

## **ONLINE REPOSITORY**

### **SUPPLEMENTAL MATERIAL**

The supplemental material accompanies “Penicillin allergy delabeling: a multidisciplinary opportunity” and is designed to provide readers with tools that may assist with penicillin allergy delabeling efforts.

### A Toolkit A Penicillin Allergy History

Date of reaction: \_\_\_\_\_  
Route of last administration:  Oral  Intravenous

Patient ID/ Sticker: \_\_\_\_\_

**Reaction details (check all that apply):**

**Intolerance histories**

Isolated GI upset (diarrhea, nausea, vomiting, abdominal pain)  Chills (rigors)  Headache  Fatigue

**Low-risk allergy histories**

Family history  Itching (pruritus)  
 Unknown, remote (> 10 yr ago) reaction  Patient denies allergy but is on record

**Moderate-high risk allergy histories (potential IgE reactions)**

Anaphylaxis  Angioedema/swelling  Bronchospasm (chest tightness)  
 Cough  Nasal symptoms  Arrhythmia  
 Throat tightness  Hypotension  Flushing/redness  
 Shortness of breath  Rash  Syncope/pass out  
 Wheezing  Dizzy/lightheadedness  
Type of rash (if known): \_\_\_\_\_

**HIGH RISK: Contraindicated penicillin skin testing/challenge (potential severe non-immediate reactions)**

Stevens-Johnson syndrome (rash with mucosal lesions)  Serum sickness (rash with joint pain, fever, myalgia)  Thrombocytopenia  Fever  
 Organ injury (liver, kidney)  Erythema multiforme (rash with target lesions)  Dystonia  Anemia  
 Acute generalized exanthematous (rash with pustules)  Drug reaction eosinophilia and systemic symptoms (rash with eosinophilia and organ injury)

**Other symptoms:** \_\_\_\_\_

### A Toolkit A (continued)

Patient ID/ Sticker: \_\_\_\_\_

**Timing/onset:**

Immediate (< 4 hrs)  
 Intermediate (4-24 hrs)  
 Delayed (> 24 hrs)  
 Unknown

**Treatment:**

None/penicillin continued  Antihistamines  
 Steroids (IV or PO)  Epinephrine  
 Penicillin discontinued  IV Fluids  
 Other: \_\_\_\_\_

**How long ago was the reaction:**

< 6 mo  6 mo-1 yr  2-5 yrs  6-10 yrs  > 10 yrs  Unknown

**Other beta-lactam use:**

Previous use of a penicillin or beta-lactam (prior to course that caused reaction)  
If yes, please list drugs: \_\_\_\_\_

Subsequent use of a penicillin or beta-lactam (after the course that caused a reaction)  
If yes, please list drugs: \_\_\_\_\_

History taken by \_\_\_\_\_ Signature: \_\_\_\_\_ Date: \_\_\_\_\_  
Print name: \_\_\_\_\_

**FIGURE E1. A**, Penicillin allergy history.<sup>E1</sup> Toolkit used to gather penicillin allergy history reaction details, stratified by risk. **B**, Penicillin allergy history algorithm.<sup>E2</sup> Algorithm designed to obtain a penicillin allergy history paired with a suggested management approach. **C**, Beta-lactam allergy history questionnaire.<sup>E3,E4</sup> Questionnaire for patients reporting a beta-lactam allergy to complete before surgical procedures. **D**, Penicillin allergy history questionnaire.<sup>E5</sup> Questionnaire for patients reporting a penicillin allergy to complete during allergy appointment. **E**, Penicillin allergy testing and delabeling.<sup>E6</sup> Procedure for military allergists to follow while assessing military recruits' penicillin allergy histories.

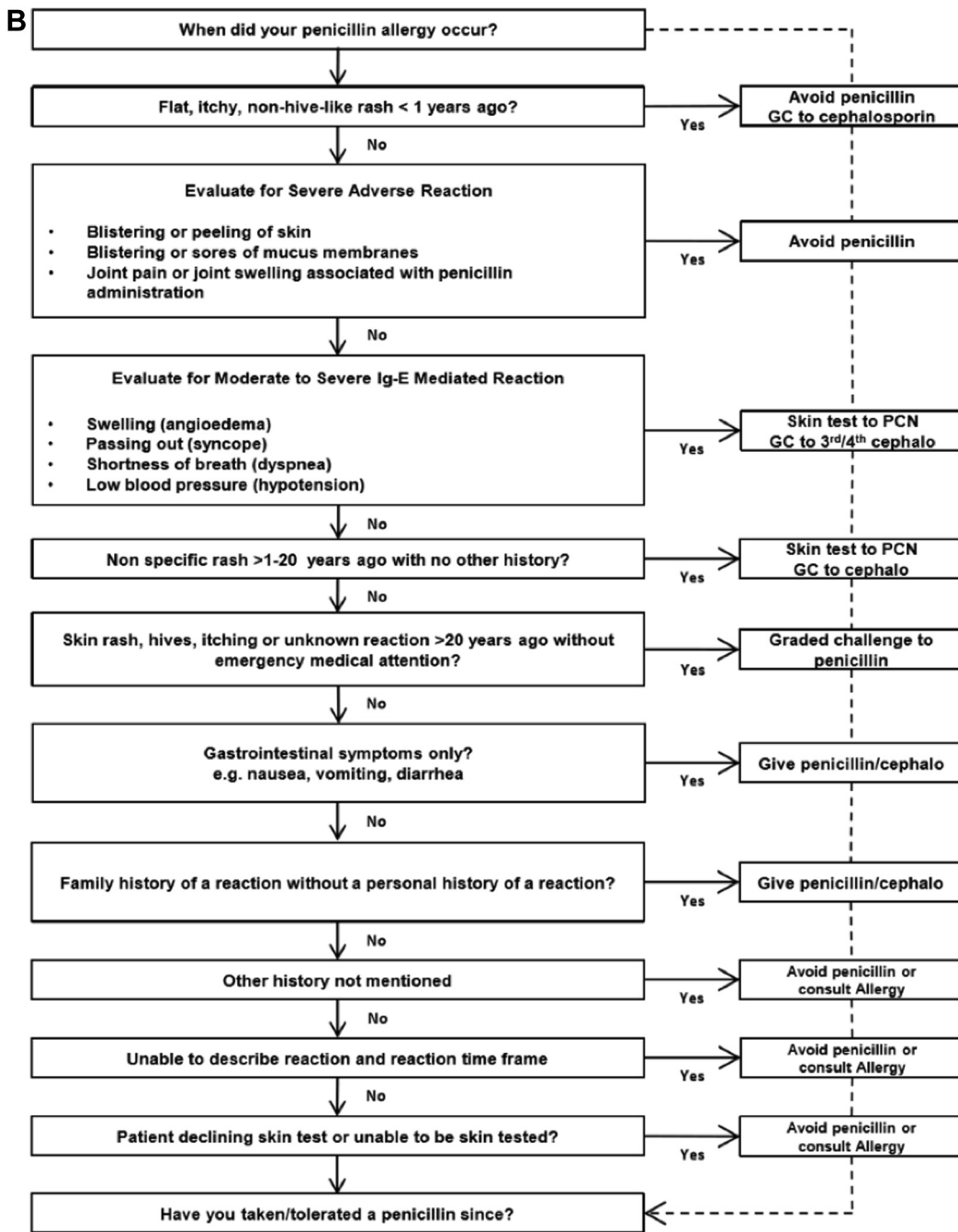



FIGURE E1. (CONTINUED).

