American Academy of Allergy Asthma & Immunology

Penicillin Allergy Delabeling Can and Should Be Performed in Pregnant Patients: A Work Group Report of the AAAAI Women's Health in Allergy and Immunology and Adverse Reaction to Drugs, Biologics, and Vaccines Committees

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Penicillin allergy is frequently reported yet rarely confirmed in pregnant women, similar to the general population. Historically, there has been hesitation to perform penicillin allergy testing in pregnant patients due to perceived risk to the patient and fetus in the event of an allergic reaction. Given the multiple clinical indications for penicillin in pregnancy and delivery, there are also risks of using non–first-line antibiotics; thus clarity is needed regarding the safety of undergoing penicillin allergy testing during pregnancy. A workgroup subcommittee of members from the American Academy of Allergy, Asthma & Immunology committees on Women's Health in Allergy/Immunology and Adverse Reactions to Drugs, Biologics, and Vaccines was convened, and a survey of current allergist practices as well as a scoping review of the literature was conducted. Although survey respondents reported mixed comfort with testing, evidence from numerous recent studies representing hundreds of pregnant patients demonstrates that penicillin allergy testing can be safely performed via an oral challenge with or without preceding skin testing. To implement this testing in clinical practice, allergists and immunologists can learn from the clinical experience of numerous institutions that have reported a successful approach to offering definitive allergy

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No funding was received for this work.
Conflicts of interest: M. T. Kraft has served as a one-time advisory board member for Sanofi in the preceding 24 months. The rest of the authors declare that they have no relevant conflicts of interest to disclose.
Received for publication November 9, 2025; revised January 6, 2026; accepted for publication January 7, 2026.
Available online March 20, 2026.
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2213-2198

https://doi.org/10.1016/j.jaip.2026.01.046

Abbreviations used
AAAAI- American Academy of Allergy, Asthma & Immunology
BPA- Best practice alert
DOC- Direct oral challenge
GBS- Group B Streptococcus
PDT- Practice, Diagnostics, and Therapeutics
PST- Penicillin skin testing
SPT- Skin prick testing

evaluation in this population. **© 2026 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2026;14:805-15)**

Key words: *Penicillin allergy; Pregnancy; Pregnant; Allergy testing*

Penicillin allergy in pregnancy is a commonly encountered clinical scenario that can have broad maternal and fetal outcomes. Although there is support for penicillin allergy testing among obstetricians, definitive guidelines for allergists are lacking.[1,2] Practice variability among allergists regarding whether and when to test pregnant patients for penicillin allergy can lead to confusion and inconsistent messaging. This workgroup report represents a collaboration between the American Academy of Allergy, Asthma &Immunology (AAAAI) committees on Women's Health in Allergy/Immunology and Adverse Reactions to Drugs, Biologics, and Vaccines, and an AAAAI Leadership Institute project. Our goal is to review the existing literature documenting the safety of penicillin allergy testing in pregnancy, assess current practices and barriers as reported in a national survey of practicing allergists within the AAAAI, and propose recommendations for implementing penicillin testing in clinical practice.

BACKGROUND

The use of β-lactam during pregnancy and delivery, and implications of penicillin allergy

β-Lactam antibiotics are used during pregnancy and delivery for various clinical indications, including group B Streptococcus (GBS) prophylaxis, preterm premature rupture of membranes prophylaxis, cesarean section prophylaxis, and treatment of asymptomatic bacteriuria and urinary tract infections.[1-3] Penicillin specifically is the preferred first-line treatment for intrapartum prophylaxis for GBS and remains the only appropriate treatment for syphilis.[1,4] Having a penicillin allergy label during pregnancy often leads to the use of alternative, less effective, and broader-spectrum antibiotics with greater risk of side effects, such as vancomycin, clindamycin, and gentamicin. These substitutions also contribute to antibiotic resistance.[5-8] In addition, a penicillin allergy label is associated with increased morbidity, including a higher risk of cesarean delivery, endometritis, wound complications, and prolonged hospital stays for both mothers and neonates.[5,9-13]

Safety of penicillin allergy testing during pregnancy

The use of penicillin skin testing (PST), oral challenges (drug provocation testing), and desensitization to allow the use of penicillins has been in practice for several decades.[14] Whereas desensitization is a procedure used to induce temporary tolerance in allergic patients, evaluation of the allergy via skin testing and oral challenges allows for definitive determination of tolerance or allergy. Penicillin allergy evaluation historically involved allergy skin testing, consisting of skin prick testing (SPT) and intradermal testing (using penicilloyl-polylysine, diluted penicillin G, and potentially ampicillin 20 mg/mL), followed by an oral challenge, typically with amoxicillin.[15] Penicillin allergy evaluation with PST and/or oral challenges is performed only in patients who have been appropriately screened and do not exhibit high-risk features, such as a history of severe cutaneous adverse reactions (eg, Stevens-Johnson syndrome and toxic epidermal necrolysis). However, pregnant women have historically largely been excluded from PST and oral penicillin and amoxicillin challenges due to concerns over safety to both the expectant mothers and the fetus, with desensitization being used for individuals in whom penicillin is considered the only safe and effective option, such as in syphilis infection.[16] Standardized PST in pregnancy was first reported in a 2006 study in which PST was performed for GBS positive women.[17] and the majority (96.4%) tolerated PST without adverse symptoms. One patient reported pruritus, and another patient vomited and fainted during the prick test but subsequently completed the intradermal testing with negative results. Of those with negative testing, 89% received at least 1 course of intrapartum penicillin for GBS, of whom 2 patients had delayed rashes and no cases of anaphylaxis. Similar results were reported in a subsequent study that demonstrated the overall tolerability and safety of PST in 28 women and that the majority of women (n = 25; 89%) were PST negative; all 25 subsequently tolerated antibiotics intrapartum.[18]

