True Rate of Allergy among Pediatric Inpatients with Penicillin Allergy Labels (TRIAL)

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ABSTRACT

Background: Penicillin allergy is a common drug allergy diagnosis in pediatric patients; however, upon appropriate allergy testing, many of these patients are found not to have a true allergy. For patients with a reported allergy, alternative antibiotics are prescribed, which are less effective, more toxic, or more expensive. There is a lack of data evaluating allergies in hospitalized children and comparing allergy assessments conducted by pediatric allergists and pharmacists.

Objective: To estimate the percentage of pediatric patients admitted with reported penicillin allergy who did not have a true penicillin allergy.

Methods: This single-centre prospective cohort study included inpatients between 6 months and 17 years of age, with a documented penicillin allergy, who were admitted to the general pediatric and oncology units of a tertiary care children's hospital between November 2019 and March 2023. The allergy history, evaluation, and risk categorization were performed by pharmacists. The history was reviewed with the allergist, and the patient was then referred, underwent skin testing, or received oral amoxicillin challenge with monitoring for 1 hour.

Results: Thirty patients were included, of whom 29 (97%) had delabelling of their penicillin allergy. Four patients (13%) had delabelling on the basis of history alone, without risk assessment. Twenty-five (83%) of the patients were assessed as having low risk; 24 of these had delabelling following oral challenge, and 1 did not complete the oral challenge because of transfer to another hospital. One patient (3%) was assessed as having moderate risk, with delabelling on the basis of results of skin testing and oral challenge. The pharmacist's and allergist's risk assessments were in agreement in 29 (97%) of the 30 cases.

Conclusions: Pediatric patients, including those with oncologic malignancies, are often mislabelled as having a penicillin allergy. Pharmacists are able to accurately determine true allergy risk and delabel penicillin allergies for pediatric patients in the hospital setting.

Keywords: penicillin, allergy, pediatric, delabelling, antimicrobial stewardship

RÉSUMÉ

Contexte : L'allergie à la pénicilline est un diagnostic d'allergie médicamenteuse courant chez les patients pédiatriques; cependant, après des tests d'allergie appropriés, bon nombre de ces patients ne présentent pas de véritable allergie. Pour ceux présentant une allergie signalée, des antibiotiques alternatifs sont prescrits, moins efficaces, plus toxiques ou plus coûteux. Peu de données permettent d'évaluer les allergies chez les enfants hospitalisés et de comparer les évaluations des allergies réalisées par les allergologues pédiatriques et les pharmaciens.

Objectif : Estimer le pourcentage de patients pédiatriques admis avec une allergie à la pénicilline signalée, mais qui n'avaient pas de véritable allergie à la pénicilline.

Méthodologie : Cette étude de cohorte prospective monocentrique comprenait des patients hospitalisés âgés de 6 mois à 17 ans, présentant une allergie documentée à la pénicilline, qui ont été admis dans les unités de pédiatrie générale et d'oncologie d'un hôpital pour enfants de soins tertiaires entre novembre 2019 et mars 2023. Les antécédents, l'évaluation et la catégorisation des risques de l'allergie ont été renseignés par les pharmaciens. L'anamnèse a été revue avec l'allergologue, et le patient a ensuite été référé, a subi un test cutané ou a reçu une provocation orale à l'amoxicilline avec surveillance pendant 1 heure.

Résultats : Sur 30 patients inclus, 29 (97 %) ont vu un désétiquetage de leur allergie à la pénicilline. Quatre patients (13 %) ont bénéficié d'un désétiquetage sur la seule base de leurs antécédents, sans évaluation des risques. Vingt-cinq (83 %) patients ont été évalués comme présentant un faible risque; 24 d'entre eux ont bénéficié d'un désétiquetage à la suite d'une provocation orale, et 1 n'a pas terminé la provocation orale en raison d'un transfert vers un autre hôpital. Un patient (3 %) a été évalué comme présentant un risque modéré, avec un désétiquetage basé sur les résultats des tests cutanés et de la provocation orale. Les évaluations des risques par le pharmacien et l'allergologue concordaient dans 29 (97 %) des 30 cas.

