Ellie J. C. Goldstein, Section Editor

Antibiotic Hypersensitivity Reactions and Approaches to Desensitization

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Before initiating antibiotic therapy, drug hypersensitivity is an important consideration, and a common strategy is to avoid giving patients medications when a high likelihood of severe reactions exists. With an increase in antibiotic resistance and a decrease in novel antibiotics, there is greater pressure to consider antibiotics in patients with a history of adverse reactions. The major concerns include IgE-mediated, or type I, reactions, anaphylaxis, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Some antibiotics with similar characteristics, such as cephalosporins and penicillins, may be given safely to patients with a certain allergy profile. There is still greater concern when considering antibiotics for patients with reported allergy. Desensitization is a strategy to safely induce drug tolerance to a specific drug to limit the possibility of a type I reaction.

Keywords. drug allergy; hypersensitivity; desensitization; β-lactam; vancomycin.

Drug hypersensitivity reactions are immunologic responses to medications. The World Allergy Organization recommends categorizing hypersensitivity reactions on the basis of the timing of the appearance of symptoms as immediate (ie, develops within 1 hour of drug exposure) or delayed-type (ie, onset after 1 hour of drug exposure) reactions [1]. Immediate-type (immunoglobulin E [IgE]–mediated) hypersensitivity reactions pose the greatest clinical concern because of the risk of life-threatening anaphylaxis; delayed-type reactions most commonly present as rashes or skin lesions.

Patient reports of reactions to antibiotics (often described as "allergies") are commonplace. A recent study of self-reported antibiotic allergy prevalence among 411 543 outpatients in San Diego County, California, found that 9.0% of patients had a penicillin allergy documented in their medical record [2]. In addition, antibiotic-associated adverse events have been implicated in 19.3% of all emergency department visits for drug-related adverse events in the United States, with the majority of adverse events due to immune mediated reactions [3]. It is thus necessary for providers to have an accurate understanding of antibiotic hypersensitivity reactions to assist in their decision-making process regarding the necessity of alternative antibiotic usage vs desensitization. Desensitization is becoming more commonly used in the current era of increasing antibiotic resistance and limited antimicrobial drug development [4]. This review focuses on the pathogenesis, clinical manifestations, diagnosis, and treatment of immediate and delayed-type hypersensitivity reactions to antimicrobial medications in addition to providing a review of standardized desensitization protocols and published case reports and case series that are available for clinical use.

IMMUNE-MEDIATED HYPERSENSITIVITY REACTIONS

Hypersensitivity reactions to drugs are mediated by immune responses to antigenic determinants within either

Received 6 September 2013; accepted 14 December 2013; electronically published 23 December 2013.

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Clinical Infectious Diseases 2014;58(8):1140–8

DOI: 10.1093/cid/cit949

Table 1. Classification of Immune-Mediated Hypersensitivity Reactions

Classification	Common Name	Pathogenesis
I	Immediate-type hypersensitivity	Antigen binding to membrane-bound IgE on mast cells, resulting in release of biogenic amines, arachidonic acid metabolites, and other vasoactive molecules.
II	Antibody-antigen binding	IgG or IgM antibodies bind to cell-surface antigens or extracellular matrix components.
III	Soluble antigen-antibody complexes	Deposition of antigen-antibody complexes formed in solution on solid substrates such as cells or tissues
IV[a]	Delayed-type hypersensitivity	Antigen-specific T-lymphocyte activation

Abbreviations: IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M.

[a] Type IV reactions are often subdivided into types a-d, depending on the cytokine-expression profile of the activated T lymphocytes.

Source: Adapted from Gell and Coombs [5].

the drug molecules themselves or epitopes formed by the association of drug with host proteins or other macromolecules. A classic and still useful scheme to classify hypersensitivity reactions was proposed by Gell and Coombs [5] (Table 1). This system describes 4 broad mechanistic pathways that result in tissue injury associated with clinical manifestations of hypersensitivity.

