

Biphasic Anaphylaxis: How Long Must Patients Be Observed?

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Anaphylaxis remains a life-threatening, systemic hypersensitivity reaction that demands immediate recognition and treatment. But the acute management is only part of the challenge; clinicians must also contend with the risk of biphasic reactions, a recurrence of symptoms after initial resolution without further allergen exposure. This phenomenon complicates discharge decisions and dictates observation periods, a practice that varies widely across institutions and specialties.

The duration of observation after an acute anaphylactic episode is a persistent clinical question, balancing patient safety against resource utilization. Current guidelines offer recommendations, but the underlying evidence for these periods, particularly concerning biphasic reactions, warrants a deeper examination.

KEY TAKEAWAYS

- **The Pivot:** The risk of biphasic anaphylaxis necessitates careful consideration of observation periods, which are often longer than for other acute allergic reactions.
- **The Data:** While specific rates vary, biphasic reactions can occur hours after initial symptom resolution, particularly in severe initial presentations.
- **The Action:** Clinicians should individualize observation periods based on initial reaction severity, patient comorbidities, and the specific allergen, rather than adhering to a rigid, universal timeframe.

Anaphylaxis is a severe, potentially fatal systemic hypersensitivity reaction, characterized by its rapid onset and life-threatening airway, breathing, or circulatory problems. The immediate treatment involves intramuscular adrenaline, often supplemented with antihistamines and corticosteroids. But the complexity extends beyond the initial resuscitation; a significant concern is the potential for a biphasic reaction, where symptoms recur hours after the initial episode has resolved and without re-exposure to the trigger. This phenomenon is not merely an academic curiosity; it directly impacts patient safety and the judicious use of emergency department resources.

The mechanism behind biphasic anaphylaxis is not fully elucidated, but it is thought to involve the delayed release of mediators from mast cells and basophils, or a prolonged effect of initial mediator release. Factors associated with an increased risk of biphasic reactions include a more severe initial anaphylactic episode, a slower response to initial treatment, and certain triggers, such as food allergens or venom. The challenge for clinicians lies in identifying which patients are at highest risk and, consequently, how long they should be observed in a clinical setting before discharge.

Defining the Risk of Recurrence

The incidence of biphasic anaphylaxis varies considerably in the literature, with reported rates ranging from 1% to 20%. This wide range reflects differences in study populations, diagnostic criteria for anaphylaxis, definitions of biphasic reactions, and observation protocols. Some studies define a biphasic reaction as any recurrence of symptoms within 72 hours, while others focus on a shorter window, typically 4 to 12 hours. The lack of a universally accepted definition complicates direct comparisons across studies and contributes to the variability in clinical practice.

The clinical presentation of a biphasic reaction can range from mild, self-limiting symptoms to a full-blown, life-threatening recurrence requiring further adrenaline. This unpredictability is a primary driver for extended observation periods. Patients who experience a severe initial reaction, particularly those requiring multiple doses of adrenaline or presenting with hypotension or respiratory compromise, are generally considered to be at higher risk for a biphasic event. The type of allergen also plays a role; food-induced anaphylaxis, for example, has been associated with a higher risk of biphasic reactions compared to drug-induced anaphylaxis.

Observation Period Recommendations

Current guidelines from various professional bodies offer recommendations for observation periods, but these are often based on expert consensus rather than robust, randomized controlled trials. The European Academy of Allergy and Clinical Immunology (EAACI) and the World Allergy Organization (WAO) generally recommend an observation period of 6 to 8 hours for most patients after an acute anaphylactic episode. For patients with more severe initial reactions, particularly those with respiratory or cardiovascular compromise, an observation period of 12 to 24 hours, or even admission to hospital, is often advised.

The rationale for these extended periods is to ensure that any recurrence of symptoms can be promptly identified and treated. But the practical implications are substantial, particularly for emergency departments already struggling with overcrowding and resource constraints. A blanket 8-hour observation for all anaphylaxis patients places a significant burden on healthcare systems, especially if a substantial proportion of these patients would not, in fact, experience a biphasic reaction. This highlights the need for better risk stratification tools to identify those who truly benefit from prolonged observation.

Factors Influencing Biphasic Risk

Several factors have been identified as potential predictors of biphasic anaphylaxis. These include the severity of the initial reaction, as measured by the need for multiple adrenaline doses, the presence of hypotension, or severe respiratory distress. Patients with a history of asthma or other atopic conditions may also be at increased risk, although the evidence for this is not universally consistent. The route of allergen exposure can also be a factor; parenteral exposure, such as from insect stings or injected medications, may lead to a more rapid and severe initial reaction, but oral exposure, particularly to food allergens, can sometimes be associated with a delayed or biphasic response.

