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Oral Amoxicillin Challenges in Low-Risk Children During a Pediatric Emergency Department Visit

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To the Editor:

An estimated 30 million children per year are seen in the pediatric emergency department (PED) and an estimated 10% present with a parent-reported allergy to an antibiotic in the penicillin (PCN) family.[1] A reported PCN allergy increases morbidity, mortality and costs[2-3] , which is especially concerning because greater than 95% of patients with a reported PCN allergy may tolerate the medication because either they never had a true allergy or they had an earlier allergy that subsequently resolved.[4] Our prior work in the PED found that 76% of families reported symptoms of allergy that were low-risk for true allergy (Table 1).[1]

We previously performed this standard “3-tier” testing on 100 children who presented to the PED with low-risk symptoms of PCN allergy and found that all 100 (100%; 95% CI 96.4% - 100%) had negative 3-tier allergy testing.[5]

With increasing evidence to support direct oral amoxicillin challenge in low-risk patients,[6] the primary outcome of this study was to evaluate whether providers and families in a PED could complete risk categorization followed by direct oral amoxicillin challenge during their PED visit. Our secondary outcome was to evaluate the effect this intervention had on PED length of stay (LOS).

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Potential Conflicts of Interest: The authors have no conflicts of interest relevant to this article to disclose.

We performed an IRB approved randomized controlled feasibility trial of a convenience sample of children (2-16 years) with a history of parent reported PCN allergy who presented to an urban PED between December 1, 2017 and December 1, 2018.

A risk stratifying questionnaire was given to families that included a “yes/no” option about interest in an amoxicillin oral challenge if the patient was eligible (Figure 1). If the child had low-risk symptoms of allergy, and no exclusion criteria, the child was randomized, using permutated block randomization, to “Oral Challenge” or “No Oral Challenge” (Table 1). Children were excluded if they had a history of developmental delay, any contraindication to allergy testing, or if they presented to the PED with a rash, vomiting or current asthma symptoms. Patients being admitted to the hospital or those who were deemed too acutely ill for participation (triage level 1 or 2 or as determined by the ED patient care team) were also excluded from the study. Children who were wards of the state, in foster care or police custody or detention were excluded as well. Prior use of oral antihistamines was not an exclusion criteria. Children with any basal condition (trauma, infection, minor accidents, etc.) were able to participate in the study provided they and their family were willing and did not meet the above-mentioned exclusion criteria. Those children with a non-basal condition, namely, those who would require an antibiotic, were approached for participation, and if consented, challenged and given an antibiotic prescription for their illness.

For the oral challenge, the child was given a non-weight-based invariable 500 mg tablet of amoxicillin or 520 mg of liquid amoxicillin if unable to tolerate pills followed by a research assistant aided mandatory one-hour observation period. Next day follow-up was attempted in all children who completed an oral challenge.

Data were managed using REDCap (Research Electronic Data Capture). Descriptive statistics were used to summarize results.

During the study, 376 questionnaires were completed (Figure 2). A majority of children (228; (60.6%)) had low-risk symptoms of PCN allergy. Half (114; (50.0%)) of low-risk children’s families were interested in an oral challenge, of which 101 (88.6%) were eligible and 82 (81.2%) consented. Randomizations to “Oral Challenge” and “No Oral Challenge” included 40 and 42 children, respectively. There was no difference in demographic characteristics or triage level between the two groups.

Nearly all the 40 children received the oral challenge (37; (92.5%)); 36 (97.3%) children tolerated the challenge and were de-labeled as PCN allergic. Of the three children whose family elected not to receive the challenge; one family did not want to wait, one child refused to take the medication, and one parent elected to not participate immediately prior to the challenge. One child developed mild urticaria after 40 minutes of observation and received an anti-histamine with symptom resolution. He was 8 years old, had otitis media, and a PED LOS of 148 minutes. His questionnaire revealed his low-risk symptom to be a maculopapular rash at 1 year of age. An additional child reported subject itching in one spot on the right shoulder 45 minutes after receiving the oral challenge. No hives were present, and the itching resolved without treatment in less than 3 minutes. This was deemed not to be

consistent with an allergic reaction. Children who received an oral challenge had an increased LOS (216 min vs 151 min, $p < 0.01$, CI 25-103).

Next-day follow-up was completed in 29 (78.4%) children who received an oral challenge, with no delayed reactions occurring. The one child with a positive reaction had no progression of symptoms.

This study characterized children as low-risk and provided an oral challenge in the PED. We randomized children whose families were willing to undergo the oral challenge to evaluate the effect that this challenge had on PED LOS. Our results showed that 97% of children who received the challenge were negative for an allergic reaction and had PCN allergy removed. Furthermore, 80% of eligible patients consented to proceed to an oral challenge in the PED.

