



Beta-lactam antibiotic skin testing and oral challenge
From the ACAAI 2015 Drug Allergy and Anaphylaxis Committee

BACKGROUND: Beta-lactam antibiotics (penicillins, semi-synthetic derivatives, and cephalosporins) are a leading cause of drug allergies in the United States. Patients at elevated risk for IgE mediated (allergic/anaphylactic) reaction to penicillin and penicillin-like drugs can undergo immediate hypersensitivity skin testing to assess or rule out risk for IgE mediated reaction; this testing, if performed with reagents that include penicillin along with major and minor penicillin determinants, is associated with excellent negative predictive value. **(1-3)**

Cephalosporins differ from penicillin in the presence of a dihydrothiazine instead of a thiazolidine ring; both possess a beta-lactam ring that participates in covalent binding to carrier proteins and can be immunogenic. There is clear evidence that clinical cross-reactivity to cephalosporins occurs in some patients with IgE-mediated potential to penicillin. The risk of cross- (anaphylactic) reaction from cephalosporins in "penicillin allergic" patients has been estimated at 0-10.5% and varies according to the 'generation' of cephalosporin; its precise incidence is unknown. Unlike evaluation of IgE mediated sensitivity to penicillin (which can be ruled out by lack of cutaneous wheal/flare reaction to Pen G and penicilloyl polylysine conjugate, with/without minor determinant mixture), **the negative predictive value of skin tests for cephalosporin or semi-synthetic penicillins has not been established, and skin testing with these drugs has not been validated.** Nonetheless, the committee recommends that this testing may be carried out in properly selected patients using published non-irritating skin test concentrations. **(1, 2)**

The 2008 Allergy Diagnostic and the 2010 Drug Allergy Practice Parameters (2) describe four scenarios:

- A patient with history of penicillin allergy who requires treatment with penicillin.
- A patient with history of penicillin allergy who requires treatment with a cephalosporin.
- A patient with history of cephalosporin allergy who requires treatment with penicillin.
- A patient with history of cephalosporin allergy who requires treatment with a cephalosporin

PURPOSE: To confirm an allergy to a penicillin, cephalosporin and/or other β -lactam antibiotic

POLICY: MD must be in the vicinity for antibiotic skin testing to be performed.

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Penicillin administration to a patient with a history of PCN allergy

Physician Instructions for penicillin skin testing

This protocol will serve as a guideline for penicillin skin testing in patients reporting history of adverse drug reaction to penicillin or a penicillin-like drug (e.g., ampicillin or amoxicillin). The committee carefully considered the agents used, concentration, amount injected, and the method and timing of the reading of the drug tests and the positive and negative controls. Realizing that various publications and clinicians vary in many of these details, the committee is suggesting that this protocol be used to standardize testing among allergists.

1. Perform history and physical examination
2. If indicated (i.e. an IgE-mediated adverse drug reaction remains in the differential diagnosis), proceed with penicillin skin testing.
3. Prick or percutaneous testing is done first with the reagents listed below.
4. If the prick test is negative, it is followed by the intradermal skin test injecting 0.02 - 0.03 ml using the same reagents.

5. Reagents for prick and intradermal (see guidelines on reconstitution described in the “Nursing Instructions” section):
 - a. Negative Control: Sodium chloride solution without preservative
 - b. Penicillin G 10,000 U/ml (a minor determinant)
 - c. Pre PEN (benzylpenicilloyl polylysine) full strength (major determinant)
 - d. Ampicillin 20 mg/ml for prick and ID testing, (4, 5) to be considered for inclusion when:
 - i. Prior reaction was to amoxicillin/ ampicillin or a semi-synthetic penicillin.
 - ii. Patient history is unclear regarding the beta lactam drug associated with past reaction, and the patient requires treatment with amoxicillin/ ampicillin or a semi-synthetic penicillin either immediately or predictably in the future
 - e. Minor Determinant Mixture (may be used if available; however, minor determinant mixture has not been approved by the FDA)
 - f. Positive Control: Histamine
 - i. Percutaneous: histamine base 6 mg/ml (histamine dihydrochloride 10 mg/ml)
 - ii. Intradermal: histamine base 0.1 mg/ml (histamine phosphate 0.275 mg/ml)

6. A positive test is defined as wheal size equal to or greater than 3 mm diameter with equivalent or greater erythema (flare) compared to the saline control done at the same time.
7. The antibiotic testing agents and controls will be read at 15 minutes