C



**MICHAEL GARRON HOSPITAL**  
TORONTO EAST HEALTH NETWORK

**BETA-LACTAM QUESTIONNAIRE**

Affix Patient Label Here

OR DATE: \_\_\_\_\_ PAC APPT DATE: \_\_\_\_\_

PROCEDURE: \_\_\_\_\_ SURGEON: \_\_\_\_\_

RECORDER: \_\_\_\_\_ Rx / RN

Name of suspected drug: penicillin \_\_\_\_\_ other: \_\_\_\_\_

Weight: \_\_\_\_\_ Height: \_\_\_\_\_ EBW: \_\_\_\_\_

Date of reaction: \_\_\_\_\_ Current Age: \_\_\_\_\_

Description of the reaction and severity:

REACTION	SEVERITY			COMMENTS
	MILD	MOD	SEVERE	
Rash – generalized? localized?				
Hives				
Urticaria				
Pruritis				
Shortness of breath				
Facial swelling				
Tongue swelling				
Throat swelling				
Swelling – other				
Nausea/vomiting/diarrhea				
Abdominal pain				
Anaphylactic shock				
Other				
Do not remember				

When did the reaction begin? \_\_\_\_\_ How long did the reaction last? \_\_\_\_\_

Any treatment from a physician? \_\_\_\_\_ Hospitalized? \_\_\_\_\_

Have you used similar antibiotics since? (names) \_\_\_\_\_

Were you tested for a penicillin allergy? \_\_\_\_\_

REFERRAL to allergist for testing? YES \_\_\_\_\_ NO \_\_\_\_\_ If yes, date faxed: \_\_\_\_\_

Powernote Entered       Email Sent to ID       ID Confirmation

ID DOCTOR CONTACTED: McCready       Powis       Date: \_\_\_\_\_

CONCLUSION: Allergy \_\_\_\_\_ Side Effect \_\_\_\_\_ Non-related \_\_\_\_\_

Antibiotic Entered       Allergy Comment Entered       Added to RASH List

Antibiotic Order \_\_\_\_\_

J. McCready, J. Powis, S. Hicks
Version 2.0, June 2018

FIGURE E1. (CONTINUED).

**D** AlerQuest, LLC AQ-2010-001  
 Subject Screening : Penicillin Allergy History

[Data](#) [Audit](#) [Queries](#)

### PENICILLIN ALLERGY HISTORY

Penicillin or Semisynthetic Derivative Taken

If Other, Specify

Route of Administration

Duration of Administration  Days # of Doses   Unknown

Indication for Antibiotic   Unknown

Any Preceding or Concurrent Medications?

If Yes, Specify

Reaction occurred on  Day Dose #   Unknown

Allergy Symptoms (check all that apply)

Symptom	Onset Time After Last Dose (Minutes)	Duration of Symptoms
<input type="checkbox"/> Urticaria (Hives)	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Angioedema	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Pruritis/Flushing	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Maculopapular Rash	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Diarrhea	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Lightheaded/Loss of Consciousness	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Shortness of Breath	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Nausea/Vomiting/Abd Pain	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Joint Pain	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Fever	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Rapid Heart Rate	<input type="text"/>	<input type="text"/>

Treatment of Reaction (check all that apply)

None  AH  Epinephrine  Steroids

Other  Unknown

If Other, Specify

Reaction Observed by Provider?

Assessment of IgE Dependent Penicillin Allergy

Penicillins Taken Since Reaction

If Yes, Provide Details

Enter additional records by clicking on ADD HISTORY ADD HISTORY

FIGURE E1. (CONTINUED).

### Penicillin De-labeling Procedures

- **Personnel –**
  - Physician (or trained licensed independent provider)
  - Nurse (or equivalent)
- **Resources –**
  - Amoxicillin 250mg capsule or liquid (pediatric weight based, up to 250mg)
  - Anaphylaxis kit (injectable epinephrine, antihistamine)
- **Procedure –**
  - Ensure patient is not on a beta-blocker or antihistamine, pregnant, or has any medical condition that would not tolerate anaphylaxis.
  - Clinical history (see questionnaire on right), vital signs, focused exam.
  - If patient has tolerated any penicillins following their prior reaction, they are CLEARED. No testing indicated.
  - Informed consent form for medication testing.
  - If all questions to 1–5 are NO, patient is LOW RISK, proceed to oral challenge. Monitor for 1 hour.
  - If any answer to 1–3 are YES, patient is at HIGHER RISK, and if testing is available, recommend skin testing first (or allergy referral).
  - If any answers to 4–5 are YES, STOP and continue to avoid.
  - If there is no reaction to the test, remove from drug allergies.
  - If the patient has a systemic reaction concerning for anaphylaxis, treat with epinephrine and antihistamine per local protocols.

Penicillin Allergy Questionnaire	YES	NO
1. Did your reaction occur within the past year?		
2. If a rash was present, did it last less than 24 hour? If unknown, mark NO.		
3. Was your reaction life-threatening (i.e. severe anaphylaxis requiring epinephrine, ER visit, ICU admission, intubation)?		
4. Did your reaction involve blistering, ulceration, sloughing of your skin or lining of your mouth, eyes, genitals – OR – were you diagnosed with Stevens Johnson Syndrome or Toxic Epidermal Necrolysis?		
5. Did your reaction involve any organ dysfunction/failure – OR – were you diagnosed with serum sickness, drug reaction with eosinophilia, acute interstitial nephritis?		

FIGURE E1. (CONTINUED).

**A** B **Toolkit B**  
Page 1 **Direct Oral Amoxicillin Challenge for Low-Risk Patients**

Patient ID/ Sticker: \_\_\_\_\_

Testing is not necessary if a penicillin class antibiotic has been tolerated since the index reaction

**DO NOT perform any penicillin allergy testing if there is a history of penicillin-associated:**

- Blistering rash • Hemolytic anemia • Nephritis • Hepatitis • Fever • Joint pains

**Direct oral amoxicillin challenge can be performed in any patient with a history of the following symptoms associated with penicillin:**

- Isolated reactions that are unlikely allergic (e.g., gastrointestinal symptoms, headaches)
- Pruritus without rash
- Remote (>10 years) unknown reactions without features of IgE/mediate hypersensitivity
- May also be used for patients with a family history of penicillin allergy or benign somatic symptoms

**First penicillin skin test if:**

- The reaction was cutaneous
- The reaction had features of IgE/mediate hypersensitivity
- The patient currently has unstable or compromised hemodynamic or respiratory status or is pregnant with low risk allergy history.

