Guidance on Antibiotic Choice for Patients with Penicillin Hypersensitivity

Key Points:

- Penicillin allergy is often over reported. Incidence of true anaphylactic reaction is 0.05% of the population and hypersensitivity occurs in 1 -10% of population
- Approximately 90% of reported penicillin allergies likely to be penicillin intolerance such as GI upset
- Obtaining clinical history (Table 2) can assist in determining nature of allergy and whether penicillin use is safe
- **Avoid** cephalosporins and other Beta-lactams in the treatment of mild-moderate infection in Type 1 allergy when alternative agents are available (**penicillin allergy options on all antimicrobial guidelines**)

Contraindicated – Antibiotics to be avoided in penicillin allergy:

Amoxicillin (in co-amoxiclav (Aumentin), Heliclear)
Ampicillin (in Co-fluampicil/Magnapen)
Benzylpenicillin/Penicillin G
Flucloxicillin (in Co-fluampicil/Magnapen)
Phenoxymethylpenicillin/Penicillin V
Piperacillin (in Tazocin)
Pivmecillinam
Ticarcillin (in Timentin)

Antibiotics to be avoided (Type 1) or used with caution in penicillin allergy:

Cephalosporins: Cefaclor, Cefadroxil, Cefalexin, Cefixime, Cefotaxime, Cefpirome, Cefpodoxime, Cefprozil, Cefrandine, Ceftazidime, Ceftriaxone, Cefuroxime

Other Beta-lactam antibiotics:

**Aztreonam, Imipenem, meropenem, ertapenem

**Refer to guidance below

Antibiotics considered safe in penicillin allergy (not complete list):

Amikacin
Ciprofloxacin
Clarithromycin
Clindamycin
Colistin
Co-trimoxazole
Doxycycline
Erythromycin
Gentamicin
Linezolid
Metronidazole
Nitrofurantoin
Minocycline
Rifampicin
Sodium fusidate
Teicoplanin
Tetracycline
Tobramycin
Trimethoprim
Vancomycin

Introduction

The aim of this document is to improve understanding of penicillin hypersensitivity and guide prescribers on safe and effective antibiotic prescribing. Adverse outcomes can result either from unnecessarily excluding penicillins from treatment or administering penicillins where there is the potential for hypersensitivity.

The phrase 'allergic to penicillin' is commonly seen in medical notes and on medicine charts. The diagnosis of 'penicillin allergy' is often simply accepted without obtaining a detailed history of the reaction. It has been reported that a significant percentage of patients labelled as 'penicillin allergic' are not truly allergic to the drug. 1% - 10% of patients who think they are allergic to penicillin are truly allergic[1]. As a result, penicillins are unnecessarily withheld from these patients, which may subsequently affect their clinical outcomes.

What is the True Incidence of 'Penicillin Allergy'?

General hypersensitivity reactions (e.g. rashes) to penicillin occur in between 1 and 10% of exposed patients but true anaphylactic reactions (which can be fatal) occur in less than 0.05%[2] of treated patients. Please note that patients who have a vague history of symptoms or gastro-intestinal intolerance are probably not truly allergic to penicillins. **Basic Immunology of Penicillin Allergy** Understanding the key classification systems and clinical presentations of penicillin allergy can help the practitioner make informed decisions about future therapy in order to treat the infection by the safest means.

Table 1. Definitions of terms relating to allergy

Adverse Drug Reaction is a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiologic function.[3]

Drug allergy is defined by The British Society for Allergy and Clinical Immunology (BSACI) as an adverse drug reaction with an established immunological mechanism.

