



3-30-2018

Penicillin Allergy Testing and Antimicrobial Stewardship

Vanessa J. Sundeen

Follow this and additional works at: <https://commons.und.edu/nurs-capstones>



Part of the [Nursing Commons](#)

[How does access to this work benefit you? Let us know!](#)

Recommended Citation

Sundeen, Vanessa J., "Penicillin Allergy Testing and Antimicrobial Stewardship" (2018). *Nursing Capstones*. 150.

<https://commons.und.edu/nurs-capstones/150>

This Independent Study is brought to you for free and open access by the Department of Nursing at UND Scholarly Commons. It has been accepted for inclusion in Nursing Capstones by an authorized administrator of UND Scholarly Commons. For more information, please contact und.common@library.und.edu.

Penicillin Allergy Testing & Antimicrobial Stewardship

Vanessa J. Sundeen

College of Nursing and Professional Disciplines

University of North Dakota

PERMISSION

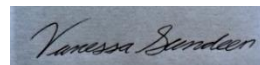
Title Penicillin Allergy Testing & Antimicrobial Stewardship

Department Nursing

Degree Master of Science

In presenting this independent study in partial fulfillment of the requirements for a graduate degree from the University of North Dakota, I agree that the College of Nursing & Professional Disciplines of this University shall make it freely available for inspection. I further agree that permission for extensive copying or electronic access for scholarly purposes may be granted by the professor who supervised my independent study work or, in his/her absence, by the chairperson of the department or the dean of the Graduate School. It is understood that any copying or publication or other use of this independent study or part thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me and to the University of North Dakota in any scholarly use which may be made of any material in my independent study.

Signature _____



Date 03/30/2018 _____

Abstract

With the progression of multidrug-resistant organisms (MDROs) and lack of novel antimicrobials, antimicrobial stewardship is of utmost importance to help protect patients and prevent a postantibiotic era. Many times, penicillin (PCN) allergy labeling restricts antibiotic prescribing from choosing first-line beta-lactam antibiotics. This leads to utilization of second-line antibiotics that are usually associated with adverse outcomes and increased hospitalization. Greater than 90% of people who have a PCN allergy history lose the anti-PCN IgE antibodies over 10-years, therefore will not have a hypersensitivity reaction to PCN. The case study, Nicole, who was used in this Independent Study, is one such patient, as she has a PCN allergy label in her medical record for a hypersensitivity reaction that occurred 25 years ago.

A literature review was compiled utilizing medical databases revealing poorer clinical outcomes and adverse future implications with usage of second-line antimicrobials. Antibiotic stewardship recommends the utilization of penicillin skin testing (PST) with the initiative of delabeling PCN allergies. The evidence reveals that PST helps to delabel close to 90% (if not more) of previously PCN allergy labeled patients. Resulting in a substantial increase in antibiotic regimen changes to first-line beta-lactam choices, and which may lead to optimized patient outcomes.

Penicillin Allergy Testing & Antimicrobial Stewardship

Currently the public and medical community is being challenged with a dilemma regarding a progression in multidrug-resistant organisms (MDROs) resulting in antibiotic resistance, an increase in healthcare-associated infections, and a lack of novel antibiotics (Blumenthal et al., 2018; Unger, Gauthier, & Cheung, 2013). Current evidence reveals that improperly labeled medication allergies influence these implications. Specifically, penicillin (PCN) allergy, as about 10%-15% of the United States (US) population reports a PCN allergy, of which only 10% have a true penicillin allergy (Unger, et al., 2013; Wada & Calhoun, 2017). Concluding, the true rate for a PCN type 1 hypersensitivity reaction is only about 1% of the US population (Narayana & Jeffres, 2017).

“Many of these patients (almost 80%) who have a well-documented allergy to PCN, lose their hypersensitivity overtime (specifically over 10 years) due to a loss in the anti-PCN IgE antibodies, deeming them nonallergic” (Unger, et al., 2013, p. 857). In addition, there is only a 0.02%-0.04% incidence of an anaphylactic reaction to PCN (Patterson & Stankewicz, 2017).