These early studies focused primarily on penicillin-allergic pregnant patients with established GBS-positive cultures and included PST only without an oral challenge.[17,18] Subsequent cohort studies have demonstrated that evaluation earlier in pregnancy with both skin testing and oral challenge is safe and effective.[15,19-26] A 2020 systematic review of 18 studies (inclusive of prospective studies, observational cohorts, and case reports of penicillin-allergic pregnant patients requiring treatment for syphilis or GBS) found that of 203 patients who had penicillin allergy skin testing, 84% were negative, and reactions to penicillin testing and challenge were rare (1.5% and 0%, respectively); the majority were tested after the first trimester.[27] Later studies have continued to add to these reassuring data regarding the safety of testing.[8,20-26] Table I summarizes the outcomes of 9 studies representing more than 1000 pregnant patients with a penicillin allergy label who underwent skin testing, oral challenge, or both. Testing was most commonly performed in the second or third trimester when gestational age was specified. The majority (95%-99%) of patients in these studies had negative skin tests, and nearly all went on to pass oral challenges. In the minority of patients who developed adverse reactions during penicillin evaluation, symptoms were typically mild and responsive to antihistamines. One study reported the use of epinephrine for 2 patients who experienced symptoms of cough, itch, and vomiting after the test dose.[20] There were no reports of serious adverse maternal or fetal outcomes after testing, including in the patients who experienced systemic reactions. After evaluation, the majority of subjects (51%-89%) went on to receive intrapartum antibiotics, primarily β-lactams.[15,17,19] Desensitization remains an option to induce temporary tolerance in pregnant patients with a confirmed or suspected high-risk IgE-mediated penicillin allergy when no acceptable alternative treatments are available.[33]

TABLE I. Summary of studies reporting outcomes of penicillin testing (skin test and/or oral challenge) in pregnant patients via a variety of pathways for evaluation, such as clinical trial protocol, dedicated e-consult or triage line, and educational intervention among obstetrics providers—there were a few reactions during testing and no serious adverse events to testing in any of the studies

Study	Pathway for evaluation	No. eligible for testing	No. actually tested	Trimester testing occurred	Type of testing	No. of PST* positive (%)	No. of tolerated OC† (%)	Reaction details
Macy, 2006[17]	Research protocol—recruited women with a history of penicillin allergy and acutely positive prenatal GBS cultures or a history of positive GBS cultures were offered PST by their obstetricians and referred to allergy	Unknown	56	Third trimester	PST only (n = 56)	3 (5)‡	N/A	Two of 47 (4%) patients who received 1 course of penicillin after evaluation developed delayed rashes
Philipson et al, 2007[18]	Prospective study of pregnant women with (+)GBS culture and penicillin allergy recruited for PST. If negative, recommended intrapartum penicillin	28	27	Third (after GBS known)	PST only	2/27 (7.4)	N/A	None
Kuder et al, 2020[19]	Retrospective chart review of patients who underwent penicillin allergy testing by allergy clinic and were pregnant at the time of evaluation	Unknown	46	Mostly second trimester; mean 25.8 weeks (SD ± 9.1 weeks)	PST (n = 46), some followed by OC (n = 18; 39%), patient choice	2 (4)	All 18 (100) who elected to pursue OC passed	28 (61%) received intrapartum antibiotics§ without reaction; 3 patients had delayed rashes with subsequent antibiotic courses postpartum

(continued)