PHARMACOLOGY

Antibiotics generally do not directly stimulate the immune system, because of their small molecular size. These small chemicals may bind with larger molecules to create a hapten-carrier complex. Penicillins have been extensively studied for their propensity to induce various types of immune-mediated hypersensitivity reactions. Once the β-lactam ring opens, it can bind with lysine to create the major determinant for allergic sensitivity, the penicilloyl-protein complex (Figure 1). As the β-lactam molecule undergoes isomerization to penicillanic acid, it may bind with other molecules that also stimulate the immune system. This isomer then becomes the minor determinant of allergy, which is a less dominant mechanism [6].

Cephalosporins, carbapenems, and monobactams may all cause allergic reactions through mechanisms similar to penicillins, but the cross-reactivity of penicillin allergy to these other classes is quite controversial. Early studies of crossover allergy rates of cephalosporins likely used reagents contaminated with trace amounts of penicillins, leading to high rates of crossover allergy [7]. Later studies show the crossover rate of allergy to be much lower, but still remaining clinically significant. The cross-reactivity rate appears to be strongly related to the characteristics of the side chains in addition to the conformation of the β-lactam ring. Carbapenems replace a carbon atom for sulfur, creating a β-lactam ring very similar to penicillins (Figure 2). The resulting crossover allergy rate ranges up to 10%, although some investigators have reported the rate to be much lower [8, 9]. Cephalosporins add a carboxyl moiety to create a 6-member β-lactam ring. The crossover allergy rate is more difficult to

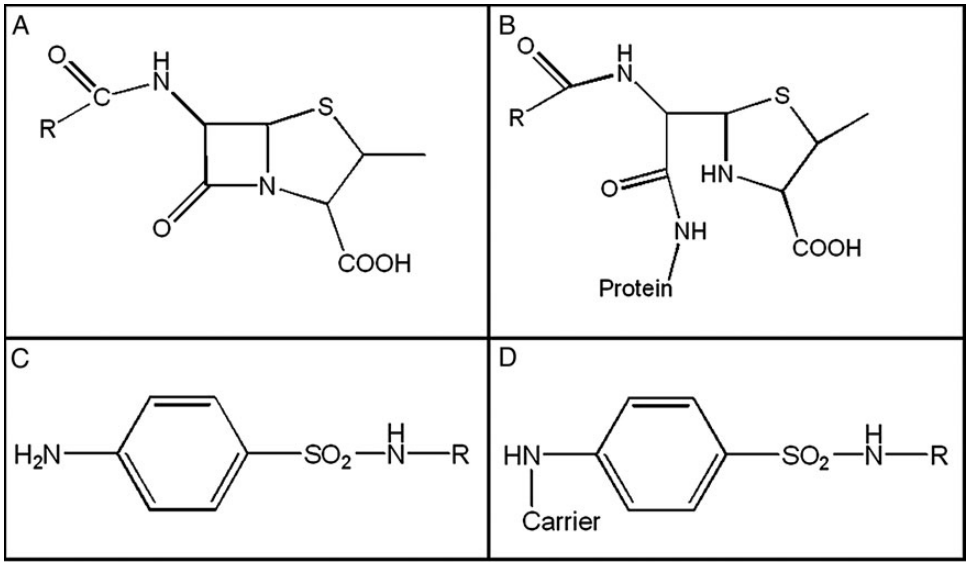

Figure 1. Chemical structures of penicillins (*A*), penicilloyl-protein complex (*B*), sulfonamides (*C*), and N^4-sulfonamidol (*D*).