Moreover, when there is a PCN allergy, first-line antibiotic choices (e.g., beta-lactams), are avoided and second-line antibiotics are used, “which may be less effective, more expensive, and lead to higher rates of adverse effects,” MDRO’s, hospital readmissions, healthcare costs, and poorer patient outcomes (Knezevic, et al., 2016, p. 1276). Also, many practitioners do not utilize cephalosporins with patients who have a PCN allergy due to the potential for cross-sensitivity of 5% to 16%; recommendation is based on those who have a type 1 hypersensitivity reaction (Moser Woo & Robinson, 2016, p. 709). To combat this predicament, antimicrobial stewardship promotes penicillin skin testing (PST) programs (Unger, et al., 2013).

Regarding the case study patient, Nicole Smith (see Appendix) reports a PCN allergy to which she was told by her parents that she developed hives after taking PCN when she was a young child; Nicole reported that she did not remember the reaction. Presently, she may not be allergic to PCN as this reaction was experienced over 25 years ago. This implication could cause her unnecessary suffering from adverse outcomes with the use of second-line choice antibiotics.

For example, if Nicole were to develop cellulitis of the upper or lower extremity (not requiring intravenous antibiotic administration), the first-line antibiotic choice is a beta-lactam as she is at low methicillin-resistant *Staphylococcus aureus* (MRSA) risk. However, due to her PCN allergy, a second-line option of clindamycin would be warranted (Robinson, 2017). This could potentially lead to problematic outcomes since clindamycin has the potential for the development of severe diarrhea and *Clostridium difficile* (*C. difficile*) infection (Moser Woo & Robinson, 2016, p. 726).

Literature Review

From a primary care perspective with influence in preventative health, especially regarding this case study Nicole Smith, it is feasible to conclude that she could benefit from having outpatient PCN allergy testing completed for PCN allergy delabeling. Although, she may not be a high-risk population target, as she is a healthy outpatient, one could argue that there is no way to predict her future health (Ramsey & Mustafa, 2018). Much of the evidence-based publications for utilization of PCN allergy testing for PCN allergy delabeling are focused on inpatient initiatives.

A review of literature was conducted for research on future implications of PCN allergy labeling and antimicrobial stewardship initiatives to combat these implications; primarily with focus on the utilization of inpatient PCN allergy testing. Literature databases utilized that

provided promising evidence were PubMed and CINAHL. Key search terms used were the following: penicillin allergy; penicillin allergy and multi-drug resistant organisms; penicillin allergy and future implications; true penicillin allergy; penicillin allergy and antibiotic stewardship; penicillin allergy and antimicrobial stewardship; and outpatient penicillin allergy testing. A filter utilized was a search with publication dates within the last 5 years. Five articles were discovered from references used in publications that were being reviewed. The Health Sciences librarian for Graduate Studies at the University of North Dakota was utilized as a resource for finding citations.

A total of twenty medical journals were reviewed: two with Level I, thirteen with Level II, three with Level IV, and two with Level V evidence (Chemeketa, 2018). Much of the literature revealed adverse outcomes in patients with a PCN labeled allergy compared to those without; primarily due to the use of second-line antimicrobials. Knezevic et al. (2016) found higher readmission rates and less favorable safety profiles due to second-line antibiotic use. Macy and Contreras (2013) found that patients with a PCN labeled allergy received treatment with flouroquinolones, clindamycin, and vancomycin that resulted in 23.4% more *C. difficile*, 14.1% more MRSA, and 30.1% more vancomycin-resistant *Enterococcus* (VRE) infections compared to controls.

In addition, PCN allergic labeled patients are given clindamycin due to avoidance of PCN, which makes these patients 3.1 times more likely to develop dental implant failures and are at 10-times higher risk of an extraction socket developing (French, Noroozi, Shariati, & Larjava, 2016). The use of second-line clindamycin, clindamycin with gentamycin, or clindamycin with metronidazole resulted in a surgical site infection rate of 27 % in PCN allergy labeled patients

who underwent microvascular free tissue transfer surgery for reconstruction of head and neck defects (Pool et al., 2016).

