

reflect the higher prevalence of contact dermatitis in women than men.¹ Second, we observed a higher prevalence of atopic dermatitis among these patients. This is consistent with higher rates of contact allergy in patients with atopic dermatitis⁵ or could reflect the higher prevalence of atopic dermatitis among patients with asthma or allergic rhinitis who may be given inhaled or intranasal corticosteroids.⁴ Third, an associated local reaction affecting the perinasal or perioral skin is more common with intranasal than inhaled routes of exposure, which may be due to intranasal corticosteroids dripping out of the nose and coming into contact with adjacent perinasal skin.⁶ Worsening asthma symptoms are an uncommon feature, possibly because allergic contact mucositis is infrequent.⁷ Fourth, budesonide was the most common corticosteroid implicated. Budesonide, a mixture of S and R diastereoisomers, belongs to group B corticosteroids that are known to cause contact sensitization.² The S isomer cross-reacts with group A and D2 corticosteroids, such as hydrocortisone-17-butyrate, that may serve as initial sensitizers.² Therefore, patch testing to budesonide isomers may be considered.³ Compared with other corticosteroids, budesonide has a slower systemic clearance,⁸ which may make it more likely to cause SCD. Finally, our review supports using standardized panels, such as the Thin-Layer Rapid-Use Epicutaneous test, to confirm the diagnosis and identify safe alternatives. Reactions to excipients have also been reported, and patch testing to these may be considered.⁹ Owing to the anti-inflammatory properties of corticosteroids, delayed readings at 6 to 7 days may enhance sensitivity.² Furthermore, a delayed positive reaction may be preceded by an edge effect, whereby a positive reaction occurs outside the patch chamber.¹⁰ Classifying corticosteroids into groups using the Coopman or the refined Baeck classification and knowledge of their cross-reactivity can assist in selecting safe alternative corticosteroids.²

Our systematic review was limited by the small number of studies and consisted mostly of single case reports (weak quality evidence). However, the development of a maculopapular or eczematous rash after initiating inhaled/intranasal corticosteroids should alert the physician to the possibility of SCD. Female sex, atopic dermatitis, associated local reactions, and budesonide use should increase suspicion. Patch testing and knowledge of cross-reactivity are useful for confirming the diagnosis and identifying safe alternatives.

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Partnering with general pediatricians to delabel penicillin allergies in children



Penicillin allergy is the most common antibiotic allergy, with nearly 10% of the US population reporting an allergy.¹ Penicillin allergy is frequently suspected because of a reported rash, family history of penicillin allergy, or non-IgE-mediated symptoms, such as headache.^{1,2} However, when tested, less than 5% of patients actually have a clinically significant allergic reaction.^{1,2} Few individuals undergo penicillin allergy testing and thus maintain the mislabeled penicillin allergy diagnosis.¹

Previous studies in adults have found that a penicillin allergy label often results in the denial of first-line antibiotics, resulting in suboptimal treatment with clear clinical consequences (eg, increased rates of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant *Enterococcus* infections).³ The effects of erroneous penicillin allergy labeling have

not yet been as comprehensively studied in children. However, it is likely that erroneous penicillin allergy labeling in children has similar effects on morbidity and health care costs, especially given that most penicillin allergies are reported during childhood and that penicillins are first-line treatments for many common childhood infections (eg, otitis media and pharyngitis).

Within the Rady Children's Hospital-San Diego system of nearly 2 million patients, more than 40,000 children have a reported β -lactam allergy.⁴ Evaluating penicillin allergies for these many patients would be no small feat. Currently, evaluation entails a specialist visit with an allergist, possibly skin testing, and finally an oral challenge. The large number of patients who would ultimately benefit from penicillin allergy testing and the limited resources and access for allergy testing suggest that alternative avenues for evaluation should be explored.

One possible solution is to partner with pediatricians to conduct oral penicillin challenges for low-risk patients in their clinics.