Conclusions : Les patients pédiatriques, y compris ceux atteints de cancers malins, sont souvent étiquetés à tort comme ayant une allergie à la pénicilline. Les pharmaciens sont en mesure de déterminer avec précision le risque réel d'allergie et de désétiqueter les allergies à la pénicilline chez les patients pédiatriques en milieu hospitalier.

Mots-clés : pénicilline, allergie, pédiatrique, désétiquetage, gestion des antimicrobiens

INTRODUCTION

Penicillin allergy, a common drug allergy diagnosis, is reported in 5%–8% of pediatric patients.[1] However, when children receive appropriate allergy testing, over 90% with a reported penicillin allergy are found to be non-allergic.[1-4] This discrepancy between reported and true penicillin allergy is often due to misclassification of reactions that occur in children who receive penicillin antibiotics.[5-7] Patients with a reported allergy typically receive alternative antibiotics that may be less effective, more toxic, or more expensive. Having a reported penicillin allergy has been associated with suboptimal antimicrobial treatment and negative clinical and administrative outcomes, including increased length of hospital stay, increased adverse events related to antibiotics, increased antibiotic-resistant infections, and greater medical costs.[8]

Many Canadian centres have no systematic approach for assessment of hospitalized patients with a reported penicillin allergy or for subsequent testing and management. Existing data are limited to pediatric quality improvement projects and adult hospital settings.[9-12] As a result, there is a lack of data describing the rates of reported versus true penicillin allergy among hospitalized children and children with malignancy. As well, there is no consensus on allergy delabelling for low-risk patients, although increasing evidence supports direct oral amoxicillin challenge without skin testing.[13-16] Furthermore, there is growing evidence to support pharmacist-led programs, which have been shown to be effective, safe, and cost-effective.[17,18] Pharmacists routinely assess and educate patients regarding their drug intolerances and allergies. As well, pharmacists have skills in assessing patients' reported allergy histories. However, to our knowledge, no previous studies have compared how different members of the team (specifically the pediatric allergist and the pharmacist) assess allergy information to make clinical decisions about a child's status.

The primary objective of this study was to determine the percentage of pediatric patients admitted to the general pediatric and oncology wards of a tertiary care hospital with reported penicillin allergy who did not have a true penicillin allergy. The secondary objective was to assess agreement between pharmacists and allergists in interpretation of patients' penicillin allergy history and skin test results.

METHODS

Study Design, Setting, and Population

The protocol for this prospective cohort study was approved by the local research ethics board. Patients older than 6 months of age and up to 17 years of age who were admitted between November 2019 and March 2023 to the general pediatrics and pediatric oncology wards of a tertiary care children's hospital and who had a reported penicillin allergy were eligible for inclusion. Patients were identified by information in the health record and/or the allergy history upon admission (Appendix 1). Patients were excluded if the family was non–English speaking; if the patient was hemodynamically unstable; if, at the time of admission, the patient had pre-existing urticaria, angioedema, or diffuse maculopapular rashes; if the patient had received medications with antihistaminic effect in the recent past (as defined below) or high-dose steroids (≥ 1 mg/kg prednisone equivalent) for more than 3 months; or if the patient had a diagnosis of infectious mononucleosis. Medications with antihistaminic effect were defined as first-generation antihistamines (diphenhydramine, dimenhydrinate) received within the past 3 days or second-generation antihistamines (cetirizine, loratadine) received within the past 5 days. Patients who had received these medications were excluded because antihistamines may interfere with skin testing and may lead to false-negative results.

For each study participant, once written informed consent had been obtained, a pharmacist (N.K.) collected an allergy history using a standardized questionnaire (Appendix 2). The questionnaire, which had been previously developed by a pediatric allergist (T.W.), was adapted from the current adult literature and history-taking questionnaires used at a local adult hospital and had been validated in a pediatric outpatient clinic setting.[19] Each patient was categorized as having low, moderate, or high risk for allergy, according to the following process. First, the pharmacist independently reviewed the questionnaire answers, completed the clinical algorithm (Appendix 3), and assigned a risk category. An allergist (R.M. or T.W.) then reviewed the history with the pharmacist and independently assigned a risk category. Cases of disagreement were discussed, with the allergist's assessment ultimately taking priority (if disagreement could not be resolved through discussion).