TABLE I. *(Continued)*

Study	Pathway for evaluation	No. eligible for testing	No. actually tested	Trimester testing occurred	Type of testing	No. of PST* positive (%)	No. of tolerated OC† (%)	Reaction details
Wolfson et al, 2021[8]	Retrospective review of e-consult program: allergist reviewed history in the electronic medical record. If appropriate for testing, scheduled during third trimester	363 recommended from e-consult; 222 had in-person evaluation	220	Third trimester	PST (n = 220), followed by OC (n = 213, 4 deferred), cleared by history (n = 1)	3 (1.5)	209 (95) passed OC‖	133 (60%) received intrapartum antibiotics. One patient developed immediate reaction (nonurticarial rash) after OC, 2 developed delayed reaction (maculopapular exanthema) after OC
Desravines et al, 2021[20]	Research protocol—recruited pregnant women with self-reported penicillin allergy who underwent allergy testing between 14 weeks and 36 6/7 gestation	127 eligible; 74 accepted	46	Second and third trimester (second trimester: n = 24 [52%]; third trimester: n = 22 [48%])	PST (n = 46, 43 negative), followed by OC (n = 45)	1 (2)	43 (93) passed OC¶	2 (4%) had systemic reactions during challenge (cough, chest tightness, pruritus, vomiting), requiring epinephrine. No adverse outcomes to mother or fetus
Zhang et al, 2021[21]	Research protocol—recruited pregnant women less than 36 weeks of GA with reported penicillin allergy	148 referred for evaluation (not specified if all eligible)	66	Third trimester	PST (n = 37) followed by OC (n = 37), DOC# only (n = 27), cleared by history (n = 2)	0	64 (100) passed OC	None
Patel et al, 2022[22]	Retrospective chart review of general allergy referrals	136 referred, 135 eligible (1 excluded for SCAR); 1349 with penicillin allergy during the same time period never referred	135	Second and third trimester	PST (n = 133), followed by OC (n = 133); 2 DOC	1 (1)	132 (99) passed OC	68 (51%) received antibiotics, 1 reported a reaction of subjective itch and throat symptoms that resolved without treatment
Mak et al, 2022[28]	Quality improvement initiative for evaluating pregnant women referred to allergy clinic	245 referred; 9 delabled by history, 1 high risk (not tested). Total 235 eligible for testing	235	Third trimester	DOC (low risk, n = 207) or PST; then OC (medium risk, n = 28)	2/28 (7) equivocal	203/207 (98) passed OC	4 (1.9%) cases of delayed cutaneous reactions treated with antihistamine and topical steroid; no immediate reactions

Kwah et al, 2022[23]	Retrospective chart review of general allergy referrals	232 referred patients, 175 underwent consultation, 167 were considered appropriate for testing	117	Mostly third trimester; median GA at testing 34.1 weeks (interquartile range, 31.1-36.8 weeks).	PST (n = 117), some followed by OC**	1 reaction**	Unknown	One patient with positive PST
Stephen et al, 2024[29]	QI study for structured referrals in third trimester	102 referred, 69 seen in A/I clinic	46	Seen between 7- and 38-week gestation, timing of testing not specified	PST followed by OC	3 (6.5)	39/42 (92.8) passed	Three reacted during OC—1 throat pain, 1 delayed rash, 1 throat/ tongue numbness. All relieved with antihistamine or no treatment
Nair et al, 2024[24]	Dedicated allergy clinic phone line provided to patients during antenatal obstetric visits	324 referred	251	Any GA: first trimester n = 9 (3.6%); second trimester n = 129 (51.4%); third trimester, n = 110 (43.8%); unknown n = 3 (1.1%)	PST (n = 239) followed by OC (n = 230), DOC only (n = 12)	5 (2), 4 were indeterminate and advised to avoid	229 (91) passed OC after PST; 12 (5) passed DOC	One patient with delayed reaction to oral challenge after negative PST
Tsao et al, 2024[25]	Prenatal penicillin allergy evaluation program including OB facing education, patient facing education, referral triage protocol	219 referred after program implementation	149	Any GA: first trimester n = 9 (6%); second trimester n= 62 (42%); third trimester n = 78 (52%)	PST only (n = 16), PST (n = 133) followed by OC (n = 132)	1 (<1)	130 (87) were delabeled, 2 (1) had positive OC	One patient developed itching and erythema after 500 mg dose, and 1 developed delayed rash on upper extremities hours after 500 mg dose; both resolved without treatment
Tucker et al, 2024[26],††	Pregnant patients referred for penicillin testing (retrospective review)	131 referred	131	Not specified	PST + OC (n = 124); 7 DOC	0	129/131 (98) delabeled (1 negative PST, skin symptoms with OC; 1 did not complete evaluation)	One had negative PST but skin itching and redness during amoxicillin administration

(continued)

TABLE I. *(Continued)*

Study	Pathway for evaluation	No. eligible for testing	No. actually tested	Trimester testing occurred	Type of testing	No. of PST* positive (%)	No. of tolerated OC† (%)	Reaction details
Wong et al, 2024[30]	Prospective cohort study at 2 centers: one offered challenge before delivery (DOC or after PST) and the other offered PST only with challenge postpartum	276 (207 in antepartum challenge site, 69 in postpartum challenge site)	230	Second trimester, third trimester or postpartum	Antepartum: PST + OC (n = 41) or DOC (162); alternative: PST only antepartum	2/44 (4.5) PST positive in the antepartum challenge group	201/204 (98.5) passed OC in the antepartum group. In the other group, 69 antepartum-negative PST; then 10/10 tolerated intrapartum challenge, 16/16 who returned for postpartum testing	Two mild cutaneous reactions, 1 episode of abdominal discomfort during oral challenge; responded to antihistamines. No epinephrine administration was required. All 3 reactions were in patients with negative PST
Godfrey et al, 2025[31]	Pregnant patients identified/referred after best practice advisory (BPA) implemented in EMR	728 BPA fired, 549 referred, 299 (41.1%) were seen, 267 tested	267	Any GA: first trimester n = 2 (0.7%), second trimester n = 121 (40.5%), third trimester n = 176 (58.9%)	PST only (8), PST + OC (100), or DOC only (159)	3	270/299 (90.3) delabeled; 3 positive PST; 3 reaction to OC; 23 other (deferred, declined, etc)	Three reactions to OC: 2 mild (singular or few hives during evaluation), 1 with rash, swelling, and vomiting 30 minutes after leaving clinic. Treated with antihistamines. No epinephrine