The time to onset of the initial reaction also appears to be relevant. Rapid onset of symptoms after allergen exposure may indicate a more severe reaction and potentially a higher risk of biphasic events. Conversely, a slower onset might suggest a less aggressive initial response, but this does not necessarily preclude a biphasic reaction. The complex relationship of these factors makes a simple, one-size-fits-all approach to observation periods problematic. Clinicians must synthesize multiple pieces of information to make an informed decision for each patient. For a comprehensive overview of general

clinical practice, the Oxford Handbook of General Practice, 5th Edition, offers practical guidance on managing acute presentations.

The Challenge of Risk Stratification

Developing reliable risk stratification tools for biphasic anaphylaxis remains an unmet need. While several scoring systems and algorithms have been proposed, none have achieved widespread clinical adoption due to limitations in validation or generalizability. These tools often incorporate variables such as initial reaction severity, allergen type, and patient comorbidities. But the predictive power of these models is often modest, meaning they may not accurately identify all patients at risk or, conversely, may lead to unnecessary prolonged observation for low-risk individuals.

The absence of a definitive biomarker for biphasic reactions further complicates risk assessment. Tryptase levels, while useful for confirming anaphylaxis, do not reliably predict a biphasic course. Research continues into other potential biomarkers, but none are currently available for routine clinical use to guide observation periods. This leaves clinicians relying on clinical judgment, which, while valuable, can be inconsistent across different practitioners and settings. This is particularly relevant in pediatric populations, where the presentation can be subtle and the risk of biphasic reactions may differ. Our previous coverage explored a model identifying anaphylaxis kids who can skip the ED, highlighting the ongoing efforts to refine risk assessment in this vulnerable group.

Practical Considerations for Observation

In practice, the decision to observe a patient for an extended period after anaphylaxis involves a careful balance of clinical factors and available resources. For patients with mild initial reactions that respond quickly to a single dose of adrenaline, a shorter observation period, perhaps 4 to 6 hours, may be appropriate. But if there is any doubt, or if the patient has significant comorbidities such as cardiovascular disease or poorly controlled asthma, a longer observation is prudent. The presence of ongoing symptoms, even if mild, should also prompt extended monitoring.

Discharge planning must include clear instructions for patients and their families, including education on recognizing recurrent symptoms and the proper use of an adrenaline auto-injector. Patients should be advised to avoid the identified allergen and to seek prompt medical attention if symptoms recur. The importance of follow-up with an allergist or immunologist cannot be overstated, as this allows for definitive diagnosis, allergen identification, and development of a long-term management plan, including prescription of additional auto-injectors and education on avoidance strategies. This comprehensive approach is vital for preventing future episodes and managing the long-term implications of severe allergic reactions. The role of allergen immunotherapy in modifying disease trajectory in other allergic conditions underscores the importance of specialized follow-up.

The lack of a definitive consensus on observation periods for biphasic anaphylaxis highlights a gap in the evidence base. While guidelines provide a framework, the individual patient's clinical presentation, risk factors, and response to initial treatment must guide the decision-making process. Future research needs to focus on developing and validating more precise risk stratification tools and biomarkers to optimize observation periods, ensuring patient safety without unduly burdening healthcare systems. Until then, a cautious, individualized approach remains the standard of care.

CLINICAL IMPLICATIONS

The persistent uncertainty surrounding optimal observation periods for biphasic anaphylaxis places clinicians in a difficult position. Balancing the rare but serious risk of recurrence against the practical realities of emergency department flow demands a careful approach. A rigid 8-hour rule for every anaphylaxis patient, regardless of initial severity, is neither efficient nor always necessary.

Instead, the focus must shift to individualized risk assessment. Patients presenting with severe initial reactions, particularly those requiring multiple adrenaline doses or exhibiting cardiovascular compromise, clearly warrant extended observation, perhaps 12 to 24 hours. But for those with mild, rapidly resolving symptoms, a shorter period may be acceptable, provided robust discharge education is given.

The industry has a role to play in developing better predictive tools. Without reliable biomarkers or validated scoring systems, clinicians are left to rely on clinical judgment, which, while valuable, is inherently subjective. Investment in research to identify objective markers for biphasic risk would significantly improve patient management and resource allocation.

For patients, this means understanding that even after initial symptom resolution, the threat of recurrence is real. Clear, concise instructions on recognizing biphasic symptoms and immediate access to an adrenaline auto-injector are paramount. The onus is on us, as clinicians, to communicate this risk effectively and ensure they are equipped to act.

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