Any patient assessed as having a high risk was excluded from study participation and referred for further assessment at the Allergy Clinic. Patients assessed as having moderate risk underwent skin testing. The allergist and pharmacist reviewed the result of the skin test independently and recorded their respective interpretations. If the result on skin testing was negative, the patient underwent a direct oral challenge (DOC), consisting of a single dose of amoxicillin 15 mg/kg orally. If the DOC result was positive, the patient was referred to the Allergy Clinic. If the patient was assessed as having low risk, no skin testing was performed and the patient underwent a DOC. For all DOCs, the pharmacist explained the monitoring parameters to the patient and family and instructed them to notify staff immediately if concerns arose regarding any possible drug reaction. An anaphylaxis kit was available at the bedside. Patients were monitored for 1 hour, and the pharmacist checked in at 30 and 60 minutes.

For patients who were originally assessed as having moderate or low risk and who had no subsequent reaction on skin testing or DOC, the penicillin allergy was delabelled. Once the penicillin allergy was delabelled, the pharmacist provided an allergy status letter to the family, to be passed along to their family physician. As well, the pharmacist updated the patient's allergy status in the electronic medical record and provincial medication profile.

Data Analysis

Descriptive analyses were used to summarize the population, and the corresponding rates of delabelling and other allergy-related outcomes.

RESULTS

Patient recruitment for this study was lower than expected because of the COVID-19 pandemic and low admission rates during the study period. Of the 33 patients with a documented penicillin allergy who were approached, 3 declined to participate. Therefore, 30 patients participated in the study. Based on history, 23 (77%) of the patients reported experiencing a maculopapular rash or urticaria (Table 1). Twenty-nine (97%) had not received epinephrine for their previous reaction, and the single patient who had received epinephrine had a reaction to cephalexin, not penicillin. Two (7%) of the patients with penicillin allergy label did not recall ever having a reaction while receiving penicillin.

TABLE 1 (part 1 of 2). Patient Demographic Characteristics and Allergy Assessment

Characteristic	No. (%) of Patients[a] (*n* = 30)
Age (years) (median and range)	8.0 (5.0–15.0)
Sex, female	17 (57)
Having ≥ 1 oncologic malignancy	5 (17)
Allergy alert on PharmaNet	3 (10)
Penicillin exposure	
Amoxicillin	22 (73)
Unknown	5 (17)
Other penicillin	2 (7)
Piperacillin/tazobactam	1 (3)
Timing of past reaction	
> 5 years	13 (43)
13 months to 5 years	8 (27)
7–12 months	6 (20)
3–6 months	1 (3)
Unknown	1 (3)
No reaction, drug avoided because of a relative's reaction	1 (3)

TABLE 1 (part 2 of 2). Patient Demographic Characteristics and Allergy Assessment

Characteristic	No. (%) of Patients[a] (*n* = 30)
Indication	
URTI	14 (47)
Pneumonia	5 (17)
UTI	1 (3)
SSTI	2 (7)
Unknown	6 (20)
Other	2 (7)
No. of penicillin doses or time before onset of reaction (*n* = 29)	
1 dose	5 (17)
1–3 days	11 (38)
4–7 days	6 (21)
> 7 days	3 (10)
Unknown	4 (14)
Nature of suspected penicillin reaction[b]	
Macular/papular rash	23 (77)
Urticaria	12 (40)
Angioedema	1 (3)
Vomiting	1 (3)
Diarrhea	2 (7)
Other	2 (7)
Unknown	2 (7)
Duration of reaction (*n* = 28)	
< 24 hours	3 (11)
24–48 hours	16 (57)
49 hours to 6 days	2 (7)
> 6 days	5 (18)
Unknown	2 (7)
Patient stopped taking antibiotic when reaction occurred (*n* = 29)	
Yes	24 (83)
No	4 (14)
Unsure	1 (3)
Treatment for allergic reaction	
Epinephrine injection	1 (3)
Antihistamines	13 (43)
Corticosteroids	1 (3)
None	15 (50)
Penicillin taken after the reaction	
Yes	3 (10)
No	25 (83)
No reaction	1 (3)
Unsure	1 (3)

SSTI = skin and soft-tissue infection, URTI = upper respiratory tract infection, UTI = urinary tract infection.
[a]Except where indicated otherwise.
[b]Sum of percentages is greater than 100 because some patients had more than 1 suspected reaction.