Graded dose or test dose challenge when PCN skin testing is negative

It is recommended that the physician administer a beta-lactam test dose with either penicillin or amoxicillin, based on patient circumstances, after a negative skin test, particularly when skin testing with a minor determinant mixture has not been performed. While some of the earlier studies suggested that an oral challenge was not needed based upon the small percentage of reactions to a subsequent oral challenge, most recent studies have included an oral challenge and the committee feels that this is a safer and more complete method of evaluation. (6, 7) The determination to challenge with penicillin or amoxicillin/ampicillin may be based on the patient’s history and/or the drug that may need to be administered immediately or prescribed in the future.(8) Patients should be observed as long as severe exposure-related reactions are anticipated. This recommendation depends on the type of previous drug reaction, the drug under investigation, and the patient’s individual condition. While the majority of Committee members advocate 60 minutes of observation following the final oral provocation dose (8), some judge 30 minutes to be adequate for many patients. For this reason, we encourage the allergist to tailor the observation time from 30 to 60 minutes, as they deem most appropriate. A commonly used protocol is the administration of full dose oral beta lactam with monitoring for 30-60 minutes, but an alternative and more cautious protocol may be used that entails a “test dose” (e.g, 1/10-¼ full oral dose), observation for 30 minutes, followed by the remaining or full oral dose with monitoring for 30-60 minutes.(9)

Penicillin induction of tolerance (desensitization) when PCN skin testing is positive:

Induction of drug tolerance (desensitization) is the progressive administration of an allergenic substance to render effector cells less reactive. This procedure typically is completed over several hours, and the typical starting dose is in the microgram range. The procedure can be performed via oral, intravenous, or subcutaneous routes. The details of conduction this procedure is beyond the scope of this skin testing protocol and the physician is referred to published protocols that can be followed. (2)

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Cephalosporin administration to a patient with a history of PCN allergy:

Unlike evaluation of IgE mediated sensitivity to penicillin (which can be confirmed by demonstration of cutaneous wheal/flare reaction to Pen G, penicilloyl polylysine conjugate, and/or a minor determinant mixture), reagents that would permit performance of cutaneous tests for cephalosporin sensitivity have not been validated. (10, 11) Recent data and common impressions among physicians imply that the overwhelming majority of "penicillin allergic" patients can tolerate cephalosporins safely. Despite this, however, severe anaphylactic reactions, including fatalities, have followed administration of cephalosporins to such individuals (2).

The committee recognizes that the clinician has several options when facing this situation. The preferred (#1) protocol discussed below is PCN skin testing which is followed by an oral challenge to PCN/Amoxicillin. An alternative option (#2) is skin testing to the cephalosporin (in a non-irritating concentration) that will be used for treatment, followed by either a graded challenge (if skin testing is negative) or by desensitization to cephalosporin (if the skin testing is positive). If this approach is chosen, follow the protocol outlined below under "Administration of cephalosporin to a patient with a history of cephalosporin allergy". A final option (#3) is to administer the cephalosporin directly under observation. This last option is recommended only in the absence of severe and/or recent penicillin allergic reaction.

Option #1 skin testing and oral challenge

A. When PCN skin testing and challenge are negative

The committee recommends that penicillin skin testing be performed in the same manner as described under the above section "Penicillin administration to a patient with a history of PCN allergy". If the penicillin skin testing is negative, a test dose challenge should be completed using PCN or amoxicillin as above discussed. If there is no adverse reaction, the patient can safely take the cephalosporin. It should be noted that some committee members would omit the test dose challenge and directly administer the cephalosporin.

B. When PCN skin testing or challenge is positive:

When the patient has positive skin testing or challenge, consensus does not currently exist for management of these penicillin allergic patients, and some are prescribed cephalosporins despite a definite and low (but difficult to quantitate) risk of severe reaction.

There are a number of possible choices for treatment as described below. Which option is chosen will be at the discretion of the treating physician who has explained the potential for benefit relative to the potential for harm, and has invited the patient to participate in the medical decision making process by expressing their values and preferences.

- a. Use an alternative non-beta lactam antibiotic.
- b. When a cephalosporin is clearly indicated, desensitization is an option.
- c. When a cephalosporin is clearly indicated, administer by graded challenge.