The vast evidence provided in the meta-analyses by Unger et al. (2013) and Narayanan and Jeffres (2017), along with the prospective cohort studies completed by Ramsey and Staicu (2017), Gugkaeva, Crago, and Yasnogorodsky (2017), and Marwood, Aguirrebarrena, Kerr, Welch, and Rimmer (2017), all strongly support the utilization of penicillin skin testing (PST) programs to promote delabeling of PCN allergy in patients. In these studies, the majority of PCN allergy testing was completed by PST (skin prick followed by the intradermal test), with a smaller portion of studies additionally completing the gold-standard dose challenge with oral PCN or amoxicillin 500 mg done in a monitored setting. Substantial majority of all PCN labeled patients who underwent PST were negative, resulting in many having a change in their antibiotic regimen to beta-lactams.

In a meta-analysis by Unger et al. (2013), nine studies were reviewed providing significant evidence with a range of 88% to 95% of patients with the a PCN labeled allergy testing negative after PST. Furthermore, studies showed ranges of 48% to 82% of those patients who tested negative had their antibiotic regimens changed to beta-lactam regimens. The authors (Unger et al., 2013) also suggest that PST programs can be adequately performed by a variety of trained personnel (e.g., physicians, pharmacists, pharmacy residents, pharmacy students, and nurses) in a variety of settings (e.g., Emergency Department, Inpatient, Outpatient, Preoperative). Marwood et al. (2017) utilized Emergency Department physicians and senior residents, Gugkaeva et al. (2017), Ramsey and Staicu (2017), and Narayanan and Jeffres (2017) utilized pharmacists for the administration of PST. “Pharmacists are well positioned to provide PST since they are readily involved with obtaining and reviewing allergy and medication histories”

(Narayanan & Jeffres, 2017, p. 51). Of note, Blumenthal et al. (2017) suggests utilization of non-allergist providers (e.g., nurse practitioners and physician assistants) due to the statistics of “more than 25 million Americans who report a PCN allergy and there are only about 5000 Allergist/Immunologists in the US (p. 7).”

The safety profile of PST is vast. Marwood et al. (2017) reported a study of 1710 patients who underwent PST showing a systemic reaction rate of 0.12%. To note, the deaths that resulted from PST were related to improper procedure, with the last published fatality from PST in 1981 (Unger et al., 2013). The authors of Unger et al. (2013) advised that intradermal testing be completed after negative skin prick testing, as 30% of PCN-allergic patients could be missed with the skin prick test. Of importance, Wada and Calhoun (2017) stress PST should not be conducted in persons who experienced a “Category 1 reaction to PCN (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, serum sickness, drug-related eosinophilia with systemic symptoms, or other severe non-IgE-mediated reactions) (p. 253).”

Another consideration is to complete the gold-standard oral dose challenge of PCN or amoxicillin, or a graded challenge after intradermal testing. One study reviewed by Narayanan and Jeffres (2017) noted that some facilities jump straight to the oral PCN or amoxicillin dose challenge due to the low incidence of confirmed type I hypersensitivity reactions to PCN. Also, “patients with a negative PST are at no greater risk of experiencing an allergic reaction to a beta-lactam than the general population (Unger et al., 2013, p 864).

Learning Points

Practitioners owe it to their patients to provide them with the utmost safety in care and prescribing to protect them from harm. Clinicians need to be more prudent in their antimicrobial stewardship because of the current movement “towards a potential postantibiotic era due to the

progression of MDROs and lack of novel antibiotics” (Unger et al., 2013, p. 856). Advanced practitioners need to be proactive in addressing medication allergies and delabeling allergies that are not of true IgE mediated hypersensitivity. Moreover, alternative second-line antimicrobials should not be prescribed “to patients reporting non-severe reactions to PCN when beta-lactams are the recommended first-line therapy” (MacFadden et al., 2016, p. 909). The evidence prominently shows that use of second-line antibiotics in PCN allergy labeled patients poses poorer outcomes and increased cost.