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Table 1
Penicillin Allergy Survey Questions

Survey question	Response choices	Responses, n (%)
How frequently do you discuss penicillin allergies with your patients if you notice them?	Sometimes, if time permits	36 (62.1)
	Always	22 (37.9)
Do you feel delabeling erroneous penicillin allergies is important?	Yes	58 (100)
	No	0 (0)
Do you currently delabel erroneous penicillin allergies?	Yes	43 (74.1)
	No	15 (25.9)
Approximately what percentage of your penicillin allergic patients do you feel has a real allergy?	<10%	31 (53.4)
	25%	18 (31)
	50%	9 (15.5)
What is the main reason parents do not want to come to the allergy clinic for penicillin allergies?	Fear of provoking a true allergy	1 (1.7)
	Fear of testing process	5 (8.6)
	Time required for evaluation	17 (29.3)
	Cost of evaluation	1 (1.7)
	Lack of concern or urgency	24 (41.4)
	Other ^a	10 (17.2)
Would you feel comfortable doing oral challenges for penicillin in your clinic in low-risk patients?	Yes	14 (24.1)
	Maybe	25 (43.1)
	No	19 (32.8)
Would you feel <i>more</i> comfortable doing oral challenges for penicillin in your clinic if allergy provided a protocol to distinguish low-risk patients?	Yes	34 (58.6)
	Maybe	17 (29.3)
	No	7 (12.1)
What are the barriers you see to having oral challenges in your clinic?	Staff not trained to treat anaphylaxis	5 (8.6)
	Lack of adequate staff	11 (19)
	Time	20 (34.5)
	Convincing families	4 (6.9)
	Other ^b	18 (31)
With organization permission, would you be willing to be a pilot test site for testing an oral challenge protocol?	Yes ^c	26 (44.8)
	No	32 (55.2)
How long have you been in practice?	1–5 y	10 (17.2)
	5–10 y	9 (15.5)
	>10 y	39 (67.2)
What is your practice size?	0–5 physicians	16 (28.1)
	5–10 physicians	20 (35.1)
	>10 physicians	21 (36.8)

^aOther (no. of responses [%]): all the above (3 [5.2%]), far drive (2 [3.4%]), unsure (3 [5.2%]), and do not refer to allergy (2 [3.4%]).

^bOther (no. of responses [%]): all the above (15 [26%]), lack of protocol (1 [1.7%]), lack of materials (1 [1.7%]), and none (1 [1.7%]).

^cPilot sites: 14 of the 29 surveyed sites had physicians willing to act as pilot test sites.

Although penicillin allergy testing has historically been most frequently performed by allergists, any physician could perform testing if appropriately trained.¹ The protocol for testing changes is based on a patient's risk (low, medium, or high).^{1,3} Low-risk patients include those with isolated gastrointestinal reactions, itching without rash, and reactions that occurred more than 10 years ago without high-risk features (eg, anaphylaxis or mucosal involvement).^{1,2} Generally, these low-risk patients can proceed directly to an observed oral amoxicillin challenge, without needing skin testing. Several studies have revealed the safety of direct oral challenges.^{4,5} We predict that oral penicillin challenges for low-risk patients could be safely performed in the pediatric clinic as long as there is a standardized protocol to safely distinguish low-risk from high-risk children. Of note, patients considered medium or high risk (having a history of anaphylaxis, mucosal involvement, drug rash with eosinophilia and systemic symptoms syndrome, recurrent reactions after penicillin administration, or reactions to multiple β -lactam antibiotics) would still require a referral to an allergist.^{1,2}

To assess pediatricians' perspectives on penicillin allergies and interest in performing testing, we surveyed the Children's Primary Care Medical Group, the largest pediatric group in San Diego (Table 1). Our survey aimed to (1) gauge pediatricians' understanding about penicillin allergies, (2) determine why patients did not come to the allergy clinic when referred, (3) identify potential barriers to performing oral challenges for low-risk patients in the clinic, and (4) assess willingness to be a pilot test site. The survey was electronically distributed to 150 Children's Primary Care Medical Group practitioners (130 pediatricians and 20 advance practice practitioners at 29 sites) during 3 weekly company-wide

chief medical officer updates. We received responses from 58 practitioners from 29 sites throughout San Diego and Riverside counties.

Our survey found that 100% of pediatricians believed that delabeling erroneous diagnoses of penicillin allergies was important, and 84% believed that 25% or less of their patients reported to be allergic to penicillin had a true allergy. Moreover, 62% of surveyed pediatricians discussed penicillin allergies with their patients if time permitted, and 74% tried to delabel erroneous diagnoses of penicillin allergies by referring their patients to an allergy or immunology clinic. The 2 most common reasons why patients did not come to the allergy clinic when referred were lack of concern or urgency (41%) and time needed for evaluation (29%); other factors included the long drive to the clinic, cost, fear of the testing process, and fear of provoking a true allergy. When asked about comfort performing oral penicillin challenges in the clinic for low-risk patients, 24% of pediatricians initially felt comfortable (43% maybe). Pediatricians practicing for less than 5 years felt most comfortable supervising low-risk challenges (40% said yes they felt comfortable vs 11% and 23% of those in practice 5 to 10 years or >10 years, respectively). However, 59% of physicians and approximately 60% of physicians in each group said they would be comfortable performing oral challenges if provided a protocol. Overall, 45% of surveyed pediatricians expressed willingness to be a pilot test site for conducting oral penicillin challenges for low-risk patients. The main single-factor barriers to conducting oral challenges in the clinic were lack of time (35%) and lack of adequate staff (19%); however, 26% cited that all the listed survey choices (staff not trained to treat anaphylaxis, lack of adequate staff, time, or convincing families) would be potential barriers.