Anaphylaxis is a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance.[4]

Immediate Onset Reactions (Type1) generally occur within 1 hour of administration of the drug. These are IgE mediated reactions and may progress to anaphylaxis.[5]

Accelerated / Immediate Reactions can be mediated by IgE and can occur up to 4 days into course of treatment but within 1-6 hours of the last dose

Non immediate without systemic involvement reactions manifest >3-4 days from the first administration or >1-2 hours from the last administration. These are usually cutaneous in presentation. Onset of rash can occur up to 2-4 weeks after starting the antibiotic or soon after discontinuation of the drug[6]

Non immediate with systemic involvement reactions have onset usually 2-6 weeks after first drug exposure or within 3 days of second exposure. These can involve drug reaction with eosinophillia and systemic symptoms (DRESS) or drug hypersensitivity syndrome (DHS). These are characterised by widespread red macules, papules or erythrodema, fever, lymphadenopathy, liver dysfunction and eosinophilia.[6]

Who should not be prescribed or administered penicillins?
Individuals with a history of Immediate Onset or Type I allergy are clinically recognisable by features of urticaria, laryngeal oedema, bronchospasm, hypotension or local swelling within 72 hours of administration, or those who develop a pruritic rash (even after 72 hours) should NOT receive a penicillin (see below regarding cephalosporins and beta-lactams).

Clinical Diagnosis

The clinician assessing a patient who presents with a history of penicillin allergy should attempt to define the type of reaction. The table below highlights some questions that may be useful

Table 2. Taking a history of Penicillin allergy. What to Ask?

1. What antibiotics has the patient reacted to in the past?
2. What antibiotics has the patient taken and tolerated since the allergy diagnosis?
3. What was the nature of the reaction?
4. If rash then:
    a. Describe nature of rash (e.g. pustular, urticarial etc)
    b. Could rash be related to underlying condition(e.g. viral)
    c. How long after commencing antibiotic did rash appear?
5. Why was the patient taking the antibiotic?
6. Did this reaction result in hospitalisation?
7. Did the reaction resolve on stopping the antibiotic?

Are there situations where cephalosporins or other beta-lactam antibiotics can be prescribed for patients with penicillin hypersensitivity?

- Patients with **no evidence** of Type I allergy to penicillin may be treated with any cephalosporin or beta lactam antibiotic for infections of any severity.
- Patients with symptoms suggestive of a Type I allergy should **avoid** cephalosporins and other beta-lactam antibiotics for **mild or moderate infections when a suitable alternative exists**. In **life threatening infections**, when use of a non-cephalosporin antibiotic would be sub-optimal, consider giving, under observation, a **second or third generation cephalosporin** (e.g. cefuroxime, ceftriaxone, ceftazidime)[1]. Seek advice from ID or Microbiology prior to prescribing.

Cross-reactivity of other classes of antimicrobials in patients with penicillin allergy?

Carbapenems (meropenem, imipenem, ertapenem) & Monobactams (Aztreonam): Early clinical research suggested that cross reactivity between carbapenems and penicillins was between 9.2% and 11% compared to carbapenem allergy of 2.7% - 3.9% in those without penicillin allergy.[1] However, recent evidence indicates that cross-reactivity between penicillins and carbapenems or aztreonam is extremely rare at <1%. [6] [7] [8] Robust clinical assessment and close monitoring advised when prescribing carbapenems in Type 1 penicillin allergy.

Aztreonam is generally tolerated by patients with confirmed immediate and non-immediate sensitivity to beta-lactams [6 7 8]; although cross-sensitivity is observed with ceftazidime on occasion.[1]

Cephalosporin allergy is dependent on the generation of cephalosporin. Cross reactivity between first and early second (pre 1980) cephalosporins e.g. cefalexin, has been reported to occur in up to 10% of patients. However, for third generation cephalosporins the risk is much lower, with as few as 2-3% of penicillin allergic patients having cross-reactivity. Second and third generation cephalosporins (e.g. cefuroxime, ceftriaxone, ceftazidime) are unlikely to be associated with cross reactivity as they have different side chains to penicillin.

Other antibiotic classes: Tetracyclines (e.g. doxycycline), macrolides (e.g. clarithromycin), aminoglycosides (e.g. gentamicin) and glycopeptides (e.g. vancomycin) are all unrelated to penicillins and are safe to use in the penicillin allergic patient.

Prescribing Issues

Always identify and document the nature of the reported allergy and drug name on the medicine chart and in the medical notes. The prescriber has the primary responsibility for ensuring that the allergy/sensitivity details are completed on all relevant medicine charts and medical notes.

What should be prescribed for truly penicillin allergic patients?

Alternative antibiotic options to use in penicillin allergic patients to treat specific infections are included in all sections of this antibiotic website.

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