Rostrum

Anaphylaxis: Unique aspects of clinical diagnosis and management in infants (birth to age 2 years)

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In this rostrum we aim to increase awareness of anaphylaxis in infancy in order to improve clinical diagnosis, management, and prevention of recurrences. Anaphylaxis is increasingly reported in this age group. Foods are the most common triggers. Presentation typically involves the skin (generalized urticaria), the respiratory tract (cough, wheeze, stridor, and dyspnea), and/or the gastrointestinal tract (persistent vomiting). Tryptase levels are seldom increased because of infant anaphylaxis, although baseline tryptase levels can be increased in the first few months of life, reflecting mast cell burden in the developing immune system. The differential diagnosis of infant anaphylaxis includes consideration of age-unique entities, such as food protein–induced enterocolitis syndrome with acute presentation. Epinephrine (adrenaline) treatment is underused in health care and community settings. No epinephrine autoinjectors contain an optimal dose for infants weighing 10 kg or less. After treatment of an anaphylactic episode, follow-up with a physician, preferably an allergy/immunology specialist, is important for confirmation of anaphylaxis triggers and prevention of recurrences through avoidance of confirmed specific triggers. Natural desensitization to milk and egg can occur. Future research should include validation of the clinical criteria for anaphylaxis diagnosis in infants, prospective longitudinal monitoring of baseline serum tryptase levels in healthy and atopic infants during the first year of life, studies of infant comorbidities and cofactors that increase the risk of severe anaphylaxis, development of autoinjectors containing a 0.1-mg epinephrine dose suitable for infants, and inclusion of infants in prospective studies of immune modulation to prevent anaphylaxis recurrences. (J Allergy Clin Immunol 2014;■■■:■■■-■■■.)

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Anaphylaxis is defined as a serious generalized allergic or hypersensitivity reaction that is rapid in onset and might cause death. It typically occurs minutes to a few hours after exposure to the trigger and involves 2 or more body organ systems. This definition applies to patients of all ages regardless of the anaphylaxis trigger (cause, inducer) or mechanism (IgE-mediated, other immunologic mechanisms, or direct mast cell activation). We focus here on the infant phenotype of anaphylaxis (birth to age 2 years), with the goals of increasing awareness of anaphylaxis in this age group and improving clinical diagnosis, management, and prevention of recurrences.[1-3]

The true prevalence of anaphylaxis in infancy is unknown. Although it remains underdiagnosed and undercoded in this population, it is reported with increasing frequency, even in newborns. In epidemiologic studies and pediatric case series, atopic infants and boys predominate, and many episodes occur in the home. Death can occur; however, the case fatality rate in hospitalized patients is low.[4-9]

RISK FACTORS AND TRIGGERS

Comorbidities that increase the risk of severe anaphylaxis, although not well defined in infants, potentially include croup, bronchiolitis, asthma, and cutaneous mastocytosis with extensive (>90%) skin involvement and/or blistering of the skin. Cofactors that amplify anaphylaxis, although also not well defined in infants, potentially include upper respiratory tract infection, fever, exertion, and emotional stress. Additionally, delayed recognition of first or subsequent episodes because of caregiver lack of awareness, depression, or substance abuse might be relevant.[3,5-11]

Anaphylaxis in infants can be triggered by a variety of agents, of which foods are by far the most common. Typical culprits are cow's milk, egg, and peanut, but any food can be implicated, including tree nuts, soy and other legumes, fish, vegetables, fruits, and grains, such as wheat and rice. Food-induced anaphylaxis can occur after direct ingestion or indirect ingestion through breast milk; rarely, it is triggered by skin contact with food or vomitus, or inhalation of vapors from cooking food.[1,3,5-9,12,13]

Drug triggers include penicillins and other antibiotics, ibuprofen and other antipyretics, and neuromuscular blockers. In infants, insect stings and bites are more likely to trigger large local reactions or urticaria than anaphylaxis. Natural rubber latex remains a potential trigger in health care and community settings, where it is found in bottle nipples, pacifiers, teethers, and toys. Vaccinations to prevent infectious diseases; topical agents, including soaps and creams; and nonimmune triggers, such as

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Abbreviations used
EAI: Epinephrine autoinjector
RCT: Randomized controlled trial

cold exposure, are uncommon triggers. In infants with apparent idiopathic anaphylaxis, novel allergens and antigens, and the possibility of a mast cell activation syndrome, should be considered.[1,3,5-10,12-14]

DIAGNOSIS OF ANAPHYLAXIS

A high index of suspicion is needed to recognize and diagnose anaphylaxis promptly in infants.[3,7-9]

Clinical criteria for diagnosis

Clinical criteria for diagnosis of anaphylaxis have been developed and validated for use in emergency departments and other health care settings and in epidemiologic studies, although not specifically for use in this age group (Fig 1).[2]