Despite the large number of children with a reported penicillin allergy, our survey suggests that the general pediatric community perceives that most of these allergies are misdiagnosed. Our study also reveals that, although all surveyed pediatricians understand the importance of addressing this public health issue, approximately one-quarter of surveyed pediatricians would currently feel comfortable conducting low-risk oral amoxicillin challenges in their clinics. Thus, this finding highlights the need for further efforts in (1) establishing a protocol to safely distinguish low-risk children from high-risk children (to begin oral challenges for low-risk patients in clinics), (2) developing educational materials to increase public awareness about the importance of delabeling misdiagnosed penicillin allergies, and (3) exploring ways to address potential testing barriers. Because there is still a potential risk of a severe anaphylactic reaction during an oral challenge, it will be especially important to address the main barriers (lack of time and lack of adequate staff) to ensure patient safety. In the end, although partnering with pediatricians to delabel misdiagnosed penicillin allergies is a step in the right direction, it is only part of the solution—this should be paired with standardized approaches to prevent mislabeling in the first place.

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Urban-rural differences in health care utilization and prescription filling for childhood asthma



Despite lower asthma prevalence in rural compared with urban children,^{1,2} studies suggest that rural children have higher asthma morbidity and uncontrolled asthma.^{2–4} Investigation into potential differences in management and health care utilization after asthma diagnosis would help provide a better understanding of these results. Potential barriers to health care access in rural areas may contribute to poor management of asthma and help explain uncontrolled disease in these areas.

We investigated urban-rural differences in health care utilization among children with asthma. Specifically, we investigated differences in physician visits and hospitalizations for asthma and asthma medication prescription filling in the year after diagnosis and during a 10-year follow-up period. This was a population-based retrospective cohort study of 66,589 children born between January 1, 1995, and December 31, 2014, who had an asthma diagnosis during this time. Data for the study were obtained from Saskatchewan Ministry of Health administrative databases, which cover approximately 99% of the population of Saskatchewan, Canada. Four databases were linked: (1) the Person Registry System, (2) the physician visits, (3) the hospital services, and (4) the outpatient prescription drug databases. Identification of asthma diagnosis was based on *International Classification of Diseases, Ninth Revision* (code 493) and *International Classification of Diseases, Tenth Revision* (code J45.x) codes. We excluded 15,021 First Nations children because no information on medication use was available, leaving 51,568 participants. Of these children, 18,086 had 10 years of follow-up

after diagnosis. The study was approved by the University of Saskatchewan Research Ethics Board.

Asthma health care utilization information and prescription filling were obtained for each year of follow-up after the index date (date of first asthma diagnosis). Physician visits for asthma required a diagnostic code of 493 listed on the claim. For asthma hospitalizations, the diagnostic code (J45.x) had to be the primary reason for admission. For asthma prescriptions, we considered filling of a prescription for inhaled corticosteroids (ICSs; yes vs no) or inhaled short-acting β -agonists (SABAs; yes vs no) in the first year after the index date and each year during the 10-year follow-up period. The number of SABA prescriptions filled during a 12-month period was categorized as less than 4 and 4 or more prescription fillings.⁵

The independent variable for this study was location of residence at the index date based on the Census Metropolitan Area⁶ and categorized as large urban (population >40,000), medium urban (population of 15,000–40,000), small urban (population of 3500–14,999), and rural (population <3500). Other covariates included were sex, age at index date, cohort group, and history of allergic condition.

We used multiple logistic regression to evaluate the associations between location of residence and health care encounters in the first year after the index date with large urban as the reference group. To determine trends in health care utilization during the 10-year follow-up period, the average annual percentage change (AAPC) was calculated by location of residence using Joinpoint trend analysis.

Most of the study population lived in a large urban area (51%) compared with medium urban (14.6%), small urban (6.9%), and rural (27.5%) areas. The sex distribution was similar across location of residence ($P = .28$).

Compared with children living in large urban areas, children living in rural areas were less likely to visit a physician or

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