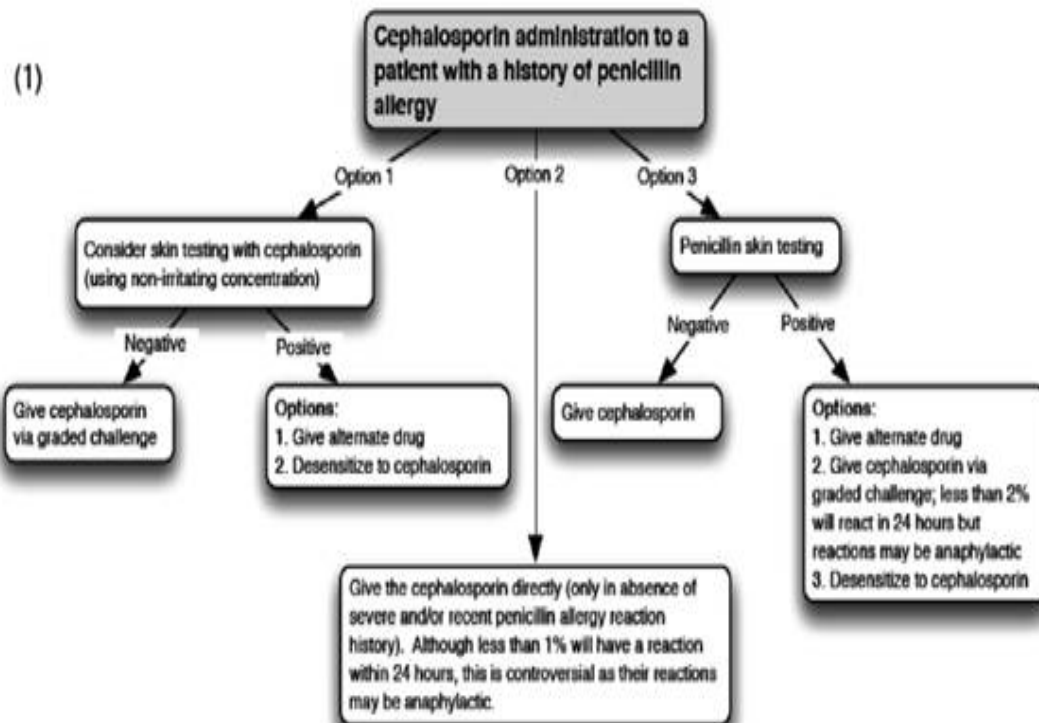
CEPHALOSPORIN GRADED DOSE CHALLENGE PROTOCOL

The committee offers this protocol as an example, but recognizes that this is not evidence based

<u>TIME</u>	<u>CEFUROXIME DOSAGE</u>	<u>(OR ALTERNATIVE AGENT)</u>
9:00 AM	25 mg	(1/10 dose and wait 30 minutes)
9:30 AM	250 mg	(give 9/10 or full dose and wait 30 minutes)
10:30 AM	END	

Note: Dosage amounts and schedule may vary based on degree of suspected sensitivity.(12)

The following algorithm taken from the JTF of PP 2010 Drug Allergy PP (2) may be used to assist in the decision-making process:



Administration of penicillin to a patient with a history of cephalosporin allergy

For the case of a patient with a history of cephalosporin allergy who requires treatment with penicillin, it is recommended that the patient have penicillin skin testing with or without an oral challenge, and if negative, the penicillin can be administered; if the penicillin skin test is positive, the patient should be desensitized to the penicillin.

Committee recommended option: Follow the same protocol for penicillin testing and graded dose/test dose challenge as outline in “Penicillin administration to a patient with a history of PCN allergy” described in the first section of this protocol.

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Administration of cephalosporin to a patient with a history of cephalosporin allergy

Note: These recommendations are based upon expert opinion and are not evidence based

The physicians has the option of 1) Skin testing and subsequent graded dose challenge to the cephalosporin that will be used for treatment 2) performing a graded or test dose challenge to the new cephalosporin after insuring that the two cephalosporin do not share the same R-side chains. This will require accurate identification of the cephalosporin causing the previous allergic reaction. 3) Desensitizing to the new cephalosporin drug. The committee recommends following the # 1 option.

1 option: Skin testing and graded dose challenge

In general, the concentration used for cephalosporin skin testing is a 10-fold dilution of the standard intravenous concentration, for both percutaneous and intradermal skin testing. See Table 18 for non-irritating concentrations for drug testing.

