Management of Apparent Life-Threatening Events in Infants: A Systematic Review

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Objective To determine in patients who are well-appearing and without a clear etiology after an apparent life-threatening event (ALTE): (1) What historical and physical examination features suggest that a child is at risk for a future adverse event and/or serious underlying diagnosis and would, therefore, benefit from testing or hospitalization? and (2) What testing is indicated on presentation and during hospitalization?

Study design Systematic review of clinical studies, excluding case reports, published from 1970 through 2011 identified using key words for ALTE.

Results The final analysis was based on 37 studies; 18 prospective observational, 19 retrospective observational. None of the studies provided sufficient evidence to fully address the clinical questions. Risk factors identified from historical and physical examination features included a history of prematurity, multiple ALTEs, and suspected child maltreatment. Routine screening tests for gastroesophageal reflux, meningitis, bacteremia, and seizures are low yield in infants without historical risk factors or suggestive physical examination findings.

Conclusion Some historical and physical examination features can be used to identify risk in infants who are well-appearing and without a clear etiology at presentation, and testing tailored to these risks may be of value. The true risk of a subsequent event or underlying disorder cannot be ascertained. A more precise definition of an ALTE is needed and further research is warranted. *(J Pediatr 2013;163:94-9)*.

An apparent life-threatening event (ALTE) was defined at a consensus development conference convened in 1986 by the National Institutes of Health to address the relationship between sudden infant death syndrome (SIDS) and apnea.[1] An ALTE was defined as "an episode that is frightening to the observer and that is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging."

There are three significant challenges for clinicians managing patients who have experienced an ALTE. First, the infant is often asymptomatic at presentation. Second, although most ALTEs represent a benign event, they can signify a more serious illness, such as sepsis or child maltreatment. Third, the decision to perform tests or hospitalize a patient is fraught with uncertainties. Clinicians may hospitalize the infant to facilitate observation, educate the parents, or complete tests. Yet, this approach may subject the patient to unnecessary risk and increase parental anxiety without improving outcomes.[2,3]

Given a lack of consensus regarding the management of infants who are initially well-appearing and without a clear etiology, an ALTE expert panel systematically reviewed the literature to answer two key questions: (1) What historical and physical examination features on presentation suggest that an infant is at risk for a future adverse event and/or serious underlying diagnosis and would therefore benefit from diagnostic testing and hospitalization? and (2) What testing is indicated on presentation and during hospitalization?

ALTE	Apparent life-threatening event
ED	Emergency department
EEG	Electroencephalogram
GER	Gastroesophageal reflux
RR	Relative risk
SIDS	Sudden infant death syndrome
URI	Upper respiratory tract

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Methods

Pertinent articles were identified using the stepwise approach specified in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.[4] PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Cochrane Library databases were searched to identify articles published in the English-language from January 1970 through May 2011 that addressed ALTEs in children less than 24 months of age. We conducted keyword searches to identify articles with at least one of the following terms in the title or abstract: *ALTE, apparent life-threatening event, life-threatening event, near-miss sudden infant death syndrome, near-miss SIDS, aborted sudden infant death syndrome, aborted SIDS, aborted crib death,* or *aborted cot death*. Additional articles were identified by examining the cited references of review articles published between January 2000 and December 2010.

Next, at least 2 reviewers independently scored abstracts (on a Likert scale) for relevance to the clinical questions using a validated methodology.[5,6] Then two independent reviewers critically appraised the full text of the identified article using a structured data collection form based on published guidelines for evaluation of the medical literature and recorded the study's relevance to the given clinical question, research design, setting, time period covered, sample size, patient eligibility criteria, data source, variables collected, key results, study limitations, potential sources of bias, and stated conclusions.[7,8] If at least 1 reviewer judged an article to be relevant based on the full text, then 2 reviewers critically appraised the article and determined by consensus what evidence, if any, should be cited in the systematic review. The lead author or another panel member served as third reviewer to resolve disagreements. The search initially identified 1388 articles, of which 1351 were systematically excluded.

Results

The review identified 37 studies. Fourteen studies investigated historical and physical examination features as potential indications for hospitalization or predictors of subsequent adverse events (**Table I**; available at www.jpeds.com). These studies evaluated age, sex, ethnicity, history of prematurity, occurrence of multiple ALTEs, concern for child maltreatment, concern for seizures, presence of upper respiratory tract (URI) symptoms, smoke exposure, severity of the ALTE event or need for cardiopulmonary resuscitation, prior diagnosis of gastroesophageal reflux (GER) or GER symptoms, birth order, and mode of delivery. Thirty-one studies evaluated diagnostic testing for GER, neurologic abnormalities, anemia, infections, toxic ingestions, metabolic disorders, and cardiac dysrhythmias (**Table II**; available at www.jpeds.com). All studies used an observational cohort design and only 4 studies used valid control groups. None of the studies completely addressed the clinical questions because of methodologic limitations. These included insufficient samples sizes to detect rare events and limited generalizability of findings when patients were recruited from high risk referral centers. Heterogeneous outcomes and follow-up periods across different studies made it difficult to pool results.

Predictors from History and Physical Examination

Age and Prematurity. Five studies investigated the relationship between chronological age and a subsequent adverse event or a significant diagnosis following presentation to an emergency department (ED), and their findings conflicted (**Table I**). Two studies found younger age to be associated with higher risk. In 1 study, infants under 30 days of age and greater than 30 weeks gestational age were more likely (OR 3.3; $P = .13$) to have a recurrent ALTE or serious diagnosis during the hospitalization or within 48 hours after discharge from the ED.[9] In another study, hospitalized infants less than 43 weeks post-conceptual age were more likely to have a subsequent event (relative risk [RR] 5.2; 95% CI 2.6-10.3) during the course of a hospitalization.[10] In contrast, two studies with different study populations found younger age to be associated with lower risk. In 1 study of infants under 6 months presenting with 1 or more ALTE features (including some patients on home monitoring), those under 2 months old were less likely to experience a recurrent ALTE during hospitalization (RR = 0.12; 95% CI, 0.03-0.52).[11] In another study of infants under 1 year of age and including some with an abnormal physical exam, age over 2 months was associated with higher risk for recurrent ALTE (RR 2.9; 95% CI, 1.3-6.8).[12] Finally, in another study with a 5-year follow-up period, age was not associated with child abuse, adverse neurologic outcome, or chronic epilepsy.[13]

Four studies identified a history of prematurity as a risk factor for subsequent ALTEs or a serious underlying diagnosis. The first reported an OR of 14 ($P = .009$),[9] and the 2 remaining studies reported RRs of 2.95 (95% CI, 1.0-8.7)[11] and 6.3 (95% CI, 3.6-11),[10] respectively, and the last 1 reporting risk attenuation at 48 weeks post-conceptual age.

Multiple ALTEs. Many studies report higher rates of underlying disorders in patients with multiple ALTEs (eg, child maltreatment and seizures), either occurring in clusters and/or recurring after discharge.[10-15] One study evaluated the risk conferred alone by a history of multiple ALTEs occurring during the 24 hours preceding ED presentation, and it demonstrated an increased likelihood (OR 4.0; $P < .001$) of recurrent ALTE or serious diagnosis during the hospitalization or within 48 hours after discharge from the ED.[9]

Suspected Child Maltreatment. Child maltreatment was reported in 0.4%-11% of well-appearing infants presenting to an ED or admitted to the hospital after an ALTE.[13,14,16-18] Documented types of child maltreatment reported to cause an ALTE included intentional smothering, intentional poisoning, non-accidental head trauma, other inflicted physical injury, emotional abuse, induced illness, and Munchausen

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