Patients recalled receiving alternative antibiotics after allergy labelling, which included azithromycin, cefazolin, cefepime, cefixime, ceftazidime, ceftriaxone, cefuroxime, cephalexin, clarithromycin, clindamycin, cotrimoxazole, erythromycin, and vancomycin.

After risk assessment, skin testing, and DOC, as appropriate, the allergy was delabelled for 29 (97%) of the patients. For 4 patients (13%), delabelling was based on history alone. An additional 25 patients (83%) were assessed as having low risk; for 24 of these, the allergy was delabelled following an oral challenge, and the 25th patient did not complete testing because of transfer to another hospital. The final patient (3%) was assessed as having moderate risk, with subsequent delabelling on the basis of skin testing and DOC (Table 2). This patient had reported having a positive skin test result in another country; however, it was unknown whether they had been specifically tested for penicillin. For one patient with reported penicillin allergy, the history completed as part of this study showed that the reaction had been to cephalexin. Overall, all patients who underwent DOC were determined to have no allergy to penicillin. Furthermore, the pharmacist and allergist assessments and risk categorizations were in agreement in 97% of cases (Table 3). There were no cases in which the pharmacist's categorization was lower risk than the allergist's.

DISCUSSION

In this study, delabelling was achieved for hospitalized pediatric patients, including those with malignancy. Our delabelling rates were higher than those reported in previous pediatric studies. We found that obtaining an accurate history was essential to properly assessing patients' allergy status. Allergies should be routinely clarified, as we found that some patients had a penicillin allergy label despite having tolerated penicillin medications, and that others were mistakenly diagnosed as having a penicillin allergy despite no evidence in the literature of cross-reactivity to another medication to which the patient was known to be allergic. Many patients experienced a maculopapular rash after receiving penicillins for an upper respiratory tract infection; however, maculopapular exanthems following amoxicillin intake can be due to viral infection directly or to the enhancement of drug allergic reactions by the virus.[20]

Pharmacists were able to collect detailed allergy histories and make independent assessments identical with those of the allergist, with appropriate risk categorization, which highlights the potential for pharmacist-driven penicillin allergy delabelling. In 1 case, the pharmacist categorized the patient as high risk, whereas the allergist categorized the patient as moderate risk because the allergy history was unknown. This patient went on to have skin testing, for which the result was negative, and ultimately tolerated a DOC. In this study, we were unable to determine pharmacists' ability to independently interpret the results of skin testing, because only 1 patient required this type of testing. However, previous studies in adults support pharmacists being able to perform and interpret skin testing.[21,22]

TABLE 2. Allergy Assessment

Variable	No. (%) of Patients (n = 30)
Risk category	
Low	25 (83)
Moderate	1 (3)
High	0 (0)
Not allergic	4 (13)
Skin testing indicated	
Yes	1 (3)
No	29 (97)
Skin prick test result (n = 1)	
Pharmacist, negative	1
Allergist, negative	1
Intradermal test result (n = 1)	
Pharmacist, negative	1
Allergist, negative	1
Oral challenge indicated	
Yes	25 (83)
No	5 (17)
Result of oral challenge (n = 25)	
No reaction	24 (96)
Not completed	1 (4)
Final assessment	
No evidence of penicillin allergy; may prescribe penicillin again	29 (97)
Severe adverse drug reaction; recommend referral	0 (0)
Patient likely has IgE allergy or requires further skin testing; recommend referral	0 (0)
Undetermined	1 (3)

IgE = immunoglobulin E.

TABLE 3. Comparison of Allergy Assessment and Categorization by Allergists and Pharmacists

Pharmacist Interpretation (Algorithm)	Allergist Interpretation		
	Not Allergic	Low Risk	Moderate Risk
Not allergic	4	0	0
Low risk	0	25	0
Moderate risk	0	0	0
High risk	0	0	1

Our study protocol did not involve graded challenges, and our findings indicate that single-dose DOC is safe in children, as well as simplifying the process and reducing the time required to determine a patient's true allergy status. In our study, skin testing was not required for most of the pediatric patients, and it may thus be better to stream moderate- or high-risk patients to a specific allergy clinic, given the high costs of and low need for skin testing. Overall, the discrepancy between reported and true penicillin allergy is often due to misclassification of reactions that occur in children who receive penicillin antibiotics.[5-7] Further education of health care professionals is needed to distinguish true allergies from intolerances, which may also allow for primary prevention of erroneous penicillin allergy labels.