Antimicrobial stewardship strongly encourages the implementation of PST to increase the likelihood of first-line choice beta-lactam antibiotics being utilized. PST utilization is safe for patients, leads to improved outcomes, can decrease healthcare costs, and can be implemented by a variety of trained healthcare personnel (e.g., pharmacists, pharmacy residents, nurses, nurse practitioners, physician assistants, and physician).

*Appendix***SUBJECTIVE**

CC: Establish Care

HPI: Nicole Smith is a 31-year-old Caucasian female who presents to the clinic today to establish care. She has no other concerns today and does not need refills for her oral contraception medication.

PMH: Appendectomy, wisdom teeth extraction

Medications: oral contraceptive daily, multivitamin daily

Allergies: PCN (hives)

Immunizations: HPV series completed, Tdap completed, Influenza completed

FAMILY Hx: Mother is alive with history of breast cancer diagnosed at age 40 years. Father is adopted with no pertinent medical history. Maternal grandmother had history of ovarian cancer; deceased at age 65 years. Maternal Aunt with history of breast cancer. Cousin with history of breast cancer.

SOCIAL Hx: Denies tobacco use. She drinks 1-2 alcoholic beverages (beer) every other week. Denies drug use. She is sexually active in a monogamous relationship with her boyfriend of 2 years; uses oral contraception. She is a school teacher. She exercises regularly and eats a healthful diet.

ROS:

General: Denies fatigue. Overall mood is positive.

HEENT: Denies changes in vision, eye pain, and congestion.

Respiratory: Denies shortness of breath and cough.

Cardiovascular: Denies chest pain, palpitations, and leg swelling.

Gastrointestinal: Denies abdominal pain and/or discomfort, diarrhea or constipation, changes in stool.

Genitourinary: Denies dysuria, urinary frequency and urgency, vaginal discharge, vaginal irritation and pain with intercourse.

Hematologic: Denies easy bruising or bleeding from gums. Negative for adenopathy.

Neurological: Negative for dizziness, numbness, and headaches.

Psychological: Denies issues with being anxious/nervous, dysmorphic mood, and troubles sleeping.

Skin: Negative for pallor and rash. Denies new lesions or changes in skin.

OBJECTIVE

Vital Signs: BP 110/66, HR 82, RR 14, Wt 155 lbs, Ht 5ft 7in, BMI 24.3 kg/m²

Physical Examination:

General: Miss. Smith is a well-developed Caucasian female who is alert and cooperative. She is a good historian and answers questions appropriately.

HEENT: Head is normocephalic and atraumatic. Nose is patent bilaterally with no polyps noted. Oropharynx without erythema or exudate. Buccal mucosa intact without lesions. Full dentition in good repair, no loose teeth. Right and left hearing, external ear, canal, and tympanic membrane normal. Right and left eye exhibit no visual abnormalities or correction, conjunctivae are normal, no scleral icterus, PERRL, red reflex present.

Neck: No tracheal deviation, no masses palpated. No thyromegaly. Neck supple. Full ROM.

Respiratory: Breath sounds clear to auscultation in all lung fields. Respiratory rate regular and easy.

Cardiovascular: Regular heart rate and rhythm, S1S2 heart sounds heard. No murmurs, gallops, or rubs. +2 pulses felt to right carotid, left carotid, right radial, left radial, right PT, left PT.

Lymphatic: No cervical lymphadenopathy palpated. No postauricular, preauricular, occipital, parotid, submandibular, and submental lymphadenopathy palpated.

Abdomen: Soft, nontender. No masses or hepatosplenomegaly palpated. Bowel sounds physiological to all four quadrants. No guarding or rebound noted. Well-healed right lower quadrant scar from previous appendectomy surgery.

GU: Pelvic exam reveals normal external genitalia. Normal vagina and cervix on speculum examination. Bimanual examination reveals no cervical motion tenderness or masses.