Patrawala et al, 2025[32]	Randomized trial of patients receiving preceding skin testing or direct oral challenge, regardless of trimester	144	144	Any GA: first trimester n = 7 (4.9%); second trimester n = 73 (50.7%); third trimester, n = 64 (44.4%)	PST followed by OC (n = 73) or DOC (n = 71)	5 (6.8%)—1 on skin prick, 4 on ID	93.2% of the skin test group (n = 68; all patients with negative PST tolerated); 100% (n = 70)	One patient in the DOC group developed generalized pruritus after the first step of the challenge that could not be distinguished between anxiety and reaction; she returned outside of the study and underwent PST and oral challenge, which were both negative. No patients who completed the oral challenge in the study had reactions

DOC, Direct oral challenge; *EMR*, electronic medical record; *GA*, gestational age; *GBS*, group B Streptococcus; *ID*, intradermal; *OC*, oral challenge; *PST*, penicillin skin testing; *QI*, quality improvement; *SCAR*, severe cutaneous adverse reaction; *SD*, standard deviation.

*Penicillin skin test.

†Oral challenge.

‡Two (4%) mild adverse reactions with PST: 1 patient had generalized pruritus with PST and 1 patient fainted and vomited with PST, but then tolerated intradermal testing and subsequently tolerated penicillin.

§History did not determine candidacy for challenge. A total of 28 patients received intrapartum antibiotics, not related to whether they had received oral challenge or not.

‖A total of 210 of the 217 (97%) skin test−negative patients had a negative oral amoxicillin challenge. There was 1 patient with a nonurticarial rash within 1 hour and 2 patients with delayed maculopapular exanthema after an oral amoxicillin challenge; 4 patients did not undergo an oral challenge. One patient's label did not get removed.

¶Two (4%) required epinephrine from the test dose but remained stable. Symptoms were coughing, itching, and vomiting.

#Direct oral challenge (no preceding skin test).

**Kwah et al[23] did not differentiate between skin testing and oral challenge results.

††Abstract only.

TABLE II. Demographics of respondents to survey of practicing allergists regarding current practice and perceptions of penicillin allergy evaluation in pregnant patients

Characteristic	Response	Value, n (%) (N = 39)*
Job position		
	Attending	36 (92.31)
	Fellow	1 (2.56)
	APP	2 (5.13)
Years in practice		
	<1 year	4 (10.26)
	1-5 years	4 (10.26)
	6-10 years	4 (10.26)
	11-15 years	8 (20.51)
	16-20 years	9 (23.08)
	>20 years	10 (25.64)
Practice environment		
	Academic medical center	11 (28.21)
	Integrated care organization	8 (20.51)
	Private practice	20 (51.28)
Clinic setting		
	Rural	2 (5.13)
	Suburban	23 (58.97)
	Urban	14 (35.90)
Geographic location of practice		
	Northeast US	6 (15.38)
	Mid-Atlantic US	6 (15.38)
	Midwest US	10 (25.64)
	Midsouth US	7 (17.95)
	Southeast US	4 (10.26)
	Rocky Mountain US	1 (2.56)
	Western US	5 (12.82)

APP, advanced practice provider.
*Not all participants answered every question; % is reflective of proportion of answers based on total n responding to the question.

The need for action

Previous studies highlight not only the safety, but also the effectiveness, of delabeling penicillin allergy during pregnancy. We, as allergists, have the tools and expertise to perform penicillin testing and/or challenges in a safe environment, and yet, many allergists defer penicillin delabeling until after delivery. The goals of this working group report included (1) surveying practicing allergists regarding current practices of testing pregnant patients with penicillin allergy, (2) identifying potential barriers to access, and (3) proposing suggestions for future practice.

METHODS

Through the AAAAI Practice, Diagnostics, and Therapeutics (PDT) committee, we delivered a survey to practicing allergists and immunologists to assess current practices and barriers to penicillin allergy testing in pregnant patients via the PDT list-serv. This 20-question survey was distributed in August and September 2024 and included questions regarding demographic and practice setting information, duration in independent practice, current or previously attempted institutional/practice interventions, and typical scheduling practices for pregnant patients presenting for evaluation of penicillin allergy. The full text of the survey can be found in this article's Online Repository at www.jaci-inpractice.org.

SURVEY RESULTS

The PDT sent an electronic request to complete the survey to 857 members of the AAAAI. A total of 61 allergists (7.1%) responded to the survey in part, 15 of whom did not treat pregnant patients and were excluded from completing the remainder of the survey. Of the remaining 46 allergists, 39 completed all of the questions in the survey, and 7 partially completed the survey; proportions for responses were calculated based on the denominator of respondents per question. The majority of respondents (n = 36; 92%) were attending physicians, 5% (n = 2) were advanced practice providers, and 3% (n = 1) were fellows. Years in practice were evenly distributed between all clinicians, with nearly half of respondents being in practice for over 15 years. Over half (51%; n = 20) of respondents were in private practice, whereas 28% (n = 11) were practicing at academic medical centers and 21% (n = 8) were hospital-employed or in an integrated care organization. Respondents were also evenly distributed across geographic locations and clinic settings (Table II).

