Apparent Life-Threatening Events in Children: Practical Evaluation and Management

Abstract

Apparent life-threatening events account for 0.6% to 0.8% of all emergency department visits for children aged <1 year. Risk factors for serious underlying pathology in a well-appearing infant have been identified as prematurity, underlying medical conditions, age <60 days (considered controversial), suspicion of child abuse, possible seizure activity, and recurrent apparent life-threatening events. A detailed history and physical examination is crucial for the management of these patients. Targeted testing is warranted, as there is little evidence to support routine testing. A period of inpatient observation is often appropriate, as well. This review seeks to: (1) present factors that may place a patient at higher risk for serious underlying disease and/or a future adverse event requiring intervention; (2) provide guidance on taking a thorough history; and (3) describe guidelines for diagnostic testing and admission to the hospital for infants with an apparent life-threatening event.
Case Presentations

A worried mother brings her previously healthy 6-month-old boy in to the ED after he began crying, turned red, and spit up his milk while he was breastfeeding. She feels that he stopped breathing for possibly 5 to 10 seconds when he turned red. During the episode, he was in her arms and, after she patted him on his back, he began to behave normally again. The mother tells you that he has had congestion and a runny nose for the past 2 days, but has not had any fever. He was born at term via a normal vaginal delivery after an uncomplicated pregnancy, and has received all vaccinations to date. The patient’s vital signs and examination are normal, and he appears well and is playful. Several questions run through your mind as you consider what steps to take next with this patient: Does this episode meet criteria for an ALTE? Is any workup necessary for this patient? Does the patient need to be observed in the hospital, or can he be safely discharged home with follow-up?

An ambulance then brings in a 6-week-old infant who had “turned blue” while she was sleeping in her mother’s arms. The mother felt her go limp and noticed that she turned blue around her mouth. She rubbed her back and tried to rouse her, and the infant responded after approximately 10 seconds. When EMS arrived, the patient was awake and alert with a normal initial examination. You place the patient on a monitor, and, after a quick assessment, she appears stable. You then gather more history from the mother. The baby was born prematurely at 35 weeks gestation, but delivered vaginally without complications. She was in the newborn nursery and discharged home in her parents’ care 2 days later. She is formula-fed and has been growing well. The mother denies any recent fever or URI symptoms, but states that this same incident occurred 1 week ago while the baby was sleeping, but she had returned to baseline much faster, so the parents did not seek medical care. The parents are the sole caregivers, and this is their first child. The infant is behaving normally in the ED, and vital signs and physical examination are normal. Again, you wonder whether this patient meets the criteria for an ALTE. What kind of workup does this patient need, if any? Does she need be observed in the hospital, or can she be safely discharged home with follow-up?

Introduction

In 1986, the National Institutes of Health Consensus Development Conference on Infantile Apnea and Home Monitoring defined an apparent life-threatening event (ALTE) 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), and choking or gagging. In some cases, the observer feels that the infant has died.”1 Infant apnea is defined by the American Academy of Pediatrics (AAP) as an unexplained episode of cessation of breathing for ≥ 20 seconds, or a shorter respiratory pause associated with bradycardia, cyanosis, pallor, and/or marked hypotonia.2 These definitions leave much to interpretation by the clinician, and assessment of the infant is further confounded by the inherently unreliable history of observers of the incident, who are often so distraught that they are unable to recall the event clearly. Therefore, timing of the event is often inaccurate. The AAP is currently developing a guideline to streamline the definition and workup for ALTE, and it is anticipated to be available in the next few years. The incidence of ALTEs has been described in population-based studies as 0.6 to 2.46 per 1000 live births and accounts for 0.6% to 0.8% of all emergency department (ED) visits for children aged < 1 year.3 This may be an underestimation, however, since ALTEs are inconsistently reported, and ALTE is not a billable diagnosis. Additionally, when an underlying etiology is found, often that is the only diagnosis noted in the medical records or diagnosis-related databases.