To our knowledge, this is the first report of a successfully implemented formal penicillin allergy delabelling program in a Canadian pediatric hospital. Our study is additionally unique because the patient assessments were led by a pharmacist, and the pharmacist's assessments agreed with those of the allergists in all but one case. Health care professionals such as pharmacists are able to accurately assess allergy information to make clinical decisions about a child's status. Notably, there were no cases in which the pharmacist's categorization of risk was lower than that of the allergist, suggesting that this may be a safe and appropriate approach.

The limitations of our study included low patient recruitment. Before the study began, a baseline analysis indicated that substantial numbers of patients admitted to the study hospital had penicillin allergy labels. However, with the onset of the COVID-19 pandemic a few months after study initiation, there were delays in recruitment for and conduct of research programs, including our study. The number of patients admitted with suspected allergy was lower than anticipated, which may have been due in part to concurrent efforts outside the hospital to raise awareness of erroneous labelling of penicillin allergy. As well, the sample size was small, which may have contributed to variable results or overestimation of the magnitude of the true association; as such, studies with larger samples would be beneficial to further assess this approach. As with any real-world scenario, there were challenges with patients or their families recalling the allergy history. Furthermore, there may have been some selection bias, given that some patients with penicillin allergy labels were not approached for recruitment because of the workload of the physician on the primary care team, particularly during respiratory surge seasons, or other logistical reasons, such as impending discharges. As well, the level of agreement between the pharmacist and the allergist might have been biased because the initial patient assessments were done independently by the pharmacist, followed by review of questionnaire answers with the allergist and then assignment of the patient's risk category by the allergist. Nonetheless, the allergist agreed with the pharmacist's assessment in 97% of cases.

Health care organizations vary in the types and numbers of medical records used for patient care, which leads to fragmentation of information and, consequently, fragmentation of care. As such, there is a logistical aspect to removing allergy labels, because allergy-related documentation may be disjointed. Despite efforts to remove penicillin labels from patient records after it has been determined that the patient does not have an allergy, the literature has identified barriers to doing so in both inpatient and outpatient settings, such as fear, reluctance, and poor documentation in the electronic medical record influencing clinicians' prescription decisions.[23] Options to mitigate poor documentation include setting up electronic alerts and promoting communication among community pharmacies, dental practices, and other health care providers.[24] Therefore, it is important to standardize the approach to documentation, understand the consequences, improve communication, and promote patient awareness and advocacy.

CONCLUSION

Pediatric patients, including those with oncologic malignancies, are often designated as having a penicillin allergy when they actually do not have such an allergy. The results of our study suggest that health care professionals other than physicians, such as pharmacists, are capable of effectively stratifying patients according to their risk, with a high rate of concordance to an allergist's assessment, and then safely delabelling penicillin allergies, if appropriate, in the hospital setting. Additional studies are needed to determine whether removal of incorrect allergy labelling prompts the use of the preferred penicillin over alternative drugs.

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Competing interests: For activities unrelated to the study reported here, Raymond Mak has received speaker's honoraria from ALK, Sanofi, CSL Behring, Pfizer, AstraZeneca, and Novartis; and Tiffany Wong has received speaker's honoraria from Valeo, Pfizer, CeraVe, and Polaris Health. Dr Wong also serves as Faculty Lead for the Spread Quality Improvement initiative of the Provincial Health Services Authority (British Columbia) and Faculty Lead for Patient Safety and Quality Improvement, Postgraduate Medical Education, Faculty of Medicine, The University of British Columbia. No other competing interests were declared.