**Proceed to amoxicillin challenge only if skin test is negative**

Continue to second page

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**B** B **Toolkit B (continued)**  
Page 2 Patient ID/ Sticker: \_\_\_\_\_

Ordered by: \_\_\_\_\_ Performed by: \_\_\_\_\_ Date: \_\_\_/\_\_\_/\_\_\_

Amoxicillin oral challenge given:  250 mg  500 mg

Time given: \_\_\_\_\_ Time observation end: \_\_\_\_\_

**Observed challenge reaction:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

Time to onset: \_\_\_\_\_

**Observed challenge reaction treatment given:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

**Delayed challenge reaction reported:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

Time to onset: \_\_\_\_\_

**Delayed challenge reaction treatment given:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

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FIGURE E2. **A**, Direct challenge.<sup>E1</sup> Toolkit for administering direct oral amoxicillin challenges for patients at low risk for true penicillin allergy. **B**, Graded challenge.<sup>E1</sup> Toolkit for administering 2-step direct oral amoxicillin challenges for patients at moderate risk for true penicillin allergy for locations without access to skin testing materials. **C**, Beta-lactam graded challenge order set.<sup>E7</sup> Electronic health record order set for beta-lactam graded challenges. **D**, Amoxicillin graded challenge order set.<sup>E8</sup> Electronic health record 3-step amoxicillin graded challenge panel.

**B**

**C** Toolkit C  
Page 1  
**2-Step Amoxicillin Challenge for Moderate-Risk Patients (Skin Testing Not Available)**  
Patient ID/ Sticker: \_\_\_\_\_

Testing is not necessary if a penicillin class antibiotic has been tolerated since the index reaction

**!** Note that this testing is recommended only in locations without access to skin testing materials. This procedure should be performed only after careful consideration of the potential benefit to the patient in question, weighed against the risk of potential harm from an allergic reaction.

**DO NOT perform any penicillin allergy testing if there is a history of penicillin-associated:**  
• Blistering rash • Hemolytic anemia • Nephritis • Hepatitis • Fever • Joint pains

**This testing is indicated if:**

- The reaction was cutaneous
- The reaction had features of IgE/immediate hypersensitivity
- The patient currently has unstable or compromised hemodynamic or respiratory status or is pregnant with low risk allergy history.

**This testing may also be used for low-risk reactions that include:**

- Remote (>10 years) unknown reactions without features of IgE
- Pruritus without rash
- Isolated reactions that are unlikely allergic (e.g., gastrointestinal symptoms, headaches)

Continue to second page

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**C** Toolkit C (continued)  
Page 2  
Patient ID/ Sticker: \_\_\_\_\_

Ordered by: \_\_\_\_\_ Performed by: \_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

**1 Amoxicillin oral challenge given:**  25 mg  500 mg  
Time given: \_\_\_\_\_ Time observed:  30 min  60 min Time observation end: \_\_\_\_\_

**Observed challenge reaction:**  
 None  Yes, please list signs and symptoms: \_\_\_\_\_  
Time to onset: \_\_\_\_\_  
**Observed challenge reaction treatment given:**  
 None  Yes, please list signs and symptoms: \_\_\_\_\_

**2 Amoxicillin oral challenge given:**  250 mg  500 mg  
Time given: \_\_\_\_\_ Time observed:  30 min  60 min Time observation end: \_\_\_\_\_

**Observed challenge reaction:**  
 None  Yes, please list signs and symptoms: \_\_\_\_\_  
Time to onset: \_\_\_\_\_  
**Observed challenge reaction treatment given:**  
 None  Yes, please list signs and symptoms: \_\_\_\_\_

**Delayed challenge reaction reported:**  
 None  Yes, please list signs and symptoms: \_\_\_\_\_  
Time to onset: \_\_\_\_\_  
**Delayed challenge reaction treatment given:**  
 None  Yes, please list signs and symptoms: \_\_\_\_\_

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**FIGURE E2. (CONTINUED).**

**C** Links to computerized guideline/app

**Order Sets**

Antibiotic Test Dose Manage My Version ▾

Please document any appropriate changes in allergy status once test dose procedure is completed.

• Penicillin Hypersensitivity Pathway

**Medications**

If possible, hold the following medications the day of the Test Dose Procedure:

A) Beta blockers: inhibit the action of epinephrine.  
B) ACE inhibitors: increase the risk of an allergic reaction.

**PO Medications**

- amoxicillin (AMOXIL) oral
- cefixime (SUPRAX) oral
- cefpodoxime (VANTIN) oral
- cephalexin (KEFLEX) oral
- penicillin V potassium (VEETID) oral

**IV Medications**

IV Antibiotic (Test dose = 10% of the full dose)

- ampicillin (OMNIPEN) IV
- ampicillin-sulbactam (UNASYN) IV
- ceFAZolin (ANCEF) IV
- ceFEPIme (MAXIPIME) IV
- ampicillin (OMNIPEN) IV  
ampicillin (OMNIPEN) 200 mg in sodium chloride 0.9% syringe  
200 mg, Intravenous, Once, Today at 1115, For 1 dose  
Vital signs per site Antibiotic Test Dose Policy. For intravenous test doses, RN to administer by IV push over 5 minutes.  
If no reaction to test dose, give full dose 30-60 min after per site policy. If rash or other symptoms develop, stop medication and treat with diphenhydramine 50 mg IV and notify RC. For anaphylactic reaction, follow site protocol.
- cefotaxime (CLAFORAN) IV
- ceFOXitin (MEFOXIN) IV
- ceftaroline (TEFLARO) IV
- ceFTAZidime (FORTAZ) IV
- ceFTRIAXone (ROCEPHIN) IV
- ceFUROXime (CEFTIN) IV
- ertapenem (INVANZ) IV
- meropenem (MERREM) IV
- nafcillin (UNIPEN) IV
- penicillin G potassium IV
- piperacillin-tazobactam (ZOSYN) IV

**Followed by**

ampicillin (OMNIPEN) 2,000 mg in sodium chloride 0.9% 100 mL IVPB  
2,000 mg, Intravenous, Once, Today at 1115, For 1 dose  
Vital signs per site Antibiotic Test Dose Policy. For intravenous test doses, RN to administer by IV push over 5 minutes.  
If no reaction to test dose, give full dose 30-60 min after per site policy. If rash or other symptoms develop, stop medication and treat with diphenhydramine 50 mg IV and notify RC. For anaphylactic reaction, follow site protocol.