The majority (82%) of allergists surveyed did not have a dedicated triage process for managing penicillin allergy referrals for pregnant patients, whereas others (9%) had charts reviewed by staff before scheduling. Nearly half (48%) of allergists report that pregnant patients are evaluated in 2 visits, whereas 20% report that evaluation and testing is completed in a single visit without prior review, and 15% report a single visit with preceding chart review (e-consult and triage). When asked what best characterizes the respondents' current practice in penicillin allergy testing in pregnancy, responses varied widely. Approximately one-third reported that all patients underwent SPT before a challenge, another 33% reported that some patients received a direct oral challenge (DOC), 20% noted that patients underwent SPT only with a challenge deferred until delivery or if needed for treatment, and 13% told patients to return for testing after delivery. The majority (80%) do not routinely use a standardized risk assessment tool such as PEN-FAST[34] to determine eligibility for skin testing or challenge. When asked when they felt the most *ideal* time is to complete a penicillin allergy evaluation (including challenge with or without skin testing), 43% reported any time in pregnancy, whereas 28% reported only when needed for acute treatment and 18% reported third trimester; similar results were found when practitioners were asked when they most frequently *actually* perform these evaluations (Figure 1). When asked what respondents felt was the most significant barrier, the majority (53%) felt that there were no barriers, whereas 16% did not feel comfortable with testing during pregnancy, 8% felt that patients had other appointments to prioritize, and another 8% reported patient apprehension being an issue (Table III). Lastly, 16% noted a difficult referral process/scheduling issue. Those who reported a difficult referral process cited lack of referrals from OB/GYN (86%), lack of a streamlined process to handle referrals between the 2 specialties (43%), absence of triage support to properly schedule patients (29%), or lack of staffing for the testing (14%). When asked whether their institution or practice has implemented any procedures to help identify or schedule pregnant patients with penicillin allergy, 72% reported no. Of those who did have procedures implemented, the majority reported educational sessions with obstetric colleagues, followed by a separate referral process for pregnant patients, quality improvement initiatives, and best practice alert (BPA) flags, respectively.

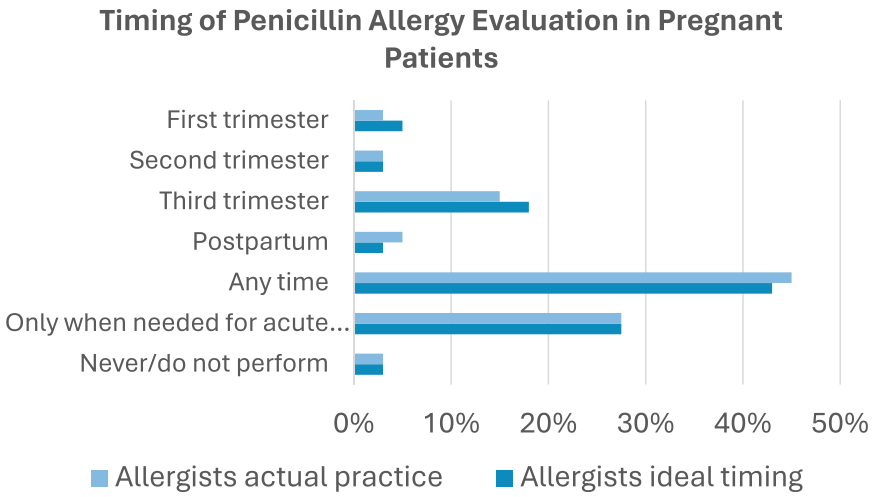

FIGURE 1. Timing of penicillin allergy evaluation in pregnant patients—both typical practice and perceived ideal timing of testing as reported by surveyed allergists (total respondents, n = 40; skipped = 21).

TABLE III. Reported barriers to evaluating pregnant patients for penicillin allergy (total respondents for this question were n = 38)

Barriers	Value, n (%)
I do not see any barriers to a pregnant patient being delabeled in allergy clinics	20 (52.63)
My own limited knowledge on allergy testing options for pregnant patients	0 (0)
I do not feel comfortable with patients undergoing allergy testing during pregnancy/I feel it is too risky	6 (15.79)
Difficult referral process/scheduling	6 (15.79)
Patients have too many other appointments to prioritize having an allergy evaluation	3 (7.89)
Patient apprehension	3 (7.89)

DISCUSSION

Penicillin allergy in a pregnant patient is a clinical scenario that allergists should expect to encounter. In our survey conducted by the AAAAI PDT, allergists from both private practice and academic settings were well represented; within this cohort, just under half of the respondents reported some barriers preventing penicillin allergy delabeling in pregnancy in their practice. However, we are limited by a low total number of respondents as well as response bias given that those most interested in this topic may be more likely to respond to the survey and may not be representative of how all allergists approach penicillin allergy evaluation in pregnant patients. There may be an even higher proportion of allergists in the community who perceive barriers to evaluation. The most frequently reported barriers were as follows: allergists did not feel comfortable testing during pregnancy, a difficult triage process, prioritization by patients of other appointments, or patient apprehension.