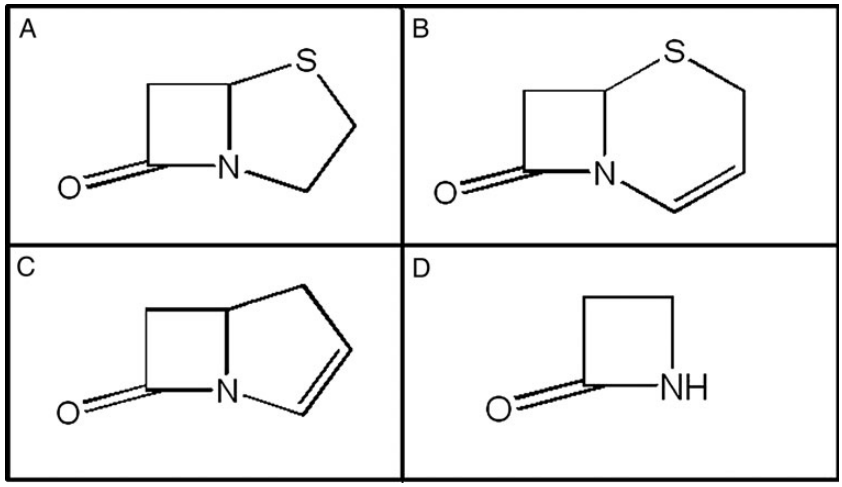

Figure 2. Ring structures for penicillins (*A*), cephalosporins (*B*), carbapenems (*C*), and monobactams (*D*).

pinpoint due to the sheer number of available medications and generations, but it is likely that early-generation cephalosporins, such as cephalexin and cefazolin, are more likely to have cross-over allergy than later generations, such as ceftriaxone and cefepime [7, 10]. Monobactams lack a second ring; crossover allergy is very rare and limited to case reports. The clinical relevance of any cross-reactivity rate depends primarily on the nature of the previous hypersensitivity reaction (ie, immediate vs delayed) and the general health of the patient, which would predict the degree of morbidity from an unexpected systemic reaction.

Sulfonamides also form hapten-carrier complexes, but unlike β-lactams, sulfonamides are stable and require acetylation or oxidation to form N^4-sulfonamidol, which can then bond to larger molecules and stimulate the immune system (Figure 1). In addition, sulfonamides may bind directly to T-cell receptors and activate the immune system with no metabolism or hapten-carrier complex necessary [6]. Vancomycin is also known to cause skin reactions such as erythema and pruritus, but it is important to differentiate between red man syndrome and a true allergic reaction. Red man syndrome is a pseudoallergic reaction that does not involve antibodies and results from direct stimulation of mast cells with severe reactions including hypotension and muscle spasm. The incidence of red man syndrome is related to the rate of infusion. Whereas 1 g of vancomycin over 30 minutes can often precipitate an episode, infusions of 10 mg/minute rarely cause reactions. IgE-mediated reactions or anaphylaxis are possible with vancomycin and carry the potential for Stevens-Johnson syndrome (SJS) [11, 12]. Drug-induced linear immunoglobulin A–mediated bullous dermatosis may be due to vancomycin with a severe case reported to mimic toxic epidermal necrolysis (TEN) [13].

Hypersensitivity reactions are possible with other antibiotic classes such as lincosamides, macrolides, and quinolones. Patient-specific factors can change the incidence of drug allergy. For example, a patient allergic to several classes of medications may be predisposed to additional allergies with other classes of drugs. Total daily dose and cumulative dose are disease-specific factors that may also influence the incidence of drug allergy [6].

CLINICAL MANIFESTATIONS OF ANTIBIOTIC HYPERSENSITIVITY REACTIONS

Type I Immediate Hypersensitivity Reactions

Penicillins and cephalosporins are the most commonly prescribed β-lactam antibiotics that can induce severe, life-threatening type I hypersensitivity reactions [14]. The onset of type I reactions occurs rapidly after administration of the inciting antibiotic, usually within 1 hour of ingestion, and requires the presence of drug-specific IgE [15]. IgE-mediated reactions are dose dependent, although this may not be clinically apparent as small doses of drug can cause a severe reaction.

The most common signs and symptoms are an urticarial rash (with a classic wheel and flare appearance), pruritus, flushing, angioedema, wheezing, gastrointestinal symptoms, hypotension, altered mental status, and anxiety [5, 15]. (Figure 3). Neither fever nor elevations in C-reactive protein are seen in a type I reaction, which can help to distinguish it from other types of drug reactions. In addition, type I reactions should not occur several days into a course of therapy, if exposure to an inciting drug is continuous.