**Rescue Medications**

- diphenhydramine (BENADRYL) 50 mg/mL injection 50 mg  
50 mg, Intravenous, Once as needed, itching, other (free text field), rash or adverse reaction, Starting Today at 1444, For 1 day
- EPINEPHrine (ADRENALIN) injection 0.3 mg  
0.3 mg, Intramuscular, Once as needed, anaphylaxis, Starting Today at 1444, For 1 day

FIGURE E2. (CONTINUED).



**D** AMOXICILLIN (PO) GRADED CHALLENGE PANEL (DOSES 1-3) ✓ Accept

Amoxicillin (PO) graded challenge panel.  
For antibiotic graded challenge in adults.

amoxicillin oral graded challenge DOSE #1 (8.75 mg)

**Allergy/Contraindication:** Penicillins **Reactions:** Unknown

8.75 mg (0.148 mg/kg), Oral, ONCE, Indications: Graded Challenge, Today at 1430, For 1 dose  
Please administer graded challenge doses 30 minutes apart. If the patient experiences a reaction during the graded challenge, do not proceed with additional doses before discussing with Allergy/Immunology.

**amoxicillin 8.75 mg**

- Specific dosing guidelines are not available for this patient's level of renal impairment. The ordered dose is within the limits that do not consider renal impairment but otherwise match the patient's conditions.
- See details for additional information on adjusting the dose for renal impairment

amoxicillin oral graded challenge DOSE #2 (87.5 mg)

**Allergy/Contraindication:** Penicillins **Reactions:** Unknown

87.5 mg (1.48 mg/kg), Oral, ONCE, Indications: Graded Challenge, Today at 1500, For 1 dose  
Please administer graded challenge doses 30 minutes apart. If the patient experiences a reaction during the graded challenge, do not proceed with additional doses before discussing with Allergy/Immunology.

**amoxicillin 87.5 mg**

- Specific dosing guidelines are not available for this patient's level of renal impairment. The ordered dose is within the limits that do not consider renal impairment but otherwise match the patient's conditions.
- See details for additional information on adjusting the dose for renal impairment

**AMOXICILLIN GRADED CHALLENGE DOSE # 3 (FINAL DOSE)**

Antibiotic graded challenge in adults.

amoxicillin oral graded challenge DOSE #3 (AMOXIL) 400 mg/5 mL SUSPENSION  
400 mg, Oral, ONCE, Starting H+120 Minutes, Please administer graded challenge doses 30 minutes apart. If the patient experiences a reaction during the graded challenge, do not proceed with additional doses before discussing with Allergy/Immunology.

amoxicillin oral graded challenge DOSE #3 (AMOXIL) CAPSULE  
Oral, ONCE, Starting H+120 Minutes, Please administer graded challenge doses 30 minutes apart. If the patient experiences a reaction during the graded challenge, do not proceed with additional doses before discussing with Allergy/Immunology.

FIGURE E2. (CONTINUED).

**A** TEST, TEST (MRN: A00000017) - Add Allergy/Adverse Effect

Type: Allergy This is the explanation for Allergy.

**\*Substance**  
 PCN Allergy Skin Test  Free text ✘ No Allergy checking is available for free text substances.

Reaction(s):

**\*Severity**: <not entered> **Info source**: <not entered>

At: <not entered> **Onset**: <not entered>

Recorded on behalf of:  **\*Category**: Drug Allergy **Status**: Active **Reason**:

Navigation: Up Home Favorites Folders Folder: Favorites

Folder: PBBOOKST\_ALLERGY

**Comments**

Patient had a negative penicillin allergy skin test on 9/25/2017. Allergy profile updated. Please refer to PHASST note for further details or page 352-1322 for questions.

FIGURE E3. **A**, Penicillin allergy testing order.<sup>E9</sup> Order form from electronic health record for penicillin skin testing. **B**, Penicillin skin testing procedure.<sup>E1</sup> Toolkit for administering penicillin skin testing before amoxicillin challenge in patients at moderate risk for true penicillin allergy.

**B**

**D** Toolkit D  
Page 1

**Penicilloyl-Polylysine (PPL)  
Skin Testing Prior to Amoxicillin  
Challenge for Moderate Risk Patients**

Patient ID/ Sticker: \_\_\_\_\_

**DO NOT perform any penicillin allergy testing if there is a history of penicillin-associated:**

- Blistering rash • Hemolytic anemia • Nephritis • Hepatitis • Fever • Joint pains

**This testing is indicated if:**

- The reaction was cutaneous
- The reaction had features of IgE/mediate hypersensitivity
- The patient currently has unstable or compromised hemodynamic or respiratory status or is pregnant with low risk allergy history.

**Skin testing:**

- Place test on arms.
- Place and read all puncture tests prior to placing any intradermal tests.
- Positive tests are defined as wheal  $\geq$ 5mm with flare > wheal.
- Do not record test if saline control is positive or histamine control is negative

Ordered by: \_\_\_\_\_ Performed by: \_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

<b>1 Prick/puncture</b>	<b>2 Intradermal</b>																														
Time placed: _____ Time read: _____	Time placed: _____ Time read: _____																														
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td></td> <td style="text-align: center;">wheal</td> <td style="text-align: center;">flare</td> </tr> <tr> <td style="text-align: center;">PPL</td> <td style="width: 40px;"></td> <td style="width: 40px;"></td> </tr> <tr> <td style="text-align: center;">Penicillin G</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">Negative control</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">Positive control (histamine)</td> <td></td> <td></td> </tr> </table>		wheal	flare	PPL			Penicillin G			Negative control			Positive control (histamine)			<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td></td> <td style="text-align: center;">wheal</td> <td style="text-align: center;">flare</td> </tr> <tr> <td style="text-align: center;">PPL</td> <td style="width: 40px;"></td> <td style="width: 40px;"></td> </tr> <tr> <td style="text-align: center;">Penicillin G</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">Negative control</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">Positive control (histamine)</td> <td></td> <td></td> </tr> </table>		wheal	flare	PPL			Penicillin G			Negative control			Positive control (histamine)		
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Negative control																															
Positive control (histamine)																															

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**D** Toolkit D (continued)  
Page 2

**3 Amoxicillin challenge**

Ordered by: \_\_\_\_\_ Performed by: \_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Amoxicillin oral challenge given:  250 mg  500 mg

Time given: \_\_\_\_\_ Time observation end: \_\_\_\_\_

**Observed challenge reaction:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

Time to onset: \_\_\_\_\_

**Observed challenge reaction treatment given:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

**Delayed challenge reaction reported:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

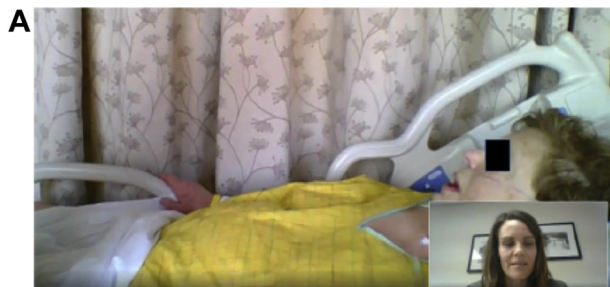
Time to onset: \_\_\_\_\_

**Delayed challenge reaction treatment given:**

None  Yes, please list signs and symptoms: \_\_\_\_\_

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FIGURE E3. (CONTINUED).