Musculoskeletal: No clubbing, cyanosis, or edema. Normal ROM to all extremities.

Neurological: No focal neurological deficits. Alert, oriented x3.

Skin: Intact, warm, dry skin. No lesions noted. No rashes present. Turgor is good.

Psychological: Normal mood and affect, speech, behavior, judgement and thought content, cognition and memory are normal.

| ASSESSMENT | ICD-10-CM |
|---|------------------|
| Encounter for general adult medical examination without abnormal findings | Z00.00 |
| Encounter for screening for human papillomavirus HPV Co-testing | Z11.51 |
| Encounter for contraceptive management | Z30.011 |
| Encounter for screening for lipoid disorders Lipid panel | Z13.220 |
| Family history of malignant neoplasm of breast | Z80.3 |
| Family history of malignant neoplasm of ovary Referral to Genetic Counseling | Z80.41 |
| Encounter for screening for other suspected endocrine disorder TSH | Z13.29 |
| Allergy status to penicillin Referral for penicillin allergy testing | Z88.0 |
| Encounter for screening for diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism CBC with differential | Z13.0 |

PLAN

- 1) Discussed with patient a referral to a genetic counselor regarding her significant family history of breast and ovarian cancer. Her mother who has a history of breast cancer has never completed genetic testing. She states she is willing to see a genetic counselor. Referral placed.
- 2) Patient's last Pap was 1 year ago and she states was normal. She states she has never had an abnormal Pap and has never tested positive for an STI. She has never had HPV testing completed. Discussed with patient the recommendation to complete HPV testing starting at age 30 years. Patient was agreeable with completing a GU examination and HPV Co-testing. When HPV test has resulted, will review and update patient with the result.
- 3) Immunizations reviewed today. Patient is up-to-date on all vaccinations. Tdap, HPV series, and annual Influenza vaccine completed.
- 4) Patient is in a monogamous relationship with her boyfriend. She currently is using oral contraception. Discussed long-term contraceptive options, as she does not foresee a planned

pregnancy in the next 3-5 years. Patient would like to research contraceptive options. She will contact the office if she decides to change contraception.

5) Recommended that since she is a woman in child-bearing years that she take a daily Prenatal Vitamin. She is agreeable.

6) Encouraged her to continue her good lifestyle choices of staying physically active and eating a healthy diet.

7) Will complete fasting Lipid panel, TSH, and CBC screening. Patient has never had testing completed. Testing will be completed today as she is fasting this morning. Will review labs when resulted and update patient with the results.

8) Discussed with patient the potential future antimicrobial implications with having the PCN allergy in her medical chart. Many people lose their anti-PCN antibodies after a span of 10 years and do not experience a hypersensitivity reaction. She is agreeable with completing PCN allergy testing. Referral placed.

Follow-up in 1 year or as needed.

References

- Al-Hasan, M.N., Acker, E.C., Kohn, J.E., Bookstaver, P.B., & Justo, J.A. (2017). Impact of penicillin allergy on empirical carbapenem use in gram-negative bloodstream infections: An antimicrobial stewardship opportunity. *Pharmacotherapy*, 38(1), 42-50. doi: 10.1002/phar.2054
- Blumenthal, K.G., Ryan, E.E., Li, U., Lee, H., Kuhlen, J.L., & Shenoy, E.S. (2018). The impact of a reported penicillin allergy on surgical site infection risk. *Clinical Infectious Diseases*, 66(3), 329-336. doi: 10.1093/cid/cix794
- Blumenthal, K.G., Li, U., Banerji, A., Yun, B.J., Long, A.A., & Walensky, R.P. (2017). The cost of penicillin allergy evaluation. *The Journal of Allergy and Clinical Immunology: In Practice*, S2213-2198(17), 1-9. doi: 10.1111/cea.13044
- Chemeketa Community College Library. (2018). Nursing: Evidence-based nursing resources. Retrieved from <http://libraryguides.chemeketa.edu/c.php?g=324667&p=2644738>
- French, D., Noroozi, M., Shariati, B., & Larjava, H. (2016). Clinical retrospective study of self-reported penicillin allergy on dental implant failures and infections. *Journal of practical dentistry*, 47(10), 861-870. Doi: 10.3290/j.qi.a36887
- Gugkaeva, Z., Crago, J.S., & Yasnogorodsky, M. (2017). Next step in antibiotic stewardship: Pharmacist-provided penicillin allergy testing. *Journal of Clinical Pharmacy and Therapeutics*, 42, 509-512. doi: 10.1111/jcpt.12530
- Knezevic, B., Sprigg, D., Seet, J., Trevenen, M., Trubiano, J., Smith, W., Jeelall, Y., Vale, S., Loh, R., McLean-Tooke, A., & Lucas, M. (2016). The revolving door: antibiotic allergy labelling in a tertiary care centre. *Internal Medicine Journal*, 46(11), 1276-1283. doi: 10.1111/imj.13223