Delayed-Type Reactions: Types II, III, and IV

Delayed-type hypersensitivity reactions (types II, III, and IV) are those in which the onset is 1 hour or more after drug exposure. These reactions are not mediated by IgE, and timing of symptoms may differ (Table 2). Type II reactions present as

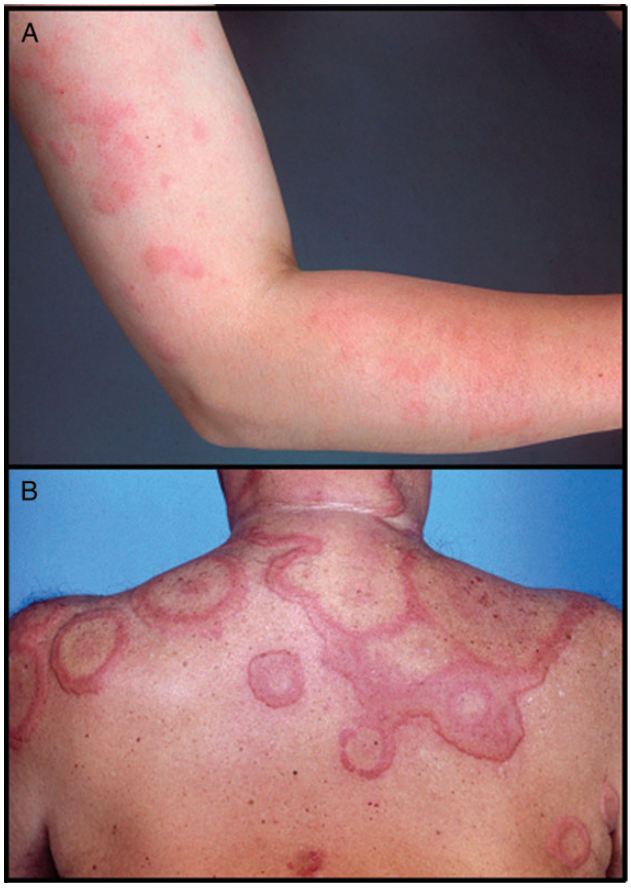

Figure 3. Examples of urticarial skin lesions resulting from drug hypersensitivity. *A,* Localized raised erythematous papules with subtle or absent central pallor. *B,* Extensive wheal and flare reaction with central blanching sharply circumscribed by and erythematous raised border. Images appears with permission from VisualDx Logical Images, Inc.

hemolytic anemia, neutropenia, and thrombocytopenia, reflecting the cell types most often affected [5, 15, 16]. Antibiotics most commonly implicated as a cause of hemolytic anemia are penicillins and cephalosporins, whereas β-lactams, vancomycin, linezolid, and sulfonamides are most commonly implicated in drug-induced thrombocytopenia. The severity of illness can range from asymptomatic to fulminant disease including hepatitis and nephritis. Clinical manifestations of type III reactions can include classical serum sickness (fever, urticarial or purpuric rash, arthralgias, lymphadenopathy, and/or acute glomerulonephritis), vasculitis (palpable purpura and/or petechiae often involving the lower extremities, fever, urticaria, arthralgias, lymphadenopathy, elevated erythrocyte sedimentation rate, and low complement levels), and drug fever. Serum sickness–like reactions (SSLRs) clinically resemble true serum sickness but are believed to be caused by different mechanisms. SSLRs are generally less severe than classic serum sickness and can include arthralgias, lymphadenopathy, and urticarial rash with and without fever; this reaction is not associated with immune complexes, vasculitis, nephritis, or hypocomplementemia. Antibiotics rarely cause classical serum sickness; however, they have been implicated in SSLR. The most common antibiotics implicated in SSLR are amoxicillin [17] and cefaclor [18, 19], although other antibiotics such as trimethoprim-sulfamethoxazole have also been implicated [20]. In addition, penicillins, cephalosporins, and sulfonamides have been shown to cause vasculitis, whereas trimethoprim-sulfamethoxazole [20] and minocycline [21] have been a cause of drug fever.

