562 Abstract

Introduction: Although penicillin allergy is the most commonly reported pediatric drug allergy, most reports do not represent IgE-mediated or late-onset severe hypersensitivity reactions. False allergy labels can lead the development of antibiotic resistance and adverse drug side effects. We hypothesize that our multipronged approach to evaluate pediatric beta-lactam allergies will "de-label" inaccurate or outdated allergies.

Methods: This quasi-experimental study included pediatric patients (0-18 years) with a documented beta-lactam allergy at a single tertiary medical center seen in clinic between 2014-2019 or admitted in 2022. Patients were prospectively recruited, screened, and stratified into risk categories determined by their reported reaction symptoms. Low-to-intermediate risk patients were referred to Allergy and Immunology (A/I) for allergy de-labeling assessment via skin (percutaneous ± intradermal) testing and/or oral challenge as deemed appropriate by A/I. We report descriptive statistics from our cohort and a two-group comparison of enrolled patients delineated by appointment attendance via one-tail *t* tests and chi-square tests.

Results: Among 107 screened participants, 54 were referred to A/I for de-labeling assessment, and a total of 19 were de-labeled (12 via A/I assessment and 7 via screening) in an average of 0.8 (±0.7) A/I visits. The majority of referred patients reported amoxicillin allergy (83%) consisting of either an urticarial (52%) or maculopapular (41%) rash with an average time of 6.0 (±3.3) years since the reaction. Only 1 patient out of the 26 low-to-intermediate risk patients who completed a de-labeling assessment was re-classified as high risk by A/I. No allergic or adverse reactions to testing were reported. Anticipated barriers to study completion of insurance type (p=0.57), travel distance to clinic (p=0.21), age of participant (p=0.38), and time since reaction (p=0.16) did not differ significantly between patients attending at least 1 A/I appointment and patients lost to follow-up.

Conclusions: Use of an inpatient and outpatient algorithm can help identify pediatric patients less likely to have a true or persistent beta-lactam allergy (delayed-onset mild symptoms, or IgE-mediated reaction >5 years ago) and who could benefit from formal allergy testing to potentially remove their allergy label. In the future, algorithm implementation within the electronic medical record may assist clinicians in thorough documentation of beta-lactam allergies and expeditious referral for allergy testing when appropriate.

Multipronged Approach to Recruitment of Pediatric Patients with Beta-Lactam Allergies for Evaluation and De-labeling

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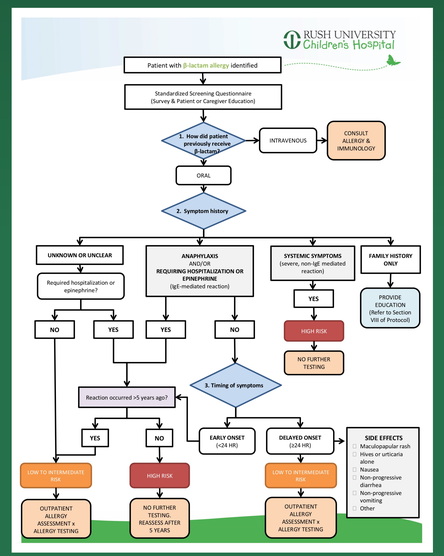
Background

- Beta-lactam allergy (often referred to as "penicillin allergy") is the most common drug allergy in the pediatric population with prevalence of 10%[1,2]
  - Of children who have IgE-mediated beta-lactam reactions, 50% no longer test positive after 5 years, increasing to 80% after 10 years – yet many are never tested
- Many penicillin adverse reactions do not represent true, life-threatening (IgE-mediated) allergy[3]
  - Unverified allergy labels in the electronic medical record (EMR) per caregiver report only
  - Rash, a common reaction symptom, may be due to underlying illness
- Labeling patients with beta-lactam allergies significantly limits treatment options
  - Providers may use more costly, broader spectrum, or more toxic antimicrobial agents that can lead to adverse drug events and the development of antimicrobial resistance[4]



Process map for pediatric beta-lactam allergy risk-stratifying algorithm

Methods

- QI initiative of Pediatric Infectious Disease and Allergy/Immunology (A/I) to address discrepancy between true and reported beta-lactam allergy
- IRB-approved quasi-experimental study of patients fulfilling the following criteria:
  - Age 0-18 years with a beta-lactam allergy in the EMR
  - Seen in Rush pediatric or medicine/pediatric outpatient clinic between 2014-2019
  - Admitted to Rush Children's Hospital beginning in 2022
  - Exclusion: uncontrolled asthma, <6 weeks from allergic reaction
- Data collection: screening conducted by trainee physicians and medical students
  - Classify reaction via algorithm into risk categories based on symptoms, timing, and age of onset
- Eligible patients (low to intermediate risk) consented and referred for outpatient A/I assessment
  - During the A/I visit, appropriate allergy testing performed
- Data analysis: summary statistics, one-tail *t* tests and chi-square tests

Demographics

Enrolled patients	*N* = 54
Sex, *n* (%)	
Female	21 (38.9)
Male	33 (61.1)
Ethnicity, *n* (%)	
Asian	1 (1.9)
Black/AA	14 (25.9)
Hispanic/Ltnx	23 (42.6)
White	13 (24.1)
Other	3 (5.6)
Insurance, *n* (%)	
Public	25 (46.3)
Private	29 (53.7)
Age, y, mean (SD)	8.2 (3.4)
Travel distance to A/I clinic[a], miles, mean (SD)	8.9 (9.2)

[a]Calculated absolute distance between participant and clinic zip codes

Results

Enrollment rate by recruitment source

	Outpatient	Inpatient	Total
Screened, *n* (%)	94 (87.0)	14 (13.0)	108
Enrolled, *n* (%)	47 (87.0)	7 (13.0)	54
Enrollment rate	50%	50%	50%

Enrollment rates did not differ between outpatient & inpatient recruitment.