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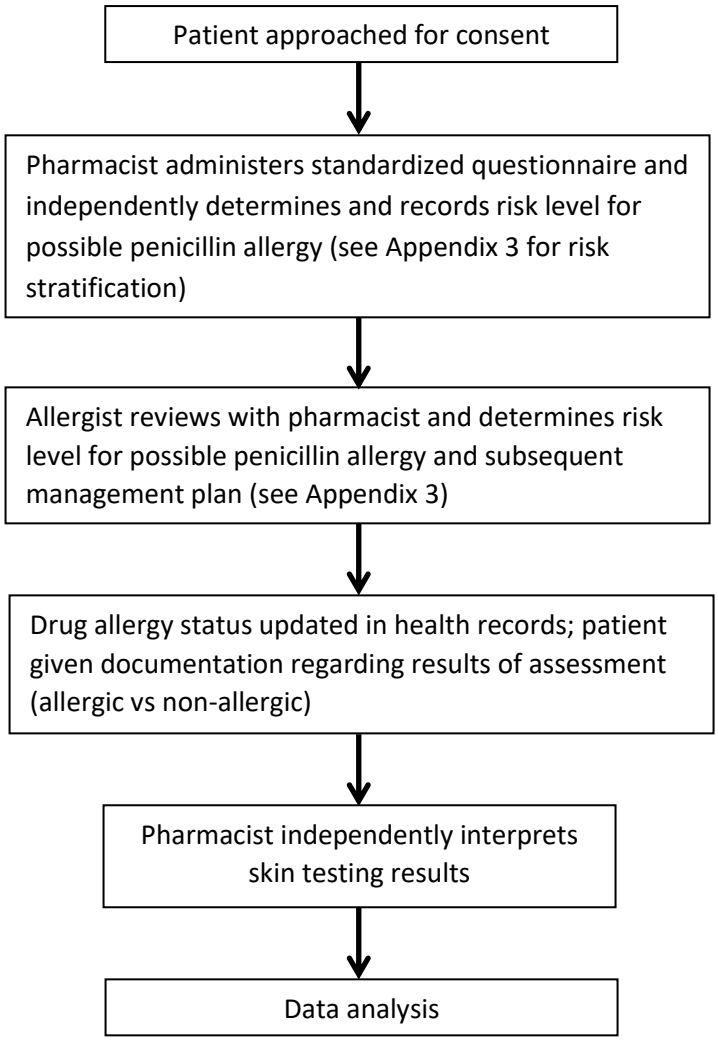
APPENDIX 1: Flow diagram of study procedure.



APPENDIX 2 (part 1 of 2): History-taking form.

Study ID: _____ **Today's Date (DD/MM/YYYY):** _____

Questionnaire: Detailed History of Penicillin Allergy

Document Start Time (00:00): _____

1. Which penicillin antibiotic was the patient suspected to be exposed to?

- ☐ Amoxicillin
- ☐ Ampicillin
- ☐ Amoxicillin/clavulanate
- ☐ Piperacillin/tazobactam
- ☐ Other penicillin: _____
- ☐ I don't know

2. Has penicillin been taken since the suspected reaction, and tolerated? ☐ Yes ☐ No ☐ I don't know

3. How long ago did the reaction to penicillin occur?

- ☐ <3 months
- ☐ 3-6 months
- ☐ 7-12 months
- ☐ 13 mo – 5 years
- ☐ >5 years
- ☐ No known reaction, drug avoided due to relative with previous reaction
- ☐ No known reaction, drug avoided due to positive skin test done for screening
- ☐ I don't know

4. What was the penicillin originally prescribed for?

- ☐ Upper respiratory tract infection (including ear infection)
- ☐ Pneumonia
- ☐ Urinary tract infection
- ☐ Skin infection
- ☐ Blood infection (sepsis)
- ☐ Stomach infection (H. Pylori)
- ☐ Other: _____
- ☐ I don't know

5. How many doses of penicillin were given prior to onset of reaction?

- ☐ 1 dose
- ☐ 1-3 days
- ☐ 4-7 days
- ☐ > 7 days
- ☐ I don't know
- ☐ Symptoms of reaction already present prior to first dose

6. How soon after the most recent dose given did the reaction begin?

- ☐ < 5 minutes
- ☐ < 1 hour
- ☐ 1-2 hours
- ☐ 2-12 hours
- ☐ 12-24 hours
- ☐ I don't know
- ☐ Symptoms of reaction already present prior to first dose