**FIGURE E4. A,** Telemedicine for penicillin skin testing.<sup>E2,E10</sup> Example of a customary telemedicine visit for penicillin skin testing between the allergist and the patient. **B,** Beta-lactam allergy algorithms/pathways.<sup>E7,E11-E13</sup> Algorithm and guideline pathway for assessing beta-lactam allergy history approved by Partners HealthCare. **C,** Aztreonam-specific usage pathway.<sup>E14</sup> Algorithm and pathway for assessing penicillin allergy history for patients receiving aztreonam.

**B** PARTNERS HEALTHCARE  
FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

### Guideline for Prescribing Antibiotics to Inpatients with Penicillin Allergy


**Why use it?** The purpose of this guideline is to provide allergy history-taking support and antibiotic prescribing recommendations for patients reporting beta-lactam allergy.

**How do I access the guideline?**

- Via your smartphone or tablet:
  - Connect to Partners wifi (password: [unclear]).
  - You will not be able to access the app via unsecured wifi (phishing risk).
  - Access the app at <https://id.partners.org/allergy>.
  - You will be prompted for your Partners username and password.
- Via a Partners PC: just go to <https://id.partners.org/allergy>.

**What's the evidence base?** This decision support tool and guideline have been in place at more than 5 Partners hospitals since 2016, setting a national standard for the inpatient approach to beta-lactam allergy.<sup>1,2</sup> Go to <https://id.partners.org/allergy/evidence/> for full papers.

**What if I still have questions?** Please watch the educational videos at <https://id.partners.org/allergy/videos/>, contact us at [allergy@partners.org](mailto:allergy@partners.org), or involve Infectious Disease and/or Allergy consultation services, if available.



### Penicillin Hypersensitivity Pathway

<p><b>Type I (or II) IBS</b> Direct IgE-mediated Severe-Johnson Syndrome Toxic Epidermal Necrolysis Acute interstitial nephritis (AIN) Drug Rash (Eosinophilic Systemic Symptoms) (DRESS) syndrome Stomatitis Drug Fever</p>	<p><b>Type I (or II) delayed IBS</b> Anaphylaxis Angioedema Wheezing or shortness of breath Laryngeal edema Hypotension Hives/urticaria</p> <p>Unknown reaction with no further details available Both allergic and toxic</p>	<p><b>Not reaction</b> Direct IgE (not toxic)</p> <p>Manufactured rash (self Type IV HSR) Record take allergy, but patient denies</p> <p>Unknown reaction, but patient denies mucosal involvement, skin desquamation, organ involvement, or joint/BC medical evaluation</p>
<p>Avoid using PCNs, cephalosporins, and carbapenems Use alternative agents by microbial coverage<sup>1</sup></p>	<p>OK to: Use 2<sup>nd</sup>/3<sup>rd</sup> generation cephalosporins by Test Dose Procedure OR Use alternative agents by microbial coverage<sup>1</sup> OR Aztreonom or carbapenem<sup>2</sup> OR If clinical indication for a beta-lactam, please involve Infectious Disease service and Allergy, if available.</p>	<p>OK to: Use 3rd dose aztreonom OR Use penicillin by Test Dose Procedure OR Use carbapenem<sup>2</sup></p>

**ALTERNATIVE AGENTS BY MICROBIAL COVERAGE:**  
 Green positive coverage: Vancomycin, linezolid, daptomycin<sup>3</sup>, daptomycin, daptomycin, TMP/SMX  
 Green negative coverage: Quinolones, sulfamethoxazole / trimethoprim, aminoglycosides, aztreonom<sup>4</sup>

**Cephalosporins by generation:**  
 1<sup>st</sup> Phosphotriester cefazolin + 2<sup>nd</sup> Phosphotriester cefuroxime  
 2<sup>nd</sup> Phosphotriester cefotaxime/ceftriaxone/cefepime/cefazolin + 4<sup>th</sup> Phosphotriester + 5<sup>th</sup> Phosphotriester

HSR: Hypersensitivity Reaction  
 IBS: Irritant/Idiosyncratic Reaction  
 \*Approval required!

**Allergy to:**

Penicillin

Was the reaction unknown?  
No

Was there a rash?  
Yes

Was there organ involvement (e.g. liver enzyme elevation, creatinine elevation or acute kidney injury)?  
No

Were there mucosal lesions or skin desquamation?  
No

Were there joint pains, fever, or myalgias?  
Yes

**Assessment**

Possible serum sickness reaction  
Type II-IV Hypersensitivity Reaction

FIGURE E4. (CONTINUED).

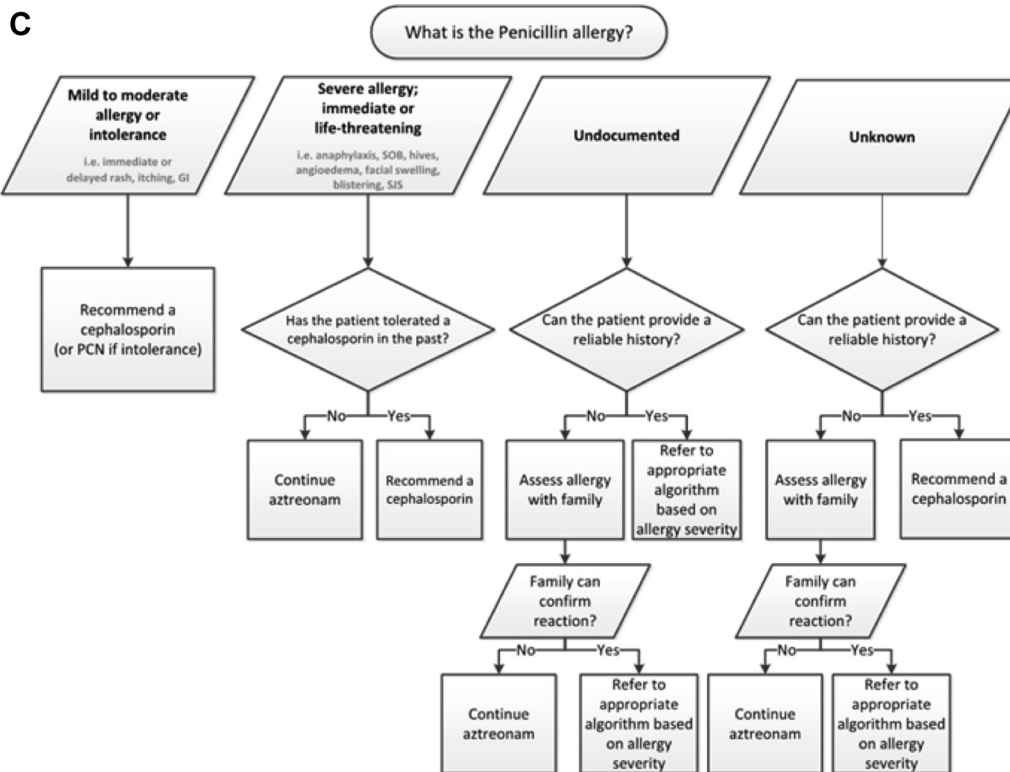


FIGURE E4. (CONTINUED).