1. Complete cephalosporin skin testing using a non-irritating concentration of the selected cephalosporin.

Use these guidelines when selecting a cephalosporin for testing:

- a. If the specific cephalosporin responsible for the adverse reaction is **unknown**, use a third generation cephalosporin, e.g., cefuroxime for which both an IV preparation for skin testing and an oral agent for graded dose challenge is available
- b. If the specific cephalosporin responsible for the adverse reaction **is known** and an alternative cephalosporin is appropriate for treatment, select a drug that does not share the same R1- or R2-side chains as the cephalosporin that caused the allergic reaction (see Tables 16 and 17 below).
- c. If the specific cephalosporin responsible for the adverse reaction **is known** but the preferred or required drug **does share** one or both of the R1- or R2-side chains, perform skin testing with the drug that is to be administered.
- d. It is not recommended to skin test to the same cephalosporin that caused the allergic reaction.

2. Skin testing procedure for cephalosporin drug:

- a. Prick test using the concentration listed in Table 18 or, if not listed, using a 10-fold dilution of the standard intravenous concentration
- b. Perform intradermal testing using the same concentration as used in 3(a) above

A. When cephalosporin skin testing is negative:

Conduct an oral graded challenge using the cephalosporin that is to be administered following the protocol outlined above under "Cephalosporin administration to a patient with a history of PCN allergy." If administering a cephalosporin agent that is identical to the one that caused the allergic reaction or shares one or more R- side chains, a more gradual graded challenge may be appropriate, based upon the clinical history and setting.

B. When cephalosporin skin testing is positive:

1. Use an alternative non-beta lactam
 2. Perform desensitization to the cephalosporin
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The following reference tables are reproduced from the 2010 Drug Allergy Practice Parameter Reference tables of β -lactam antibiotics classified according to R1- and R2- side chains.⁽²⁾

Table 16. Groups of β -Lactam Antibiotics That Share Identical R₁-Group Side Chains^a

Amoxicillin	Ampicillin	Ceftriaxone	Cefoxitin	Cefamandole	Ceftazidime
Cefadroxil	Cefaclor	Cefotaxime	Cephaloridine	Cefonicid	Aztreonam
Cefprozil	Cephalexin	Cefpodoxime	Cephalothin		
Cefatrizine	Cephadrine	Cefditoren			
	Cephaloglycin	Ceftizoxime			
	Loracarbef	Cefmenoxime			

^a Each column represents a group with identical R₁ side chains.

Table 3 (Modified from Pichihera ME 2014(13))

Cephalosporin drugs with similar R1 side-chain structures

Group I	Group II	Group III	Group IV	Group V	Group VI	Group VII	Group VIII
Identical	Identical	Identical	Identical	Identical	Identical	Identical	Dissimilar
Cefaclor	Cefadroxil	Cefdaloxime	Cefepime	Cephaloridine	Cefozopran	Cefazolin	Cefazedone
Cephaloglycin	Cefatrizine	Cefdinir	Cefteram	Cephalothin	Cefclidine	Ceftazidime	Cefbuperazone
Loracarbef	Cefprozil		Ceftiole		Cefluprenam		Cefoperazone
Similar			Cefmenoxime				Cefpiramide
Cefamandole			Cefodizime				Cefsulodin
Cefonicid			Cefoselis		Less similar		Cefuroxime
			Cefotaxime		Ceftaroline fosamil		Cephacetrile
			Cefpirome				Cephapirin
			Cefpodoxime				Cephadrine
			Ceftizoxime				Flomoxef
			Ceftriaxone				Moxalactam
			Cefquinome				
			Similar				
			Ceftazidime				
			Less similar				
			Ceftibuten				
			Cefcapene				

^aThis grouping contains a benzylmethanamine core except for cefamandole and cefonicid, which contains a core of benzylmethanol.

^bThis grouping contains a 4-(aminomethyl)phenol core.

^cThis grouping contains a (*E*)-2-aminothiazole-4-carbaldehyde oxime core.

^dThis grouping contains a (*E*)-2-aminothiazole-4-carbaldehyde *O*-methyl oxime core except for cefixime, which contains an attached formic acid to *O*-methyl oxime; ceftazidime, which contains an attached propionic acid to *O*-ethyl oxime; ceftibuten, which contains a *but*-3-enoic acid moiety in place of the formaldehyde *O*-methyl oxime moiety; and cefcapene, which contains a but-1-en-1-yl moiety in place of the formaldehyde *O*-methyl oxime group.