Table 2. Approximate Timing of Onset of Symptoms Due to Hypersensitivity Reactions in Previously Sensitized and Nonsensitized Patients

Type of Reaction	Previously Sensitized Patients	Patients Not Previously Sensitized
I	0–1 h	0–1 h
II	24–36 h	7–14 d
III	24–36 h	7–14 d
IV	48–96 h	14 d

The predominant findings in type IV hypersensitivity reactions typically involve the skin. There are several commonly recognized patterns of cutaneous involvement that can occur: contact dermatitis, morbilliform eruptions, SJS, TEN, and drug-induced hypersensitivity syndrome (DiHS). Contact dermatitis is a reaction to topically applied medications characterized by erythema and edema with vesicles or bullae that often rupture and leave a crust. Morbilliform eruptions are characterized by diffuse, pink plaques that generalize within 2 days [22]. The most common inciting antibiotics are penicillins and sulfonamides. Morbilliform eruptions may be exaggerated by a coexisting viral infection as seen when ampicillin or amoxicillin is given for fever during Epstein-Barr infection [22]. SJS and TEN are serious cutaneous eruptions characterized by extensive exfoliation and mucosal membrane involvement. Epidermal detachment is present in <10% in SJS, 10%–30% in SJS/TEN overlap, and >30% in TEN [23]. Erythroderma, target-like lesions, extensive erosions, and/or bullae in addition to sloughing of the skin and mucosal sites are common findings (Figure 4). Lesions usually begin on the face and upper trunk before spreading; the palms and soles are commonly involved. Antibiotics more commonly causing SJS/TEN include sulfonamides, tetracyclines, and dapsone. In particular, an increased risk for SJS/TEN due to trimethoprim-sulfamethoxazole has been reported in patients with HIV [24], perhaps due to toxic hydroxylamine metabolites and depleted systemic glutathione reserves [25]. Finally, DiHS, also called drug rash with eosinophilia and systemic symptoms (DRESS), is a severe type IV hypersensitivity reaction characterized by fever, rash, and multiorgan failure

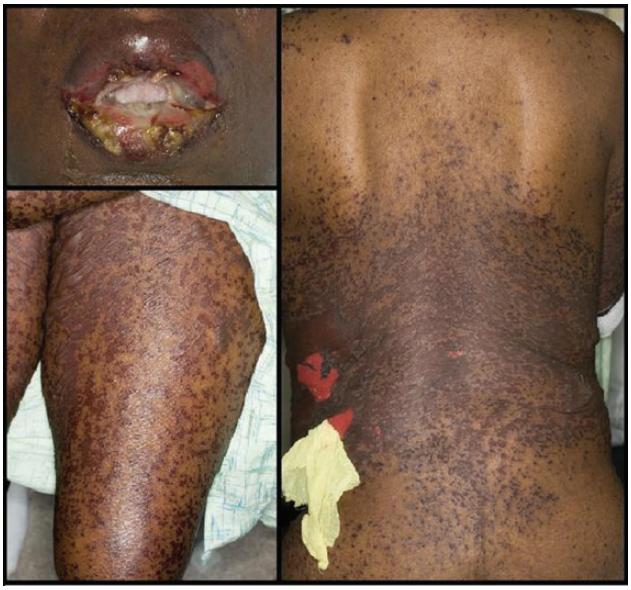

Figure 4. Mucosal membrane involvement with skin desquamation in a human immunodeficiency virus–infected patient with toxic epidermal necrolysis caused by a sulfonamide allergy.

with the liver, kidneys, heart, and/or lungs most commonly affected. Additionally, drug fever may be the sole manifestation of a type IV hypersensitivity reaction, although hepatic or renal dysfunction, pulmonary involvement, and/or mucosal ulceration may be present. The timing of the onset of fever in this case is not a reliable diagnostic clue [26]; in most cases fever can occur several days to 3 weeks after the offending medication has been started but may take up to several year(s) in some patients. Withdrawal of the offending medication usually results in defervescence in 72–96 hours.

DIAGNOSIS AND TREATMENT OF ANTIBIOTIC ALLERGY

Evaluation of the patient reporting a hypersensitivity reaction to an antimicrobial medication should begin with a detailed history and assessment of the type of clinical reaction experienced [27]. Important information to obtain includes

- source of the reported allergy history (patient, family member, healthcare professional, etc);
- indication;
- dose/route of medication;
- signs/symptoms experienced;
- the timing of onset of the reaction in relationship to the initiation of the medication;
- whether or not the reaction necessitated hospitalization;
- treatment(s) given for the reaction and response;
- whether or not the patient has taken the medication again since the prior reaction;
- whether or not any recurrent signs or symptoms occurred with subsequent drug exposure; and
- concurrent medications at the time that the reaction occurred and if any of these were newly started.