Characteristics of reported reactions

Enrolled patients	*N* = 54
Antibiotic, *n* (%)	
Amoxicillin	45 (83.3)
Amoxicillin-clavulanic acid	2 (3.7)
Penicillin	5 (9.3)
Cephalosporins	2 (3.7)
Age at reaction, y, mean (SD)	2.2 (1.9)
Time since reaction, y, mean (SD)	6.0 (3.3)
Algorithm outcome prompting referral, *n* (%)	
Non-IgE mediated	20 (37.0)
Maculopapular rash	19 (35.2)
Unknown	1 (1.9)
IgE-mediated, >5 years ago	18 (33.3)
Urticaria <24 hours	13 (24.1)
Anaphylaxis	1 (1.9)
Maculopapular rash	3 (5.6)
Diarrhea	1 (1.9)
Delayed-onset urticaria	15 (27.8)
IV route	1 (1.9)
Referral outcomes, *n* (%)	
De-labeled	12 (22.2)
Maintained allergy label	6 (11.1)
Did not complete study	36 (66.7)

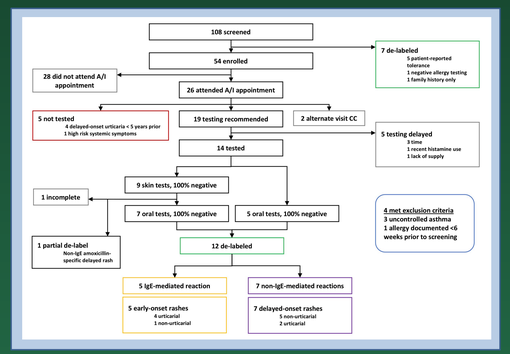
Outcomes

De-labeled patients	*N* = 19
Source, n (%)	
Outpatient	18 (94.7)
Inpatient	1 (5.3)
Age at reaction, y, mean (SD)	2.2 (1.9)
Time since reaction, y, mean (SD)	6.1 (2.9)
Reactions, n (%)	
Maculopapular rash	10 (52.6)
Urticaria <24 hours	4 (21.1)
Delayed-onset urticaria	3 (15.8)
Family history only	1 (5.3)
Unknown	1 (5.3)
De-label method, n (%)	
Phone screening	7 (36.8)
Patient-reported tolerance	5 (26.3)
OSH testing	1 (5.3)
Family history only	1 (5.3)
Referred to A/I	12 (63.2)
Oral challenge	5 (26.3)
Skin test + oral challenge	7 (36.8)

Barriers to appointment attendance

	Attended A/I appointment: *Yes* *n* = 26	*No* *n* = 28	*P* Value
Age at screening, y, mean (SD)	8.0 (3.3)	8.3 (3.6)	0.38
Time since reaction, y, mean (SD)	5.5 (3.0)	6.4 (3.5)	0.16
Travel distance to A/I clinic[a], miles, mean (SD)	7.9 (9.1)	9.9 (9.3)	0.21
Insurance, public, *n* (%)	11 (42.3)	14 (50.0)	0.57

Anticipated barriers to appointment attendance were not significantly different.
[a]Calculated absolute distance between participant and clinic zip codes



Flowchart of study outcomes for outpatients and inpatients screened with risk-stratifying algorithm

Summary of Results

18% of screened patients (*N* = 108) de-labeled

For every 6 patients screened, 1 de-labeled

22% of enrolled patients (*N* = 54) de-labeled

For every 5 patients enrolled, 1 de-labeled

50% of A/I visits where beta-lactam allergy discussed (*N* = 24) de-labeled

100% A/I tests negative

A/I visits to de-label[a] mean (± SD)

0.79 (±0.71) visits
Overall, *n* = 19

1.25 (±0.45) visits
De-labeled via A/I, *n* = 12

[a]A/I clinic visits attended by 1 de-labeled patient

Conclusions

- Risk-stratifying algorithm identifies low to intermediate risk patients with beta-lactam allergy label eligible for testing
  - Prominent features: amoxicillin allergy label, rash (non-IgE and urticarial) as a toddler, on average 6 years prior to screening
  - IgE and non-IgE-mediated reactions de-labeled, many in one A/I visit
  - All tested patients resulted negative for true allergy without adverse reactions
  - Limitation in identifying delayed-onset urticaria as possible distinct risk group
  - We predict this will increase first-line antibiotic prescribing, which is estimated to save $1893 per de-labeled patient[5]
- Anticipated barriers did not predict appointment attendance
  - Similar clinic travel distance, % public insurance, and timing of reaction
  - Limitation of small sample size and % study completion
- Future directions:
  - Identifying barriers to de-labeling
  - Increasing inpatient recruitment to improve yield
  - Triaging beta-lactam reactions at the initial allergy documentation
  - EMR automated reminders using algorithm for A/I referral

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