^eThis grouping contains a 2-methylthiophene core, except for cefoxitin, which also contains a 7-methoxy group on the β -lactam ring.

^fThis grouping contains a (*E*)-5-amino-1,2,4-thiadiazole-3-carbaldehyde *O*-methyl oxime core except for ceftobiprole, which contains *O*-methyl oxime replaced with oxime; ceftuprenam, which contains *O*-methyl oxime replaced with *O*-fluoromethyl oxime; and ceftaroline fosamil, which contains the (*E*)-5-amino- group replaced with a (*E*)-5- phosphonoamino- group and the *O*-methyl oxime replaced with a *O*-ethyl oxime group.

^gThis grouping contains a 1-methyl-1*H*-tetrazole core.

Table 17. Groups of β -Lactam Antibiotics That Share Identical R₂-Group Side Chains^a

Cephalexin	Cefotaxime	Cefuroxime	Cefotetan	Cefaclor
Cefadroxil	Cephalothin	Cefoxitin	Cefamandole	Loracarbef
Cephradine	Cephaloglycin		Cefmetazole	
	Cephapirin		Cefpiramide	

^a Each column represents a group with identical R₂ side chains.

Nonirritating concentrations of cephalosporins to be used for drug testing. ⁽²⁾

Table 18. Nonirritating Concentrations of 15 Antibiotics⁴²⁸

Antimicrobial drug	Full-strength concentration	Dilution from full strength	Nonirritating concentration
Azithromycin	100 mg/mL	10 ⁻⁴	10 μ g/mL
Cefotaxime	100 mg/mL	10 ⁻¹	10 mg/mL
Cefuroxime	100 mg/mL	10 ⁻¹	10 mg/mL
Cefazolin	330 mg/mL	10 ⁻¹	33 mg/mL
Ceftazidime	100 mg/mL	10 ⁻¹	10 mg/mL
Ceftriaxone	100 mg/mL	10 ⁻¹	10 mg/mL
Clindamycin	150 mg/mL	10 ⁻¹	15 mg/mL
Cotrimoxazole	80 mg/mL	10 ⁻²	800 μ g/mL
Erythromycin	50 mg/mL	10 ⁻³	50 μ g/mL
Gentamicin	40 mg/mL	10 ⁻¹	4 mg/mL
Levofloxacin	25 mg/mL	10 ⁻³	25 μ g/mL
Nafcillin	250 mg/mL	10 ⁻⁴	25 μ g/mL
Ticarcillin	200 mg/mL	10 ⁻¹	20 mg/mL
Tobramycin	80 mg/2 mL	10 ⁻¹	4 mg/mL
Vancomycin	50 mg/mL	10 ⁻⁴	5 μ g/mL

TREATMENT OF THE ACUTE REACTION

An impending generalized reaction to immediate hypersensitivity skin testing is unusual. However, this may be anticipated if patient has a sensation of throat irritation, seems apprehensive, is pale, has a rapid heartbeat, breaks out with perspiration, complains of weakness or faint feeling, nasal/ocular symptoms, appears flushed or has increased rate of respiration.

If patient displays systemic/anaphylactic symptoms:

Rapid onset:

- Have patient lie down
- Take blood pressure (**do not** inflate cuff over skin test site!) and pulse administer epinephrine; explain effects of epinephrine to patient (palpitations, shakiness, etc.)

Gradual onset:

- Have patient lie down
- Take blood pressure (**do not** inflate cuff over injection site!) and pulse
- Notify physician
- Have immediate access to emergency medications

The following supplies and reagents must be readily available:

- Stethoscope and sphygmomanometer.
- Tourniquet, syringes, and hypodermic needles.
- Epinephrine 1:1000 for IM administration.
- Oxygen with nasal cannula/mask.
- Intravenous fluids.

- Oral airway and large bore (16 + 14-gauge) needles.
- Diphenhydramine (for IM or IV injection)
- Cetirizine (oral)
- Glucagon for injection
- Solumedrol 125 mg

NOTE: Hospital admission is required for poor response or lack of resolution of anaphylactic episode with the above measures.