There are other classes of medications in addition to antibiotics that can cause hypersensitivity reactions, such as antiepileptics, antihypertensives, antiretrovirals, muscle relaxants, nonsteroidal anti-inflammatories, allopurinol, therapeutic foreign proteins, platinum-based chemotherapy, and opiates [16]. The patient's medical record should be reviewed to obtain any further details regarding the reported allergy, including any laboratory abnormalities present during the time of the reported event (ie, peripheral or urine eosinophilia, hematuria, etc). In some circumstances, patients reporting an allergy to an antibiotic medication may have actually experienced a nonallergic adverse effect. Examples may include gastrointestinal side effects caused by macrolides and tetracyclines or photosensitivity caused by tetracyclines.

Nevertheless, history alone is not always sufficient for establishing antibiotic hypersensitivity. Skin testing is a next step in the diagnostic process. However, it is important to note that there are comparatively few validated antibiotic skin test procedures available. Of these, penicillin testing has the longest history and is the most frequently used methodology. Penicillin skin testing can provide additional useful information regarding an individual's risk for a type I hypersensitivity reaction if exposed to the antimicrobial medication in question. Importantly, an evidence-based analysis including original studies describing the precision of skin testing in the diagnosis of penicillin allergy found that only 10%–20% of patients reporting this allergy were truly allergic. Patients with positive skin test results should undergo desensitization [28]; virtually all patients with negative penicillin skin tests results can take penicillin without serious sequelae [27].

If a patient with a reported allergy is deemed not allergic or if the allergy is simply an expected side effect, the medical record should be updated to reflect this change. Failure to do so may deprive the patient of receiving essential antibiotics when no allergy exists. Documentation of tolerance to a similar class or product (ie, penicillin-allergic patient able to tolerate cephalosporins) is also important. This documentation should stay with the patient across hospital admissions and outpatient records. This task may be best accomplished during medication reconciliation, but evaluation of allergy is an ongoing process.

The majority of deaths from anaphylaxis result from respiratory failure followed by cardiovascular compromise [29]. Maintenance of the airway and cardiovascular system comprise the critical foundation of anaphylaxis management. Epinephrine

should be administered immediately. Outside the healthcare setting, intramuscular epinephrine given in the anterior lateral thigh is the preferred route. If intravenous access is available, a bolus of epinephrine (0.2 μg/kg) should be given and followed by a low-dose infusion of a vasopressor such as norepinephrine titrated to a systolic blood pressure ≥90 mm Hg. Fluid administration with large volumes of crystalloids should occur concurrently with vasopressor infusion when the response to epinephrine is not immediate and sustained.

Secondary therapeutic modalities such as antihistamines and corticosteroids do not immediately support blood pressure or reduce inflammation, but are commonly included in anaphylaxis protocols. Antihistamines are useful for preventing or blunting angioedema or urticaria associated with IgE-mediated drug reactions. Simultaneous treatment with both an H_1 and an H_2 antagonist is recommended over a single agent for anaphylaxis [30]. Corticosteroids have little value in the acute phase of anaphylaxis, but they have well-known anti-inflammatory properties and are frequently included in anaphylaxis treatment algorithms because of their utility in preventing delayed anaphylactic reactions.

PRINCIPLES OF DESENSITIZATION

Classical desensitization protocols are designed to treat type 1 (IgE–mediated) mast cell reactions [31]. The typical request for drug desensitization may better be described as induction of drug tolerance without an adverse reaction [32]. This term more accurately reflects the diverse mechanisms that may be responsible for a specific drug reaction including IgE-mediated, non-IgE-mediated, and non-immune-mediated processes [16].

