



SPANISH ASSOCIATION OF PAEDIATRICS

**Spanish Society of Paediatric Infectious Diseases,  
Spanish Society of Paediatric Clinical Immunology and  
Allergy, Spanish Association of Paediatric Primary  
Care, and the Spanish Society of Extra-hospital  
Paediatrics and Primary Health Care consensus  
document on antibiotic treatment in penicillin or  
amoxicillin allergy<sup>☆</sup>**

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**KEYWORDS**

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**Abstract** The suspected allergy to beta-lactam antibiotics, especially penicillin and amoxicillin, is the most frequent reason for consultation in Child Allergy Units. In this consensus document, the clinical and diagnostic criteria of allergic reactions are described, as well as alternative antibiotic treatment for the most common infections diagnosed in paediatrics for patients with known or suspected allergy.

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**PALABRAS CLAVE**

Alergia;  
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Tratamiento

**Documento de consenso de la Sociedad Española de Infectología Pediátrica, Sociedad Española de Inmunología Clínica y Alergia Pediátricas, Asociación Española de Pediatría de Atención Primaria y Sociedad Española de Pediatría Extrahospitalaria y Atención Primaria sobre antibioterapia en alergia a penicilina o amoxicilina**

**Resumen** La sospecha de alergia a antibióticos betalactámicos, especialmente penicilina y sobre todo amoxicilina, suponen el motivo de consulta más frecuente en las Unidades de Alergia Infantil. En este documento de consenso se describe la clínica y los criterios diagnósticos de las reacciones alérgicas, así como el tratamiento antibiótico alternativo de las infecciones más habituales en pediatría, para los pacientes con sospecha diagnóstica o confirmación de la alergia.

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## Introduction

Beta-lactam antibiotics account for approximately 80% of visits to paediatric specialty clinics due to allergies to medication. Penicillins are the most frequent family involved, of which aminopenicillins (amoxicillin) are currently the leading group.<sup>1-3</sup>

The prevalence of self-reported beta-lactam allergy in children ranges from 1.7% to 5.2%,<sup>4,5</sup> although only a minority of these children (<20%) receive an actual diagnosis of allergy.<sup>6</sup> Anaphylactic reactions occur in 0.01–0.05% of the population, and they are rare and usually less severe in children.<sup>1</sup>

When penicillin is metabolised, different allergenic determinants are released, such as benzylpenicilloyl (95% of the total), which is the major determinant and is responsible for most allergic reactions, and minor determinants that cause a minority of reactions, which can nevertheless be just as severe.<sup>2,3</sup>

Semisynthetic penicillins (ampicillin, amoxicillin) also produce unique antigenic determinants located in their side-chains.<sup>1,2</sup>

The most frequent reactions are selective responses to amoxicillin (its side chain) in the absence of penicillin allergy. When the allergic reaction occurs in response to the major determinant of penicillin, all penicillins are involved.<sup>7</sup>

## Suspicion of beta-lactam allergy

Immediate allergic reactions, which manifest with urticaria, angioedema, bronchospasm or laryngeal oedema within an hour from antibiotic administration, are easy to recognise. However, many reactions may be delayed (occurring hours or days after administration) and present only with nonpruritic maculopapular or morbilliform rashes.<sup>1</sup>

The prevalence of viral infections that cause rashes is high in children, so it is important to differentiate between these two conditions. They are most commonly confused in cases of roseola (which may present with maculopapular rash or hives, or even with eyelid oedema [Berliner sign]), infectious mononucleosis (due to the frequent development

of bilateral eyelid oedema and of rash following administration of amoxicillin) and infectious urticaria. The rational use of antibiotics, avoiding their administration in cases of fever without source or pharyngotonsillitis with negative results in the rapid test for streptococcus, is the best strategy to avoid such confusions. Adverse reactions that are not immune-mediated, such as vomiting or diarrhoea developed during treatment, should not be considered allergic reactions.

Taking an accurate history is of the essence when allergy to penicillin or amoxicillin is suspected, with a thorough investigation of the clinical manifestations, the time elapsed since antibiotic administration, and the previous use of the drug or other drugs with a similar antigenic structure. The child (regardless of age) must be referred to the allergy clinic.

During the evaluation, the suspected drug and other drugs with which it may be cross-reactive will be avoided.<sup>1-3,7</sup> The suspected allergy to the involved drug must be visibly noted in the chart of the patient, removing the flag once it is ruled out.<sup>8</sup>

## Types of reactions

At present, reactions are classified into immediate and non-immediate<sup>1-3,9-11</sup> for the purposes of clinical assessment and determining the underlying mechanism (Table 1).

*Immediate reactions:* develop immediately following antibiotic use, generally within an hour. They are IgE-mediated reactions, can progress rapidly, are potentially fatal and tend to increase in severity with repeated exposure.<sup>1</sup> They include urticaria, angioedema and anaphylaxis with its most severe features (laryngeal oedema, bronchospasm and hypotension).

*Non-immediate reactions:* they develop after a variable period of time that ranges between hours and days. They include accelerated reactions (>1 to <72 h) and delayed reactions (days to weeks), and manifest with urticaria and rashes that are usually not IgE-mediated and more rarely with severe presentations such as Stevens–Johnson syndrome, toxic epidermal necrolysis (TEN) or drug reaction with eosinophilia and systemic symptoms (DRESS). Other

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