**A**

This patient has indicated an allergy to Penicillin or Cephalosporin medication. Please review the  
⚠ Acknowledge reasons below and place a consult order for Allergy clinic if indicated and IF patient is included in the target population. ( BPA-id # 2350 ).

DO NOT SEND AN DRUG ALLERGY CONSULT FOR THE FOLLOWING REASONS:

1. The initial allergic reaction consisted only of nausea, vomiting and/or diarrhea OR
2. After the allergic reaction, the patient has taken the SAME medication without an adverse reaction OR
3. Patient denies having an allergy to the listed medication (IF YES, REMOVE THE ALLERGY)

SIGN AND SEND A DRUG ALLERGY CONSULT IF THEY DO NOT MEET THE CRITERIA ABOVE

[🏠 OUTPATIENT CONSULT INT MED - ALLERGY/IMMUNOLOGY](#)

Acknowledge Reason \_\_\_\_\_

▼

**FIGURE E5. A**, Outpatient allergy consult.<sup>E15</sup> Electronic health record alert ordering an outpatient allergy consult in penicillin- or cephalosporin-allergic patients with specific reaction histories. **B**, Beta-lactam hypersensitivity pathway.<sup>E16</sup> Alert from electronic health record prompting physicians to consult the beta-lactam hypersensitivity pathway. **C**, Update allergy history.<sup>E17</sup> Alert from electronic health record prompting clinicians to update a patient’s allergy history after receiving an antibiotic test dose.

**B**

BestPractice Advisory - Bcnvalidate, Bahamas

**Important (1)**

⚠ Consider Narrow Spectrum Beta-Lactam [provide feedback](#)

The [Penicillin and Cephalosporin Hypersensitivity Pathway](#) has decision support for safe and appropriate antibiotic prescribing for patients with beta-lactam allergies.

Remove the following orders? \_\_\_\_\_

Apply the following? \_\_\_\_\_

⚠ Acknowledge Reason \_\_\_\_\_

**FIGURE E5. (CONTINUED).**

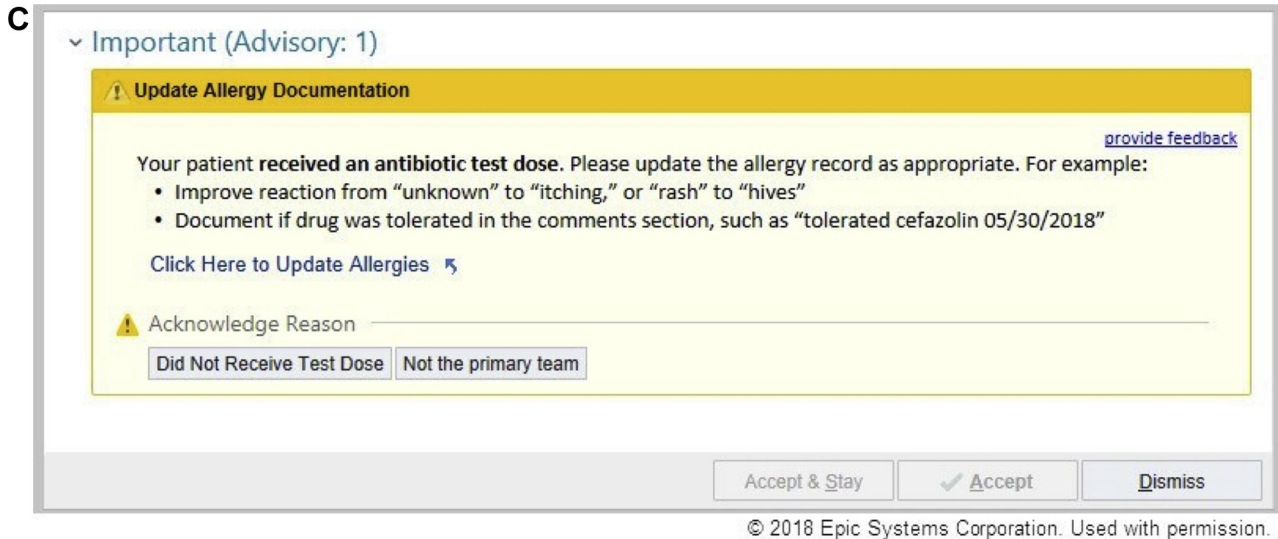


FIGURE E5. (CONTINUED).

