized Patients. *Arch Intern Med* 2000;160:2819-2822.; Shebab N, Patel PR, Srinivasan A, et al. Emergency Department Visits for Antibiotic-Associated Adverse Events. *Clin Infect Dis* 2008;47:735-743.; Shenoy ES, Macy E, Rowe T, et al. Evaluation and Management of Penicillin Allergy: A Review. JAMA 2019;321(2):188-199.

Discussion/Conclusions

- 51 patients completed a BL GC between September 1, 2019 and September 1, 2021.
- Majority of the GC procedures were managed by the NMH allergy consult service (92%; 47/51) vs. ASP.
  - Reasons for this are believed to be due to the complex nature of our hospitalized patients who had a mean CCI of 3.8 (0-11), a history of immunosuppression (41%; 21/51) and/or a psychiatric condition (27%; 14/51) with a moderate to high-risk for a severe hypersensitivity reaction based on their reported allergy history (67%; 34/51).
- With consideration of baseline risk(s) for a BL challenge with or without a preceding PST, 2 of the 51 hospitalized patients challenged with a BL required termination of the GC procedure due to non-life threatening events.
- 39% (20/51) were challenged with and tolerated a *penicillin* or first-generation cephalosporin (ie. cephalexin) even in those with a moderate to high risk for a severe reaction based on allergy history.
  - Significant time since the index reaction (eg. >10 years) may offer safe challenge opportunities for moderate risk hospitalized patients without the need for a formal allergy consult.
- 73% (37/51) were switched to a BL with a mean duration of therapy of 27 days (1-140 days).
  - Exerting the GC averted the use of a second-line, alternative, antibiotic and possibly mitigated untoward events given the lengthy course of antibiotic therapy for several patients.
- 49% (25/51) and 16% (18/51) of patients had their β-lactam antibiotic allergy label either de-labeled or clarified, respectively, in the allergy profile of the electronic medical record.
- The GC procedure in our hospitalized patients was well tolerated even for those with a moderate-high risk allergy history concerning for a severe hypersensitivity reaction. As a result, most infections completed treatment using a first-line, preferred, BL agent. Ongoing efforts to improve documentation of BL allergies is warranted.