Management of Children with Hypersensitivity to Antibiotics and Monoclonal Antibodies

Allison Eaddy Norton, MD[a,*], Ana Dioun Broyles, MD[b,*]

KEYWORDS

• Pediatric drug allergy • Drug hypersensitivity • Allergy skin testing • Desensitization • Antibiotic allergy • Monoclonal allergy • Drug provocation

KEY POINTS

- Testing in young children should not be avoided because of parental or physician fear of testing because it has been confirmed to be safe.
- Accurate diagnosis for both antibiotic allergy and monoclonal antibody allergy leads to better workup and management of these allergies.
- The range of hypersensitivity reactions that occur in monoclonal antibody allergy overlaps with antibiotic allergy but is also distinctly different.
- Graded challenges are the gold standard in diagnosis and have been proven to be safe in children.
- Desensitization should only be pursued if there are no alternatives and is contraindicated in drug reactions with severe skin disease.

INTRODUCTION

Proper management of drug allergy in children is based on accurate diagnosis. Unfortunately, there is a lack of understanding of drug allergy in this population as well as provider or parental fear of testing children, which can lead to incomplete workup and misdiagnosis. Overlabeling in antibiotic allergy is a huge health burden and leads to drug-resistant bacteria.[1] Overdiagnosis is rather common in children, likely because

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[a] Division of Pediatric Pulmonary, Allergy and Immunology, Vanderbilt Children's Hospital, School of Medicine, 100 Oaks, 719 Thompson Lane, Nashville, TN 37204, USA; [b] Division of Allergy and Immunology, Boston Children's Hospital, Harvard Medical School, 300 Longwood Avenue, Boston, MA 02115, USA
* Corresponding authors.
E-mail addresses: Allison.norton@vanderbilt.edu (A.E.N.); ana.broyles@childrens.harvard.edu (A.D.B.)

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of the frequency of rashes that occur during an antibiotic course in a child and reluctance of testing to confirm allergy.[2,3] However, proper management should be based on a thorough history, in vitro testing (if available), in vivo testing, and if negative, drug challenge for delabeling because accurate diagnosis and management of the antibiotic allergic child are key factors in preventing children from carrying drug allergy labels that persist until adulthood.

It may also be difficult to determine the precise timing that a reaction begins in an infant or young child, making it challenging to ascertain immediate reactions from nonimmediate reactions. Distinguishing the type of reaction is important because the workup and management vary depending on the timing and associated symptoms of the reaction. In addition, providers often choose avoidance over testing in children, although intradermal testing and drug challenge have been proven to be safe and well tolerated in children.[4,5]

Monoclonal antibodies are proteins, of human or murine origin, increasingly used in oncologic and autoimmune diseases in children. Their larger protein structure, as opposed to the small chemical structures of antibiotics, promotes immunogenicity and can elicit hypersensitivity reactions.[6,7]

This article focuses on the workup, management, and treatment of pediatric antibiotic and monoclonal antibody allergy.

EPIDEMIOLOGY

It is difficult to obtain a true incidence of drug allergy in the pediatric population.[8] Epidemiologic studies indicate that drug allergy affects more than 10% of children and adolescents, although community studies suggest that this number is grossly overestimated.[2] When these children undergo diagnostic studies, including skin testing or drug provocation testing (DPT), less than 10% are confirmed to be truly allergic to the suspected drug.[4,9,10]

Penicillin allergy is the most commonly reported drug allergy, with a prevalence rate of 5% to 10% in adults and children.[11–14] Amoxicillin has now replaced benzyl penicillin as the most frequently reported drug allergy in children.[15] Non–beta-lactam (BL) allergy is rare in children and estimated to affect 1% to 3% of this population. In regards to the most commonly reported reactions to non-BL drugs, sulfonamides are the most commonly reported, followed by macrolides.[16]

In contrast to antibiotic allergy, monoclonal antibody allergy is infrequently reported in children and is limited to case reports and case series.[6,7,17–19]

GENERAL PRINCIPLES

The general principles of drug allergy are based on the classic mechanisms initially described by Gell and colleagues[20] in 1968 and updated by Pichler in 2003 to include subtypes IVa to IVd as demonstrated in **Table 1**.[20–23] However, as new approaches to drug allergy have emerged, an additional classification based on precision medicine has recently been proposed. This newer classification is based on phenotype, endotypes, and biomarkers in drug allergy.[24]

Phenotypes are determined by specific clinical symptoms associated with timing from exposure to the culprit drug. Phenotypes are divided into the following 2 broad categories:

- Immediate-onset drug allergy: occurs within 1 to 6 hours of exposure to the drug and is associated with cutaneous, respiratory, gastrointestinal symptoms, or anaphylaxis.