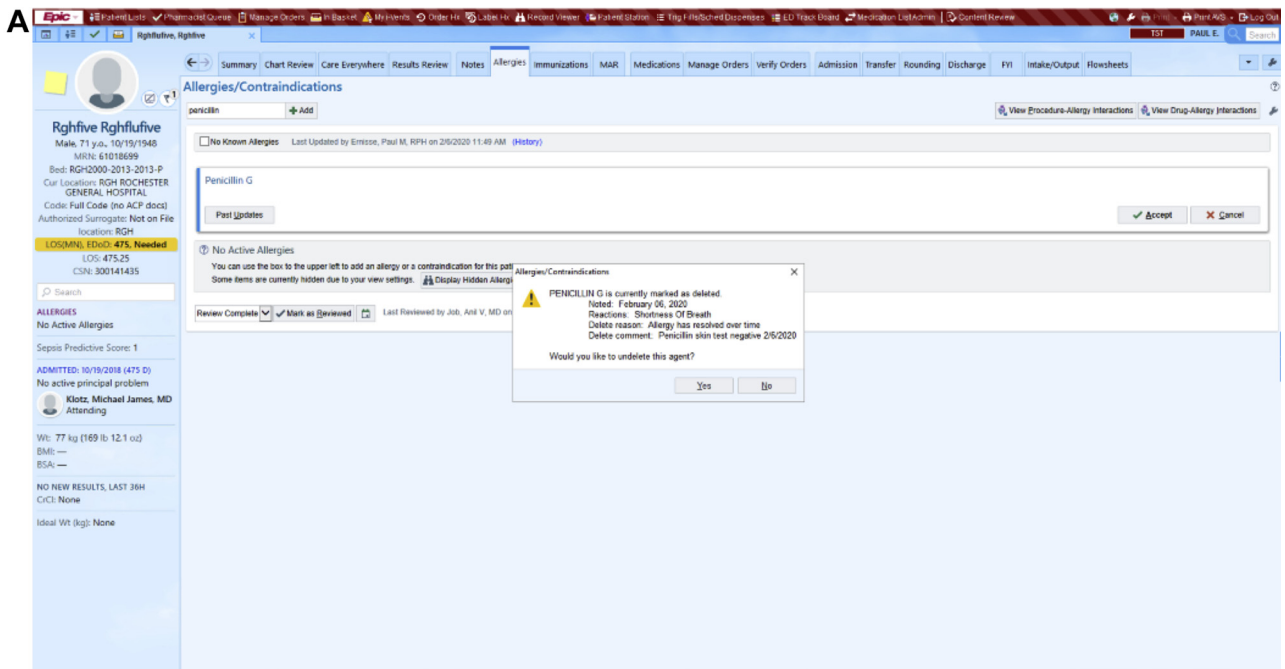


FIGURE E6. A, Relabeling alert.<sup>E9</sup> Electronic health record notification informing clinicians about details that led to the delabeling of the penicillin allergy. B, Relabeling alert. Alert from electronic health record prompting physicians to review a previous negative penicillin allergy challenge before relabeling an allergy.

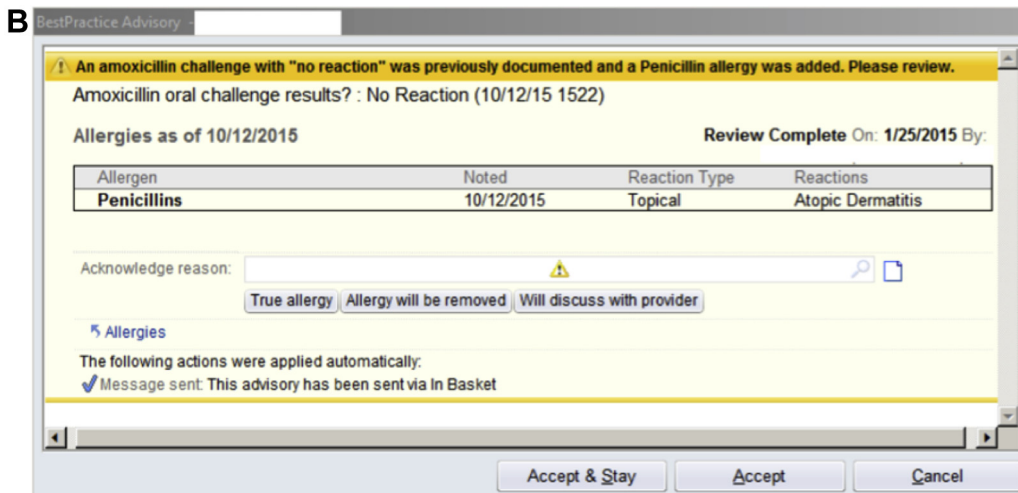


FIGURE E6. (CONTINUED).

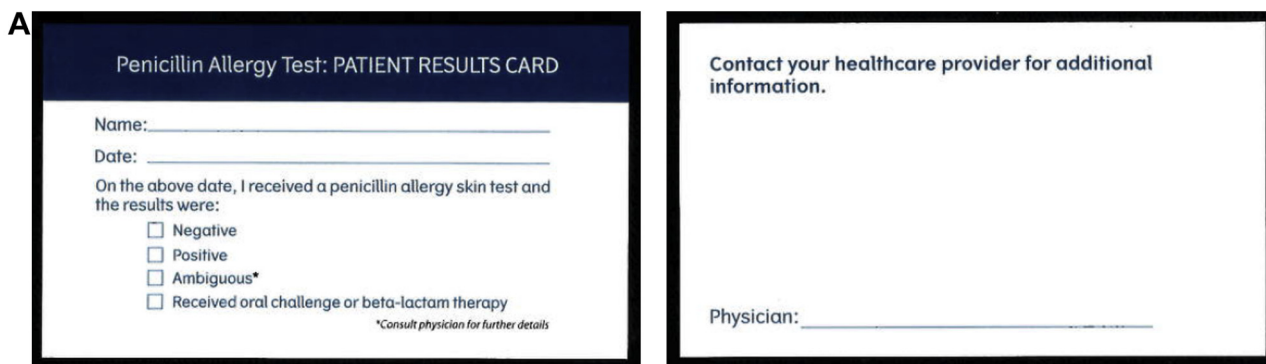


FIGURE E7. **A**, Wallet card (ALK). Card patient can carry in wallet that details allergy information, provided by ALK. **B**, Wallet card (Vanderbilt Drug Allergy Center). Card patient can carry in wallet that details allergy information, provided by Vanderbilt Drug Allergy Center. **C**, Allergy Passport, a free mobile application on iTunes for apple/IOS. IOS-friendly application patients can download to their mobile device to document allergy information for future health care providers.

**B** [Your Logo Here]  
 \_\_\_\_\_ [Name]  
 Tolerated a penicillin allergy challenge with  
 \_\_\_\_\_ [Drug/Dose] on \_\_\_\_\_  
 [Date] and no longer needs to be considered allergic to  
 penicillin. Mild delayed rashes may still occur in 2-5% of future  
 treatments.  
 Signed \_\_\_\_\_

FIGURE E7. (CONTINUED).