7. What was the nature of the reaction to penicillin? (check all that apply)

- ☐ Macular/papular rash
- ☐ Urticaria (hives)
- ☐ Angioedema (swelling)
- ☐ Erythema multiforme
- ☐ Blistering/peeling skin or mucous membrane
- ☐ Cough
- ☐ Wheeze
- ☐ Stridor
- ☐ Breathing difficulties
- ☐ Rhinorrhea, conjunctivitis
- ☐ Nausea
- ☐ Vomiting x1
- ☐ Vomiting multiple times
- ☐ Abdominal discomfort/pain
- ☐ Diarrhea
- ☐ Palpitations
- ☐ Syncope/decreased level of consciousness
- ☐ Arthritis/arthralgia
- ☐ Unexplained fever (unrelated to illness for which antibiotic was prescribed)
- ☐ Liver involvement
- ☐ Kidney involvement
- ☐ Other: _____
- ☐ I don't know

8. **How long did the reaction last?** ☐ <24 hours ☐ 24-48 hours ☐ 49 hours - 6 days ☐ >6 days ☐ I don't know

9. **Did the patient stop taking the antibiotic when the reaction occurred?** ☐ Yes ☐ No ☐ I don't know
If no, then what happened?_____

10. **Was any medical advice sought?** ☐ Yes ☐ No ☐ I don't know
If yes, what kind of health care professional was seen?

- ☐ Family physician
- ☐ Pediatrician
- ☐ Emergency room physician
- ☐ Other specialist
- ☐ Nurse practitioner
- ☐ Other: _____

APPENDIX 2 (part 2 of 2): History-taking form.

11. **Was any treatment given for the reaction?** ☐ Yes ☐ No If yes, the treatment was (select all that apply) ☐ I don't know

☐ Epinephrine injection (intramuscular)
☐ Epinephrine injection (subcutaneous)
☐ Antihistamines (eg. Diphenhydramine, cetirizine, loratidine, etc)
☐ Short acting inhaled beta agonist (salbutabmol, terbutaline)
☐ IV fluids
☐ H2 antagonists (eg. ranitidine, cimetidine)
☐ Corticosteroids (eg. Dexamethasone, prednisone)
☐ Other: _____

12. **If penicillin has been taken since the reaction, what was the nature of the reaction to penicillin?** (check all that apply)

☐ No reaction
☐ Macular/papular rash
☐ Urticaria (hives)
☐ Angioedema (swelling)
☐ Erythema multiforme
☐ Blistering/peeling skin or mucous membrane
☐ Cough
☐ Wheeze
☐ Stridor
☐ Breathing difficulties
☐ Rhinorrhea, conjunctivitis
☐ Nausea
☐ Vomiting x1
☐ Vomiting multiple times
☐ Abdominal discomfort/pain
☐ Diarrhea
☐ Palpitations
☐ Syncope/decreased level of consciousness
☐ Arthritis/arthralgia
☐ Unexplained fever
☐ Liver involvement
☐ Kidney involvement
☐ Other: _____
☐ I don't know

13. **Have other antibiotics been taken since the reaction?**
☐ Yes please specify which Antibiotics: _____

☐ No
☐ I don't know

14. **How many times was a penicillin medication prescribed and taken prior to the reaction?**
☐ One course
☐ Two courses
☐ Three or more courses
☐ None

☐ I don't know

15. **Has penicillin allergy skin testing been done in the past?** ☐ Yes ☐ No ☐ I don't know

If yes, what was the result? ☐ Positive ☐ Negative

16. **Was there a previous diagnosis or constellation of the following symptoms associated with penicillin?**

a. Erythema Multiforme/Stevens Johnson Syndrome/Toxic Epidermal Necrolysis (Target lesion, Skin peels off, involvement of mouth, eyes, anus, often requires hospitalization or ICU stay)
☐ Yes ☐ No

b. Serum sickness related to penicillin? (Joint swelling/redness/pain, fever, enlarged lymph nodes)
☐ Yes ☐ No

c. Drug reaction with eosinophilia and systemic symptoms (DRESS) - rash, hematologic abnormalities (eosinophilia, atypical lymphocytosis), lymphadenopathy, and internal organ involvement (liver, kidney, lung), occurring 2-8 weeks after drug exposure
☐ Yes ☐ No

APPENDIX 3: Flow chart for risk assessment.