Penicillin testing in pregnancy—when and how to test

Despite the robust evidence that penicillin allergy testing in pregnancy is generally safe, with low risk and significant benefit,[8] we note that survey respondents continue to report discomfort with testing. Over the past 20 years, there has been an evolution in published outcomes of penicillin testing, from skin testing only without an oral challenge before the intrapartum period[9,17,18] to skin testing with an oral challenge,[8,20-22,29] and most recently including DOC in low-risk patients.[21,24,28,31,32] In consecutive articles, a collaborative group at British Columbia Women's Health and Hospital Centre examined the safety of DOC in pregnancy.[21,28] They initially created an institutional risk algorithm in which low-risk patients received DOC (n = 28) and medium-risk (n = 14) patients underwent SPT first, and compared outcomes with individuals who received the prior standard of care, in which all pregnant patients underwent SPT followed by a challenge (n = 24); all 66 patients were able to be delabeled.[21] The same institution subsequently adopted the validated PEN-FAST[34] decision tool after its publication in 2020 for the remainder of its evaluations. Although PEN-FAST has not been specifically validated in the pregnant population, this risk assessment tool has gained popularity because of its simple 5-question format (history of penicillin allergy, timing of reaction, clinical symptoms, and need for treatment) with a high negative predictive value of very low risk patients (score 0) having a <1% chance of positive penicillin testing.[34] Patients who were deemed low risk either via their initial algorithm or who had a PEN-FAST score of zero underwent DOC (n = 207), with none having immediate or delayed reactions.[28] Godfrey et al[31] reported on the results of another institution's referral program in which a BPA fired in the electronic medical record for pregnant patients with a penicillin allergy who were subsequently referred to a drug allergy clinic and offered an oral challenge with or without preceding skin testing based on risk stratification. In the 2 years after adaptation of the BPA, 299 patients were evaluated, the majority (53.2%) via a DOC. Reactions were minimal and treated with oral antihistamines; none required epinephrine.[31] Ultimately, 270 of 299 patients were delabeled; the majority of those who were not (n = 29) either declined (34.5%) or deferred (20.7%) evaluation or had a possible type IV reaction (17.2%). Only 6 patients had positive testing—3 of 108 (2.8%) positive SPT and 3 of 259 (1.6%) positive oral challenges (1 after negative skin testing and 2 after DOC).[31] Finally,

Patrawala et al[32] reported outcomes of a randomized trial of 144 pregnant patients with low-risk penicillin allergy history, regardless of trimester, who underwent evaluation via either skin testing first or DOC, and found that the vast majority (93.2% in the skin testing group and 100% in the DOC group) had negative evaluation; none required epinephrine.

With respect to the timing of penicillin allergy evaluations in pregnancy, most of the studies have completed PST and oral challenges during the late second to early third trimester of pregnancy.[19,21,28] Desravines et al,[20] however, recruited women from the beginning of the second trimester to the late third trimester (14w0d to 36w6d) to overcome the tight turnaround time accompanying GBS testing, which occurs at 36 weeks. They found that pre-emptive evaluations were safe and allowed for increased use of β-lactam antibiotics. Generally, evaluations have been avoided in the first trimester due to the nausea and vomiting common at this gestational age, which can confound oral challenges, the low but potential risk for anaphylaxis posing risk to the fetus,[5] and concern for coincidental timing of penicillin testing with early pregnancy loss or congenital abnormalities. In their randomized trial, Patrawala et al[32] performed testing regardless of trimester, but only 5% (n = 7) of subjects were in the first trimester, likely related to the timing of evaluation; most initial prenatal visits are performed by 10 weeks of gestation, and subsequent specialist referral, such as to allergy, can take several weeks.[32] Other institutions represented by the authors of this workgroup report time their evaluations during the third trimester in order to decrease risk to the fetus if epinephrine is necessary; none defer until after GBS status is known or after delivery. Importantly, to the authors' knowledge, there have been no adverse outcomes reported from testing in the first trimester since the advent of standardized screening and testing protocols. The only known report of a significant adverse outcome to penicillin testing stems from a 1958 case report in which anaphylaxis to intradermal penicillin led to fetal demise, before the development of robust screening protocols.[5,35] Another consideration for timing is the higher rate of naturally occurring miscarriage in the first trimester of pregnancy, which could be temporally attributed to testing, even if causation is unlikely. Ultimately, the timing of PST and/or oral challenge can be decided through shared decision-making with the pregnant patient. In one report regarding patient perspectives of penicillin evaluation during pregnancy, a common theme was preference for testing during the second or early third trimester. Patients cited concerns with testing in the first trimester due to information overload and physical changes in early pregnancy, and some patients were influenced by risk and benefit discussions with reference to specific indication (ie, known GBS status), among others.[36]

Although clarifying penicillin allergic status before delivery is preferred, some have reported a successful approach of postpartum testing on the labor and delivery ward with risk-stratified direct challenges.[37] It is important to note, however, that delaying challenge to intrapartum or postpartum increases the chances for lost follow-up and missed opportunities to delabel. Wong et al[30] compared strategies in 2 centers, one of which offered testing antepartum with an oral challenge (with or without preceding skin test), whereas the other center offered only penicillin skin test antepartum and deferred challenge to intrapartum or postpartum depending on the need for penicillin. They found that 97% (201 of 207) patients at antepartum challenge sites were delabeled compared with 38% (26 of 69) in the postpartum challenge site (Table I). The majority of this discrepancy in delabeling could be attributed to loss to follow-up (n = 37 in the postpartum clinic) as opposed to positive testing (5 in the antepartum group and 0 in the postpartum group) or patient decline (n = 1 in the antepartum group).[30]

Features of successful delabeling programs

In our survey, over 70% of allergists reported that their practice had not implemented any procedures to help identify or schedule pregnant patients with penicillin allergy, which likely contributes to the cited barriers and hesitancy among allergists and obstetric providers to refer patients for evaluation.[38] However, when a penicillin allergy evaluation program is established between allergy and immunology and obstetrics, the result is increased first-line antibiotic use.[8] Several institutions have optimized their triage processes to allow for streamlined consultation and to allow for consultation and testing to occur on the same day, minimizing the number of appointments required at a busy time for pregnant women. We discuss several of these examples below as an illustration.