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Nursing Instructions (1)

EQUIPMENT AND SUPPLIES:

REAGENTS FOR PENICILLIN SKIN TESTING:

- Penicillin G (1,000,000 unit vial or 5,000,000 unit vial)
- Pre-Pen (benzylpenicilloyl polylysine) --full strength
- Positive Control: Histamine
 - i. Percutaneous: histamine base 6 mg/ml (histamine dihydrochloride 10 mg/ml)
 - ii. Intradermal: histamine base 0.1 mg/ml (histamine phosphate 0.275 mg/ml)
- Negative Control: Sodium chloride solution without preservative

REAGENTS FOR OTHER ANTIBIOTIC SKIN TESTING

- Ampicillin Sodium 1 gram, 500 mg, or 250 mg
- Cefuroxime (Zinacef) 750 mg vial [second-generation cephalosporin]
- Cefazolin Sodium (Kefzol) 1 gram vial [first generation]
- Ceftriaxone (Rocephin) 500 mg vial [third generation]
- Cefotaxime Sodium (Claforan) 1 gram vial [third generation]

ANTIBIOTICS FOR ORAL CHALLENGE

- Amoxicillin 250 mg tablet or 125 mg/5 ml oral suspension
- Penicillin V potassium 250 mg tablet or 125 mg/5 ml oral solution
- Cefuroxime axetil (Ceftin) 125 or 250 mg tablet or 125 mg/5 ml oral suspension [2nd generation cephalosporin]
- Ceftibuten (Cedax) 200 mg capsule or 90 mg/5 ml oral suspension: closest drug to use for oral challenge following skin testing with ceftriaxone [3rd generation cephalosporin]
- There are no oral forms of Cefazolin or Cefotaxime for oral challenge

EQUIPMENT NEEDED

- Timer
- Marker
- Percutaneous skin test needles
- Alcohol soaked cotton or gauze
- Intradermal skin test syringes
- Alcohol swabs
- 10 ml sterile vials
- Sterile water for injection (no preservative) for dilution

- Normal saline (Sodium chloride) for injection (no preservative) for dilution
- Syringes for mixing dilutions
- Filter needle with micron filter (to draw up Prepen from ampule)

RECONSTITUTION

A. **Penicillin G 1,000,000 Units**

Shake well between dilutions.

1. Reconstitute PEN G 1,000,000 U with sterile water (no preservative) according to manufacturer's instructions to make a dilution of 100,000 U/ml. This dilution expires in one week when refrigerated. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, (12)and expiration date/time after reconstitution. The remaining PEN G 100,000 U/ml can be divided into 10 ml sterile vials and frozen for future use. Frozen vials expire in 1 month. Once thawed, they expire in 1 week, and need to be relabeled to indicate the new expiration.
2. If necessary, thaw above dilution. Add 0.5 ml of 100,000 U/ml PEN G to 4.5 ml normal saline for injection (no preservative) in a sterile 10 ml vial. This will equal 10,000 U/ml. The expiration is 12 hours after mixing. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated. **This dilution is used for testing (prick and intradermal).*

B. **Penicillin G 5,000,000 Units Reconstitution**

Shake well between dilutions.

1. Reconstitute PEN G 5,000,000 U with sterile water for injection (no preservative) according to manufacturer's instructions to make a dilution equal to 1,000,000 U/ml. The expiration is one week. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.
2. Add 0.5 ml of 1,000,000 U/ml PEN G to 4.5 ml normal saline for injection (no preservative) in a sterile 10 ml vial. This will equal 100,000 U/ml. This dilution expires in one week when refrigerated. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Additional PEN G 100,000 U/ml can be prepared in 10 ml sterile vials and frozen for future use. Frozen vials expire in 1 month. Once thawed, they expire in 1 week, and need to be relabeled to indicate the new expiration.
3. Add 0.5 ml of 100,000 U/ml PEN G to 4.5 ml normal saline for injection (no preservative) in sterile 10 ml vial. This will equal 10,000 U/ml. Expiration is 12 hours after mixing. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated. **This dilution is used for testing (prick and intradermal).*

C. **Ampicillin Sodium**

Shake well between dilutions.

1. Dilute 1 gram, 500 mg, or 250 mg ampicillin with sterile water (no preservative) according to manufacturer's instructions to make a 500 mg/ml stock solution. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated. The expiration is 4 days.
2. As an example of making a 100 mg/ml ampicillin solution, dilute 1 ml of stock solution (ampicillin 500 mg/ml) with 4 ml of normal saline (no preservatives) in sterile 10 ml vial. This will equal 100 mg/ml. Expiration is 12 hours after mixing. Label vial with medication name,

strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.