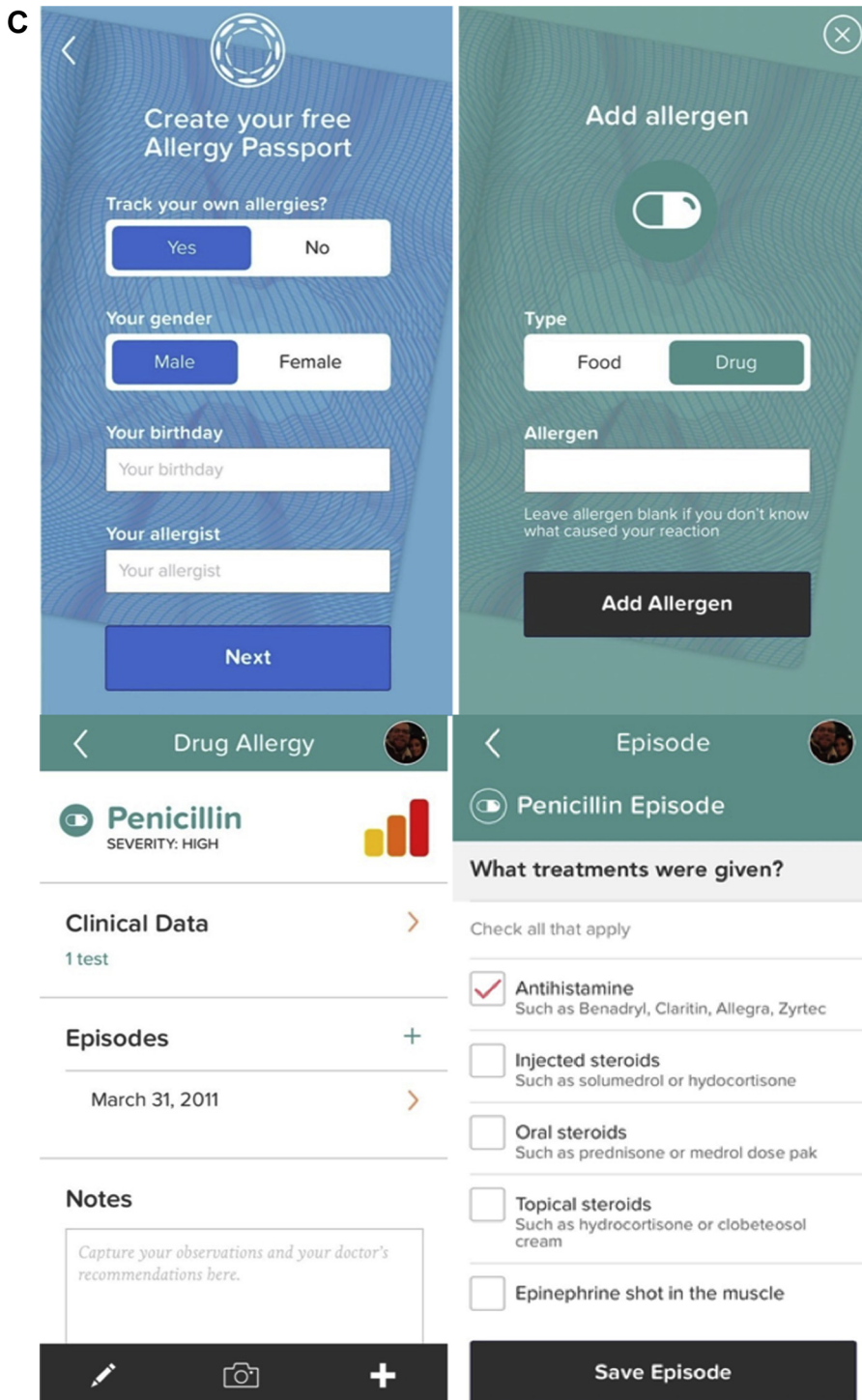


FIGURE E7. (CONTINUED).

## REFERENCES

- E1. Shenoy ES, Macy E, Rowe T, Blumenthal KG. Evaluation and management of penicillin allergy: a review. *JAMA* 2019;321:188-99.
- E2. Ramsey A, Staicu ML. Use of a penicillin allergy screening algorithm and penicillin skin testing for transitioning hospitalized patients to first-line antibiotic therapy. *J Allergy Clin Immunol Pract* 2018;6:1349-55.
- E3. Chiriac AM, Banerji A, Gruchalla RS, Thong BYH, Wickner P, Mertes PM, et al. Controversies in drug allergy: drug allergy pathways. *J Allergy Clin Immunol Pract* 2019;7:46-60.e4.
- E4. Vaisman A, McCready J, Hicks S, Powis J. Optimizing preoperative prophylaxis in patients with reported beta-lactam allergy: a novel extension of antimicrobial stewardship. *J Antimicrob Chemother* 2017;72:2657-60.
- E5. Solensky R, Jacobs J, Lester M, Lieberman P, McCafferty F, Nilsson T, et al. Penicillin allergy evaluation: a prospective, multicenter, open-label evaluation of a comprehensive penicillin skin test kit. *J Allergy Clin Immunol Pract* 2019;7:1876-1885.e3.
- E6. Lee RU, Banks TA, Waibel KH, Rodriguez RG. Penicillin allergy...maybe not? The military relevance for penicillin testing and de-labeling. *Mil Med* 2019;184:e163-8.
- E7. Blumenthal KG, Shenoy ES, Wolfson AR, Berkowitz DN, Carballo VA, Balekian DS, et al. Addressing inpatient beta-lactam allergies: a multihospital implementation. *J Allergy Clin Immunol Pract* 2017;5:616-625.e7.
- E8. Staicu ML, Plakosh M, Ramsey A. Prospective evaluation of electronic medical record penicillin allergy documentation at a tertiary community teaching hospital. *Ann Allergy Asthma Immunol* 2017;119:94-5.
- E9. Bland CM, Bookstaver PB, Griffith NC, Heil EL, Jones BM, Ann Justo J, et al. A practical guide for pharmacists to successfully implement penicillin allergy skin testing. *Am J Health Syst Pharm* 2019;76:136-47.
- E10. Staicu ML, Holly AM, Conn KM, Ramsey A. The use of telemedicine for penicillin allergy skin testing. *J Allergy Clin Immunol Pract* 2018;6:2033-40.
- E11. Blumenthal KG, Li Y, Hsu JT, Wolfson AR, Berkowitz DN, Carballo VA, et al. Outcomes from an inpatient beta-lactam allergy guideline across a large US health system. *Infect Control Hosp Epidemiol* 2019;40:528-35.
- E12. Blumenthal KG, Shenoy ES, Varughese CA, Hurwitz S, Hooper DC, Banerji A. Impact of a clinical guideline for prescribing antibiotics to inpatients reporting penicillin or cephalosporin allergy. *Ann Allergy Asthma Immunol* 2015;115:294-300.e2.
- E13. Blumenthal KG, Wickner PG, Hurwitz S, Pricco N, Nee AE, Laskowski K, et al. Tackling inpatient penicillin allergies: Assessing tools for antimicrobial stewardship. *J Allergy Clin Immunol* 2017;140:154-161.e6.
- E14. Staicu ML, Brundige ML, Ramsey A, Brown J, Yamshchikov A, Peterson DR, et al. Implementation of a penicillin allergy screening tool to optimize aztreonam use. *Am J Health Syst Pharm* 2016;73:298-306.
- E15. McDanel DL, Azar AE, Dowden AM, Murray-Bainer S, Noiseux NO, Willenborg M, et al. Screening for beta-lactam allergy in joint arthroplasty patients to improve surgical prophylaxis practice. *J Arthroplasty* 2017;32:S101-8.
- E16. Ramsey A, Sheikh A. Innovations in health care delivery: drug allergy. *J Allergy Clin Immunol Pract* 2019;7:2143-50.
- E17. Wright A, Rubins D, Shenoy ES, Wickner PG, McEvoy D, Wolfson AR, et al. Clinical decision support improved allergy documentation of antibiotic test dose results. *J Allergy Clin Immunol Pract* 2019;7:2919-21.