Infants cannot describe symptoms, such as pruritus, throat tightness, or feeling of impending doom. Some potential signs of anaphylaxis can be difficult to interpret because they also occur in healthy infants; examples include behavioral changes, such as irritability, clinging to a caregiver, inconsolable crying, and somnolence, as well as flushing, dysphonia, drooling, regurgitation, and incontinence of urine and stool. Vital signs should be recorded and interpreted by using age-specific reference ranges (rapid resting respiratory rate, rapid resting heart rate, and low baseline blood pressure in comparison with children). Oxygen saturation should be measured by using pulse oximetry.[1,3]

The initial presentation of anaphylaxis in infants typically involves the following organ systems: skin and subcutaneous tissue in 98% (95% CI, 94% to 100%), the respiratory system in 59% (95% CI, 47% to 71%), and the gastrointestinal system in 56% (95% CI, 44% to 67%).[8] Cardiovascular signs are seldom reported; however, blood pressure is not always documented. In one study only 6% of the infants who met the clinical criteria for diagnosis of anaphylaxis were assigned an emergency department discharge term that included the term "anaphylaxis."[8]

Differential diagnosis

Congenital abnormalities of the respiratory or gastrointestinal tracts, an apparent life-threatening event, aspiration of a foreign body, food protein–induced enterocolitis syndrome with acute presentation, and intussusception are important considerations in the differential diagnosis of anaphylaxis in infants (Table I).[3]

Laboratory confirmation of the clinical diagnosis

The standardized assay for mast cell total tryptase is widely available in clinical laboratories, although not performed on an emergency basis. Tryptase levels are seldom increased in patients with food-induced anaphylaxis, even in optimally timed blood samples obtained 15 minutes to 3 hours after symptom onset. In young infants interpretation of serum tryptase levels presents additional complexities because their baseline levels can be increased, reflecting mast cell burden in the developing immune system. Median baseline levels of 14.2 ± 10.2 μg/L in atopic infants and 6.13 ± 3.47 μg/L in healthy infants have been reported before age 3 months, after which they gradually decrease and reach the normal reference range (3.85 ± 1.8 μg/L) by age 9 to 12 months.[1,15,16]

INITIAL TREATMENT OF ANAPHYLAXIS

A high level of preparedness, including a written protocol, is important because life-saving initial treatment needs to be started promptly. Remove any suspected relevant trigger. Rapidly assess circulation, airway, breathing, skin, and body weight (Fig 2). Without delay, call to request help from a resuscitation team in health care settings or from emergency medical services in community settings. Place the infant supine or semireclining in a position of comfort in the caregiver's arms. Inject epinephrine (adrenaline) intramuscularly in the mid-outer thigh in a dose of 0.01 mg/kg in health care settings. Use an epinephrine autoinjector (EAI; 0.15 mg) in community settings.[1-3,13,17-19]

When indicated at any time, provide high-flow supplemental oxygen (8-10 L/min) through a tightly fitting infant face mask. Establish intravenous access and start fluid resuscitation with 0.9% saline, initially at a dose of 10 to 20 mL/kg over 5 to 10 minutes. Begin continuous electronic monitoring of respiratory rate, heart rate, and blood pressure with an appropriately sized blood pressure cuff and monitor oxygenation by using pulse oximetry.[1-3,13] When indicated, start cardiopulmonary resuscitation with chest compressions at a rate of 100 per minute and a depth of 4 cm with minimal interruptions and start rescue breaths at a rate of 15 to 20 per minute.[1]

Antihistamines and glucocorticoids are commonly given; however, these medications should not be used as initial treatment or as monotherapy because they do not rapidly reverse laryngeal edema, bronchospasm, or hypotension.[1,2,20-22] Biphasic anaphylaxis can occur in infants.[23] Recommendations for pharmacologic treatment of anaphylaxis in this age group are extrapolated from recommendations for treatment of anaphylaxis in older patients.[1,2,17,20-22]

Infants who do not respond to initial anaphylaxis treatment should, if possible, be transferred promptly to the care of a pediatric emergency medicine team that is trained, experienced, and equipped to provide skilled airway management and ventilation, and optimal shock management guided by continuous electronic monitoring of respiratory and cardiovascular outcomes.[1]

MANAGEMENT AFTER RESOLUTION OF AN ANAPHYLACTIC EPISODE

Long-term management focuses on treatment and prevention of anaphylaxis recurrences in community settings. The importance of follow-up with a physician, preferably an allergy/immunology specialist, should be emphasized (Fig 3).[1,12,13,17-34]

Management at discharge after treatment of anaphylaxis in a health care setting

Caregivers should be trained how to recognize anaphylaxis and inject 0.15 mg of epinephrine in the mid-outer thigh with an EAI.[1-3,12,13,24-27] A personalized written anaphylaxis emergency action plan that lists common symptoms and signs of anaphylaxis in infants and outlines prompt initial treatment should be provided.