There are several challenges facing clinicians when evaluating these patients in the ED. While most ALTEs are a presentation of a benign event, there is concern by the emergency clinician that this may represent the rare instance of a serious condition. After experiencing an ALTE, infants will often be asymptomatic and well-appearing in the ED. The necessity for performing diagnostic testing and/or hospitalizing these patients for observation may not always be clear. These patients are often subjected to extensive and, at times, unnecessary testing and treatment, which may incur high stress and cost to the family.4 At present, there is no standard recommended approach to the ED evaluation of infants with ALTEs, and limited clinical trials exist examining such outcomes. Recent clinical decision rules have been developed; however, they remain to be validated.5,6

Critical Appraisal Of The Literature

A systematic search of the literature from January 1988 to April 2013 was undertaken using PubMed and the Cochrane database. The search was performed using the terms apparent life-threatening event, ALTE, near-miss sudden infant death syndrome, and aborted crib death. A total of 42 articles were reviewed, which included 9 review articles with consensus statements and 33 observational cohort studies. Limitations of the studies include small sample sizes and lack of valid control groups for comparison. In all studies, the definition of an ALTE was based on the National Institutes of Health Consensus Development Conference (as described in the Introduction section). Of the 33 studies, 14 were pro-
Etiology And Pathophysiology

In infants with an ALTE, after investigation, approximately one-half have an identified underlying cause for the event. The most common comorbid conditions associated with ALTEs are gastroesophageal reflux disease (GERD), seizure, and lower respiratory tract infection. Other less common (but potentially serious) conditions include cardiovascular disorders, central nervous system disorders, metabolic disorders, drug toxicity or poisonings, and nonaccidental trauma. Up to 50% of infants with ALTEs ultimately have no identifiable underlying cause and remain asymptomatic. Several studies report that patients who experience recurrent ALTEs have higher rates of underlying disease that may predispose them to apnea and ALTE-like episodes. ALTEs have previously been considered to fall within the spectrum of sudden infant death syndrome (SIDS). There is a vast body of literature on SIDS, and recent literature has outlined that infants with ALTEs and infants with SIDS may be distinct and different risk groups. According to a 2008 study, ALTE differed from SIDS in that ALTE patients lack the clear male predominance seen in SIDS. ALTE infants were more likely to be full-term at birth compared to infants with SIDS, who were more likely to be premature and/or have a low birth weight. Infants with ALTEs were significantly less likely to be small for gestational age compared to infants with SIDS. Maternal age of < 20 years was seen more commonly in infants with SIDS. Most notably, the peak age for SIDS is between 2 and 4 months of age, while infants who experience an ALTE are more commonly aged < 2 months. The incidence of SIDS has decreased since the Back to Sleep Campaign (now known as Safe to Sleep) was instituted in 1994, whereas the incidence of ALTEs has remained unchanged. Approximately one-half of ALTEs occur during wakefulness, while SIDS usually occurs during sleep.

Although an ALTE is now not considered to be a precursor to SIDS, these conditions do share some risk factors. In a retrospective study performed in Sweden, maternal smoking was found to be a significant risk factor, where 33.3% of infants who experienced an ALTE (and who subsequently died of SIDS) had dual risk factors of a prone sleeping position and late prenatal smoke exposure as compared to 13.3% of ALTE survivors. Although SIDS and ALTE patients may have a few common risk factors, their differences are more prominent than their similarities. The AAP Task Force on SIDS recommends that infant home monitoring is not an effective strategy to prevent SIDS, but it may be useful in some infants who have had ALTEs.

Differential Diagnosis

While the differential diagnosis for an ALTE is wide and comprises conditions in most body systems, 3 diagnoses deserve further discussion, as they are the most commonly identified in infants who present with ALTEs. These are: (1) GERD; (2) seizure disorder; and (3) lower respiratory tract infection. See Table 1 for a more comprehensive list of possible differential diagnoses.