3. Dilute 1 ml of 100 mg/ml ampicillin with 4 ml of normal saline (no preservatives) in sterile 10 ml vial. This will equal 20 mg/ml. Expiration is 12 hours after mixing. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated. **This dilution is used for testing (prick and intradermal).*
4. Prick testing is done first with the testing dilution (20 mg/ml). A sodium chloride (no preservative) negative control and a histamine phosphate control are also applied.
5. If the prick test is negative, proceed with the intradermal testing to the same testing dilution (20 mg/ml) by injecting 0.02 – 0.03 ml intradermally along with the negative and positive controls.

D. Cefuroxime (Zinacef) 750 mg vial

Shake well between dilutions.

1. Dilute Cefuroxime 750 mg vial with 7.5 ml of sterile water for injection (no preservative). This will equal 100 mg/ml stock solution. The expiration is 4 days. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.
2. Dilute 1.0 ml of Cefuroxime 100 mg/ml with 9.0 ml of normal saline for injection (no preservatives) in sterile 10 ml vial. The expiration is 12 hours. This will equal 10 mg/ml. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated. ** This dilution is used for testing (prick and intradermal)*
3. Prick testing is done first using the 10 mg/ml dilution. A sodium chloride control and a histamine phosphate control are also applied.
4. If prick test is negative, then proceed with intradermal testing with the same testing dilution (10 mg/ml), injecting 0.02 – 0.03 ml. intradermally, along with the negative and positive controls.

E. Cefazolin Sodium

Shake well between dilutions.

1. Dilute Cefazolin 1 gm with 9.6 ml of sterile water for injection (no preservative). This will equal 100 mg/ml stock solution. The expiration is 4 days. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.
2. Dilute 0.6 ml of Cefazolin 100 mg/ml with 2.4 ml of normal saline for injection (no preservatives) in sterile 10 ml vial. The expiration is 12 hours. This will equal 20 mg/ml. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated. ** This dilution is used for testing (prick and intradermal)*
3. Prick testing is done first using the 20 mg/ml dilution. A sodium chloride control and a histamine phosphate control are also applied.
4. If prick test is negative, then proceed with intradermal testing with the same testing dilution (20 mg/ml), injecting 0.02 – 0.03 ml. intradermally, along with the negative and positive controls

F. **Ceftriaxone (Rocephin) 500 mg vial**

Shake well between dilutions.

1. Dilute Ceftriaxone 500 mg vial with 4.8 ml of sterile water for injection (no preservative). This will equal 100 mg/ml stock solution. The expiration is 10 days refrigerated. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.
2. Dilute 1.0 ml of Ceftriaxone 100 mg/ml with 9.0 ml of normal saline for injection (no preservatives) in sterile 10 ml vial. The expiration is 12 hours. This will equal 10 mg/ml. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.
** This dilution is used for testing (prick and intradermal)*
3. Prick testing is done first using the 10 mg/ml dilution. A sodium chloride control and a histamine phosphate control are also applied.
4. If prick test is negative, then proceed with intradermal testing with the same testing dilution (10 mg/ml), injecting 0.02 – 0.03 ml. intradermally, along with the negative and positive controls.

G. **Cefotaxime Sodium (Claforan)**

Shake well between dilutions.

1. Dilute 1 gm Cefotaxime with 9.5 ml sterile water (no preservative). This will equal 100 mg/ml stock solution. The expiration time is 4 days. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.
2. Dilute 1ml of 100 mg/ml Cefotaxime with 9 ml normal saline (no preservative) in sterile 10 ml vial. This will equal 10 mg/ml stock solution. The expiration is 12 hours. Label vial with medication name, strength, manufacturer, lot number, expiration date of the stock vial, diluent used and volume, and expiration date/time after reconstitution. Keep refrigerated.
**This dilution is used for testing (prick and intradermal).*
3. Prick testing is done first with the testing dilution (10 mg/ml), also applying a sodium chloride (no preservative) control and a histamine phosphate control.
4. If the prick test is negative, proceed with the intradermal testing to the same testing dilution (10 mg/ml), by injecting 0.02 – 0.03 ml intradermally, along with the negative and positive controls.

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