Wolfson et al[8] used a model of the initial obstetrics provider obtaining the history of penicillin allergy, including the year the allergy occurred and the major symptoms. An e-consult, which is a physician-to-physician request to review the electronic medical record, was then sent to the allergy/immunology division. Allergists assessed appropriateness for evaluation: a history of intolerance alone (eg, headache) was delabeled without further assessment, a history of severe cutaneous reaction or recent anaphylaxis was advised to continue to avoid penicillins, and patients who had a low-risk clinical history of potential IgE-mediated reaction more than 5 years prior were scheduled for in-office evaluation during their third trimester to perform PST/oral challenges. Although not all patients recommended for evaluation presented to the clinic (222 of 363, 61%), nearly all of those who did (95%, n = 220) were successfully delabeled at their visit (Table I).

Stephen et al[29] implemented a referral pathway to achieve the same goal, using obstetric clinician education and prioritizing referral scheduling promptly to facilitate delabeling. After obstetrics clinicians identified patients with a penicillin allergy label, a scheduling team contacted patients by phone to schedule appointments within 2 weeks. The allergy clinic was alerted to accommodate same-day testing whenever feasible, with a dedicated allergy clinic testing nurse to allow for 2 to 3 simultaneous challenges.

The use of the electronic medical record's BPA to automate the process of identifying eligible patients for referral holds particular promise. In the 2 years after its implementation, Godfrey et al[31] reported that the BPA was triggered for 728 patients who were seen in 1 of 7 obstetric clinics in their health care system, and a referral was made for 549 (75.4%) of patients; 299 were ultimately seen in the drug allergy clinic.

As a final example, Patel et al[22] demonstrated the clinical utility of preappointment screening in pregnant patients with penicillin allergy via a triage questionnaire administered through the electronic medical record. The questionnaire was reviewed by nurses to ensure that penicillin allergy testing was appropriate and to exclude those with high-risk histories, such as severe cutaneous reaction or anaphylaxis within the preceding 1 year.[22] By prescreening patients, nearly all were able to proceed with skin testing and challenge (Table I). Future larger scale referral pathways can build off this existing body of work, using them as

key components of penicillin delabeling programs in pregnant patients.

CONCLUSION

Penicillin allergy labels continue to pose challenges for the optimal clinical care of pregnant patients. The knowledge of the low rate of true penicillin hypersensitivity in those with an allergy label and the implications of using broader-spectrum, second-line antibiotics for perinatal infections favors allergy testing during pregnancy, although a history of severe reaction, for example, Stevens-Johnson syndrome, should exclude the patient from rechallenge. Allergists' comfort with testing should not continue to be a barrier to care as numerous studies representing hundreds of patients have now demonstrated that pregnant patients can be safely skin tested and challenged to penicillin. Indeed, as allergists, we have an obligation to advocate for this testing and actively seek opportunities for community outreach and partnership with local OB/GYN practices to ensure that all pregnant patients have appropriate care. Through the shared experience of multiple different institutional approaches to streamline, screen, and effectively implement such testing, we are equipped to bring proactive penicillin allergy delabeling as a clear standard of care in pregnant patients.

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ONLINE REPOSITORY

Q1. DEFINITION: For the purposes of this survey study, delabeling is defined as removal of a drug allergy label (penicillin) from their medical record by means of history taking, skin testing and/or drug challenge.
Do you see pregnant patients and/or women of childbearing age for penicillin allergy evaluation in your office?
Yes
No

If No, stop survey

Q. I am a(n):
Attending physician
Fellow
Advanced practice provider
Other (comment box)

Q. How many years have you been in independent practice?
Currently still in training
Less than 1 year
1-5 years
6-10 years
11-15 years
16-20 years
>20 years

Q. How would you describe your practice environment?
Academic center
Community (hospital-based, nonacademic center or integrated care organization)
Private practice (single provider, multiple allergy or multiple specialty group, large group, private equity)
Other [**Free Text**]

Q. Which best describes the setting of your clinic
Rural
Suburban
Urban

Q. Geographic location in which you practice
Northeast (Connecticut, Massachusetts, Maine, New Hampshire, New York, Rhode Island, and Vermont)
Mid-Atlantic (New Jersey, Pennsylvania, Delaware, Maryland, Virginia, West Virginia, Ohio, and Washington DC)
Midwest (Iowa, Indiana, Illinois, North Dakota, Nebraska, Michigan, Montana, South Dakota, and Wisconsin)
Mid-South (Arkansas, Kansas, Louisiana, Missouri, Mississippi, Oklahoma, and Texas)
Southeast (Alabama, Florida, Kentucky, Georgia, North Carolina, Tennessee, and South Carolina)
Rocky Mountain (Alaska, Arizona, Colorado, Idaho, Montana, New Mexico, Nevada, Wyoming, and Utah)
Western (California, Oregon, Washington, and Hawaii)