If an IgE-mediated sensitivity is established and the need for the drug confirmed, a standard desensitization protocol can be initiated. The goal of this procedure is described by some as controlled anaphylaxis—that is, the drug is administered at a concentration and rate that will cause drug-specific IgE-armed mast cells to degranulate at low rates that do not precipitate a systemic reaction. Serial doses of medication are gradually increased (usually doubled) for each administration (often at 15- to 20-minute intervals), and the number of IgE receptors on the mast cells are suppressed, which deceases the sensitivity of the mast cell to the point where a full dose of drug can ultimately be safely given. This defines a clinically tolerant state to the continued administration of the drug with little risk of a significant mast cell–mediated reaction during the course of therapy. It is critical to note that this procedure does *not* eliminate the IgE-mediated drug sensitivity; rather, it desensitizes the individual to allow him/her to receive the therapeutic course safely. Once desensitized, the patient usually does not react to administration of the drug for the duration of therapy. Once therapy is completed, the desensitized state will only last for up to 4 half-lives ($T_{½}$) of the drug. After that, sensitivity is assumed to have returned, and future therapeutic courses will require repeated desensitization protocols.

In cases where IgE-mediated sensitivity cannot be confirmed but the patient history strongly suggests that an immediate hypersensitivity state exists, drug allergy is assumed and the patient is subjected to a standard desensitization protocol [16]. In contrast, for cases where the history suggests that IgE-mediated hypersensitivity is not responsible for a previous reaction, a graded challenge protocol can be instituted [32]. A graded challenge is not intended to induce drug tolerance, and is designed primarily to demonstrate that administration of a specific drug will not result in an immediate reaction. A patient who tolerates a graded challenge without reaction can then be considered nonallergic, with a risk of future reaction no greater than the population at large.

There is further consideration to interpreting the results of a graded challenge. If the mechanism responsible for the reaction is a non-IgE-mediated or non–immune mediated, although there may be no initial reaction after the graded challenge, a delayed reaction (such as rash or other organ dysfunction) may still occur. This is why, in the initial assessment, establishing the temporal relationship between initial drug exposure and

Table 3. Sample Desensitization Protocol[a] for a 1-g Final Dose

Dose	Strength, mg	Volume, mL	Preparation Instructions
1	1	30	Add 29.75 mL D5W and 0.25 mL stock solution A[b] to empty 50-mL bag
2	2	30	Add 29.5 mL D5W and 0.5 mL stock solution A to empty 50-mL bag
3	4	30	Add 29 mL D5W and 1 mL stock solution A to empty 50-mL bag
4	8	30	Add 28 mL D5W and 2 mL stock solution A to empty 50-mL bag
5	16	30	Add 26 mL D5W and 4 mL stock solution A to empty 50-mL bag
6	32	30	Add 22 mL D5W and 8 mL stock solution A to empty 50-mL bag
7	64	30	Add 14 mL D5W and 16 mL stock solution A to empty 50-mL bag
8	128	50	Add 18 mL D5W and 32 mL stock solution A to empty 50-mL bag
9	250	50	Remove 2.5 mL from 50-mL D5W bag and add 2.5 mL of stock solution B[c]
10	500	50	Remove 5 mL from 50-mL D5W bag and add 5 mL of stock solution B
11	1000	50	Remove 10 mL from 50-mL D5W bag and add 10 mL of stock solution B

Administer first 10 doses over 15 minutes and last dose over 30 minutes.

[a] Supplies needed: eight 50-mL bags, three 50-mL D5W bags, stock solution A, stock solution B.

[b] Stock solution A: 4 mg/mL.

[c] Stock solution B: 100 mg/mL.