Within the past few years, multiple studies have demonstrated that direct oral amoxicillin challenges are safe and effective in select populations to de-label patients with reported PCN allergy.[7-9] A joint statement by The American Academy of Allergy, Asthma, and Immunology, the Infectious Diseases Society of America, and the Society for Healthcare Epidemiology of America supports a shift from the traditional 3-tier model of PCN allergy testing to an oral challenge only paradigm in select patient populations.[6] However, with an estimated 10% of the US population reporting a PCN allergy there remains a need to identify novel, non-allergy clinic testing environments that could effectively de-label large volumes of patients. Factors such as cost, insurance, time and regional differences in provider availability may limit their ability to go to an allergy clinic for PCN allergy testing.

By completing our study in the PED, we demonstrated the feasibility of addressing PCN allergy in a PED setting using direct oral amoxicillin challenge. We found that there was a significant difference in LOS between randomized groups, however the elimination of the research consent process and randomization, if this testing became routine, would eliminate most of the increased LOS. Subsequently, the health and lifetime economic benefits associated with addressing PCN allergy in childhood outweigh any negative associated with increased LOS.

This study is limited by our use of convenience sampling and the number of studied patients was too low to be able to draw a reliable conclusion on the tolerability and safety of oral amoxicillin challenges in the ED.

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Clinical Implications: The Pediatric Emergency Department appears to be an effective location to de-label patients with penicillin allergy; however, efforts need to be made to minimize associated increased length of stay.

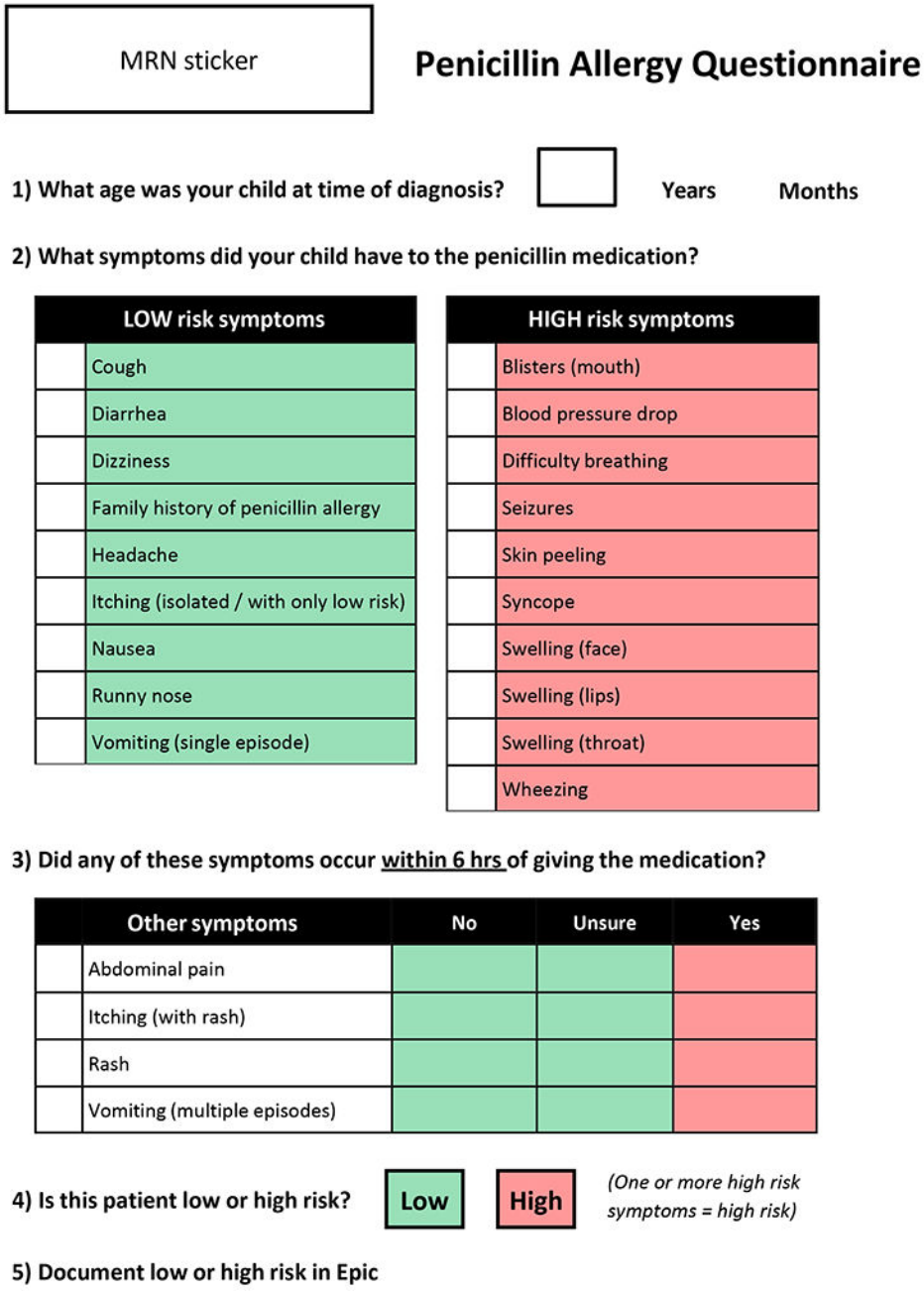

Figure 1 (online repository).
Screening questionnaire for penicillin risk stratification.