Q. How frequently do you receive a referral for penicillin allergy in a pregnant patient in your practice?
Never
1-5 times per year
6-11 times per year
Once per month or more

Q. How do you triage pregnant patients referred for penicillin allergy in your current practice?
No dedicated triage process before medical consultation (eg, health care professional sees patient to review)
Review by Allergy RN/APP/Clinical staff before scheduling e-consultation (video, telephone, or chart review) by health care professional before in-office visit
Other (write-in option)

Q. Which of the following, if any, best characterizes your current practice for penicillin allergy testing in a pregnant patient? (choose all that apply)
All pregnant patients receive penicillin skin testing before oral challenge
Some pregnant patients receive direct oral challenge (without preceding skin testing)
Pregnant patients receive penicillin skin testing only (without current challenge in office; challenge deferred until delivery or if needed for treatment)
Patients are not tested while pregnant (return after delivery)

Q. Do you routinely use a standardized risk assessment tool (eg, PENFAST) to determine eligibility for penicillin testing (skin test and/or oral challenge) in a pregnant patient?
Yes
If yes, branching question to write in: which tool do you use?
No

Q. In a pregnant patient with a listed penicillin allergy, **when do you feel is most ideal** to complete the penicillin allergy evaluation (including drug challenge, with or without preceding skin testing)?
First trimester
Second trimester
Third trimester
Anytime during pregnancy
Postpartum (after delivery)
Only when needed for acute treatment of active infection (GBS and syphilis)
Never

Q. In your current practice, **when do you most frequently** perform procedures (skin testing, drug challenge) to complete penicillin allergy evaluation in pregnant patients?
First trimester
Second trimester
Third trimester
Anytime in pregnancy
Postpartum (after delivery)
Only when needed for acute treatment of active infection (GBS and syphilis)
Never/do not perform

Q. In your current practice, how are penicillin evaluations typically scheduled for pregnant patients?
Single-visit consultation and testing same day without prior review
Single-visit—chart review prior (e-consult, triage, etc) and patients scheduled for testing visit

Two visits—consultation on first visit, return for testing
Variable—consultation first, testing offered same day depending on time, staffing, and patient preference

Q. Do you address penicillin allergy before pregnancy in non-pregnant patients of child-bearing age (that are not being seen specifically for penicillin allergy evaluation)?
Yes, always
Yes, sometimes
No
Additional comments—text box (optional)

In each of the following clinical scenarios, what is your current recommendation to patients?

Answer options: (a) skin test and oral challenge, (b) direct oral challenge, (c) avoid penicillin/desensitize if critically necessary during pregnancy, (d) clear by history

- A pregnant patient who experienced anaphylaxis to penicillin 15 years ago
- A pregnant patient who experienced a rash to amoxicillin in childhood
- A pregnant patient with an unknown reaction to penicillin in childhood
- A pregnant patient who experienced hives 4 years ago to penicillin
- A pregnant patient who endorses headache with amoxicillin/clavulanic acid 3 years ago
- A pregnant patient with prior anaphylaxis to cephalosporin

To the PDT committee, To the PDT committee, when converting this question in the Survey platform, please make it a table with multiple options similar to below.

	Skin test and oral challenge	Direct oral challenge	Avoid penicillin/ desensitize if critically necessary during pregnancy	Clear by history
A pregnant patient who experienced anaphylaxis to penicillin 15 years ago				
A pregnant patient who experienced a rash to amoxicillin in childhood				
A pregnant patient with an unknown reaction to penicillin in childhood				
A pregnant patient who experienced hives 4 years ago to penicillin				
A pregnant patient who endorses headache with amoxicillin/clavulanic acid 3 years ago				
A pregnant patient with prior anaphylaxis to cephalosporin				

Q What do you feel is the most significant **barrier**, if any, for a pregnant patient with a penicillin allergy to be delabeled in allergy clinics?

I do not see any barriers to a pregnant patient being delabeled in allergy clinics

My own limited knowledge on allergy testing options for pregnant patients

I do not feel comfortable with patients undergoing allergy testing during pregnancy

Difficult referral process/scheduling—if yes, please specify (choose all that apply)

Lack of referrals from the OB/GYN office

Lack of a streamlined process to handle referrals between OB/GYN and allergy

Lack of triage support to identify pregnant patients separately for scheduling

Lack of staffing for testing/challenge

Patients have too many other appointments to prioritize having an allergy evaluation

Patient apprehension

Other **[include area to write in]**

Q Does your institution have an automatic alert or dedicated referral process for pregnant patients with a penicillin allergy?

Yes

No

If yes, please clarify:

- Best practice alert (BPA) flags in the electronic health record (EHR) for all pregnant patients with penicillin allergy.
- Separate referral process for pregnant patients (triage, direct contact to Allergy office, e-consultation, OB/GYN office is able to schedule in Allergy clinic, etc).
- Educational sessions (eg, OB/GYN providers are encouraged to refer patients to allergy clinic if they identify penicillin allergy).