- MacFadden, D.R., LaDefa, A., Leen, J., Gold, W.L., Daneman, N., Weber, E., Al-Busaidi, I., Petrescu, D., Saltzman, I., Dvlinn, M., Andany, N., & Leis, J.A. (2016). Impact of reported beta-lactam allergy on inpatient outcomes: A multicenter prospective cohort study. *Clinical Infectious Diseases*, 63(7), 904-910. doi: 10.1093/cid/ciw462
- Marwood, J., Aguirrebarrena, G., Kerr, S., Welch S.A., & Rimmer, J. (2017). De-labelling self-reported penicillin allergy within the emergency department through the use of skin tests and oral drug provocation testing. *Emergency Medicine Australasia*, 29, 509-515. doi: 10.1111/1742-6723.12774
- Moser Woo, T. & Robinson, M.V. (2016). *Pharmacotherapeutics for advanced practice nurse prescribers (4th edition)*. Philadelphia, PA: F. A. Davis Company.
- Narayanan, P.P. & Jeffres, M.N. (2017). Feasibility, benefits, and limitations of a penicillin allergy skin testing service. *Annals of Pharmacotherapy*, 51(6), 504-510. doi: 10.1177/1060028017690854
- Patterson, R.A. & Stankewicz, H.A. (2017). *Penicillin, allergy*. Treasure Island, FL: StatPearls Publishing. Available from <https://exproxylr.med.und.edu:2243/books/NBK459320/>
- Pool, C., Kass, J., Spivack, J., Nahumi, N., Khan, M., Babus, L., Teng, M.S., Genden, E.M., & Miles, B.A. (2016). Increased surgical site infection rates following clindamycin use in head and neck free tissue transfer. *Otolaryngology – Head and Neck Surgery*, 154(2), 272-278. doi: 10.1177/0194599815617129
- Ramsey, A. & Mustafa, S.S. (2018). A penicillin skin testing initiative in an outpatient allergy office. *The Journal of Allergy and Clinical Immunology: In Practice*, S2213-2198(18), 1-2. doi: 10/1016/j.jaip.2018.01.001

- Ramsey, A. & Staicu, M.L. (2017). Use of a penicillin allergy screening algorithm and penicillin skin testing for transitioning hospitalized patients to first-line antibiotic therapy. *The Journal of Allergy and Clinical Immunology: In Practice*, S2213-2198(18), 1-7. doi: 10.1016/j.jaip.2017.11.012
- Robinson, M. (2017). Cellulitis. *Epocrates*. Retrieved from <https://online.epocrates.com/diseases/6311/Cellulitis/Key-Highlights>
- Unger, N.R., Gauthier T.P., & Cheung, L.W. (2013). Penicillin skin testing: Potential implication for antimicrobial stewardship. *Pharmacotherapy*, 33(8), 856-867. doi: 10.1002/phar.1288
- Wada, K.J. & Calhoun, K.H. (2017). US antibiotic stewardship and penicillin allergy. *Current opinion in otolaryngology head & neck surgery*, 25, 252-254. doi: 10.1097/MOO.0000000000000364