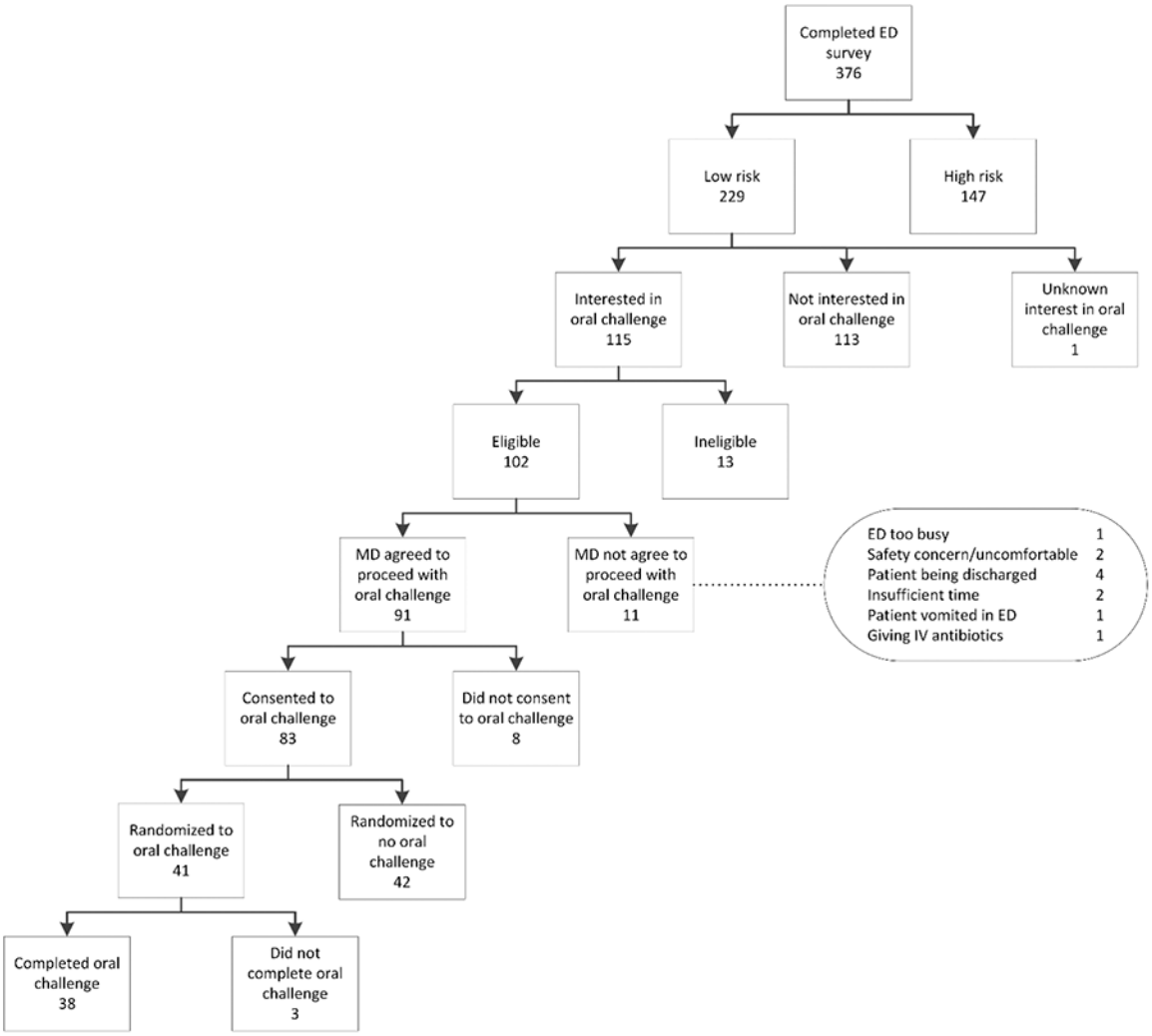

Figure 2.
CONSORT diagram showing patient flow from survey completion to oral challenge.

TABLE 1.

Categorization of allergy symptoms

Low-risk group		High-risk group	
Nonallergic symptoms	Low-risk symptoms	High-risk symptoms	
Runny nose	Rash	Facial swelling	Seizures
Diarrhea	Itching	Difficulty breathing	Rash *
Headache	Dizziness †	Lip swelling	Itching *
	Vomiting	Wheezing	Vomiting *
	Nausea	Throat swelling	Abdominal pain *
	Cough	Skin peeling	
	Family history	Mouth blisters	
	Vomiting with med administration	Drop in blood pressure	
		Syncope	

* Within 6 hours of antibiotic administration.

† High-risk if combined with rash, itching, and vomiting.