Table 4. Medication Desensitization Protocols

Medication	Concentration, mg/mL	Infusion Time	Interval Between Doses	Time to Complete	Dose Range, mg	Level of Evidence[a]	Final Dose
Ampicillin [33] IV	Not reported	Not reported	20 min	6 h	0.05–2000	IV	2000 mg
Cefepime [34] IV	0.04 2 20	5 min	15 min	4 h	0.032–2000	III	2000 mg
Ceftazidime [35] IV	0.1 1 2	15 min	15 min	2 d	0.025–2.5 6–307 0.5–586	I	Various
Ciprofloxacin [36] IV	0.1 1 2	10 min 20 min last dose	15 min		0.1–0.8 0.16–0.64 0.6–120	II	400 mg
Clarithromycin [37] oral	0.05 0.5 5 50	NA	15 min	5 h	0.005–0.2 0.4–3.2 6–24 50–500	III	500 mg
Clindamycin [38] oral	NA	NA	8 h	7 d	20–600	II	600 mg
Daptomycin [39] IV	Not reported	15 min	30 min	3 h	0.00035–350	II	350 mg
Imipenem [40] IV	0.0001 0.001 0.01 0.1 1	30 min	30 min	4 h	0.0003 0.01–0.03 0.1–0.3 1–3 10–21	II	1000 mg/d
Linezolid [41] oral	0.018–1.5	NA	30		0.0366–400	II	600 mg
Meropenem [42] IV	0.00008–20	20 min	20 min	5 h	0.004–1000	III	1000 mg
Penicillin [43] IV	0.1 1 10 100 1000	Unknown	15 min 30 min after last dose	9 h	0.01–0.08 0.16–0.64 1.2–4.8 10–80 160–640	I	1000 mg IV
Penicillin [43] oral	0.5 5 50	NA	15 min 30 min after last dose	4 h	0.05–3.2 6–24 50–400	I	1000 mg IV
TMP/SMX [43] oral	40 TMP/200 SMX per 5 mL	NA	1 h	5 h	0.04/0.02–160/800	I	160 mg/800 mg
Tobramycin [44] IV	0.0005–0.8	20 min	30 min	8 h	0.001–16	II	80 mg
Vancomycin [12] IV rapid	0.0002–2	Various	Continuous	4 h	0.02–500	I	Usual dose over 2 h
Vancomycin [12] IV slow	0.001–4	5 h	5 h	3 d	0.5–1000	I	1000 mg

Abbreviations: IV, intravenous; NA, not applicable; TMP/SMX, trimethoprim/sulfamethoxazole.

[a] I, desensitization successful in >1 patient with confirmed allergy to that medication; II, desensitization successful in 1 patient with confirmed allergy to that medication; III, desensitization successful in 1 patient with confirmed allergy to a medication in class; IV, desensitization successful in 1 patient without confirmed allergy.

first appearance of adverse clinical event is so important. As newer and more accurate techniques are developed to identify specific mechanism of antibiotic sensitivity, more specific and effective protocols will be developed to induce drug tolerance in susceptible patients.

Before beginning a desensitization procedure, several considerations must be reviewed to limit any major complications. The best clinical setting should be determined (office, medical ward, intensive care unit). The desensitization protocol should be reviewed with the pharmacist and nurse to ensure optimal creation of formulas and strict adherence to the schedule. The pharmacist should be aware that a dose may have to be remixed in the event of a dose failure. Adequate personnel should be available during the desensitization with the expectation that the process may take several hours or longer. Vital signs and adverse reactions should be monitored before and after each incremental dose. Medications for anaphylaxis should be immediately available, and some protocols advocate scheduling diphenhydramine throughout the desensitization with epinephrine at the bedside, whereas others recommend an intravenous

line, electrocardiography monitor, and spirometer. An adverse reaction does not necessarily require stopping the desensitization protocol and may proceed by repeating the last tolerable dose and rechallenging. Patients missing a dose may have to be desensitized again. A sample adaptable desensitization protocol is listed in Table 3, and medication-specific desensitization protocols are listed in Table 4 [12, 33–44].

CONCLUSIONS

Antibiotic allergy remains an important barrier in providing ideal care, and with fewer new antibiotics available on the market along with increasing antibiotic resistance, the chance of an allergy–treatment mismatch is increasing. Many patients with declared allergy may be given that medication after differentiating between allergy and intolerance. When a true drug allergy is highly likely based on history and skin testing (when available), desensitization protocols can be used to give the patient an antibiotic in the safest and most responsible manner possible. Fully understanding the mechanisms of allergy and engaging specialists in treatment further reduces risk.

Notes

Author contributions. Conception and design: D. P. L., C. A. M., E. S.; drafting of manuscript: D. P. L., C. A. M., E. S., G. D. M.; content oversight: E. S., G. D. M.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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