Table 1. Differential Diagnosis For Apparent Life-Threatening Events

<table>
<thead>
<tr>
<th>Central Nervous System</th>
<th>Respiratory</th>
<th>Infectious</th>
<th>Gastrointestinal</th>
<th>Hematologic</th>
<th>Nonaccidental Trauma</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Central apnea</td>
<td>• Airway anomaly</td>
<td>• Encephalitis</td>
<td>• Gastroenteritis</td>
<td>• Anemia</td>
<td>• Blunt trauma</td>
<td>• Drug toxicity/poisoning</td>
</tr>
<tr>
<td>• Hydrocephalus</td>
<td>• Apnea of infancy</td>
<td>• Meningitis</td>
<td>• Gastroesophageal reflux disease</td>
<td>• Bleeding disorders</td>
<td>• Münchausen syndrome by proxy</td>
<td></td>
</tr>
<tr>
<td>• Infantile spasm</td>
<td>• Bronchiolitis</td>
<td>• Pneumonia</td>
<td>• Intussusception</td>
<td>• Hematologic malignancies</td>
<td>• Shaken baby syndrome</td>
<td></td>
</tr>
<tr>
<td>• Intracerebral bleeding</td>
<td>• Breath-holding spells</td>
<td>• Sepsis</td>
<td>• Volvulus</td>
<td>• Anemia</td>
<td>• Smothering (accidental or nonaccidental)</td>
<td></td>
</tr>
<tr>
<td>• Intracranial bleeding</td>
<td>• Croup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Neuromuscular disorders</td>
<td>• Foreign body aspiration</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>• Seizure</td>
<td>• Pertussis</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>• Stroke, vascular event</td>
<td>• Pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Tumor, mass</td>
<td>• Respiratory syncytial virus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Differential Diagnosis For Apparent Life-Threatening Events

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GERD is the predominant discharge diagnosis found in studies on ALTEs, with a reported incidence ranging from 20% to 54%. A retrospective study of 469 patients with ALTEs subsequently diagnosed with GERD found a low rate of adverse outcomes (3.8%) and noted that significant risk factors included a long length of stay in the hospital and the development of neurologic impairment. In a retrospective study examining 313 infants with ALTEs, 49% had a discharge diagnosis of GERD. However, 10 of these patients had an event requiring intervention during admission (including apnea, choking, desaturation, and cyanosis). Five of these 10 infants had another unrelated diagnosis identified within 24 hours of hospitalization. This reinforces the concern that a diagnosis of GERD does not exclude other meaningful entities that may cause an ALTE. This study suggests that, in patients with ALTEs, admission to the hospital may be beneficial despite a suspected diagnosis of GERD.

ALTE episodes may be the first manifestation of seizure disorder. In a 2013 systematic review, seizures were reported in up to 10% of ALTE patients. However, a prospective study following 471 patients over approximately 5 years reported that positive findings on inpatient neurologic evaluation at the time of the ALTE had low yield for predicting which patients would go on to develop chronic epilepsy.

Lower respiratory tract infections (including respiratory syncytial virus [RSV] infection and pertussis) is the third most common final diagnosis in patients presenting with ALTEs, with a reported occurrence rate of up to 8%.

Prehospital Care

There are limited studies examining prehospital care of infants who experience ALTEs. One study in 2004 examined demographic characteristics, clinical characteristics, and outcomes for a population of infants with ALTEs for whom an ambulance in an urban emergency medical services (EMS) system was summoned. Paramedics were prospectively trained in the recognition of ALTEs and in the standardized assessment of infant physical distress. Using a consistent method, the EMS personnel prospectively recorded their level of concern for each patient, and > 80% of the patients were considered to have no clinical abnormalities and did not require any interventions. Nonetheless, approximately 45% of the patients ultimately did have an underlying illness as the probable cause for the ALTEs. EMS is often called in the setting of an ALTE because of the frightening nature of the initial presentation, though the infant may appear well upon their arrival. This study illustrates the importance of EMS staff being familiar with the criteria for defining an ALTE and understanding that infants with ALTEs may have serious medical conditions that require a timely and thorough medical evaluation, despite a well appearance.

Emergency Department Evaluation

The ED evaluation of a patient with a suspected ALTE should always begin with a rapid cardiorespiratory assessment and identification of the need for life-sustaining procedures; however, most patients who have experienced ALTEs are well-appearing and stable upon presentation to the ED. Once a patient is stabilized, a careful and detailed history is critical and will guide the extent and direction of ED management.

History

The observer of the ALTE is often distraught and has difficulty recalling the exact details of the events. The emergency clinician must remain reassuring and foster a calming and supportive environment. The interview should aim to identify objective data and include a framework for the caregiver to report the event in a reliable manner. A checklist for obtaining a history on a patient presenting with an ALTE is included in Table 2. (See page 5.)

Risk Factors For An Apparent Life-Threatening Event

Specific factors have been studied to identify patients who may be at increased risk for ALTEs.

Prematurity

Three different retrospective studies identified prematurity (defined as < 37 weeks gestation) as a risk factor for a serious diagnosis and/or the need for a medical intervention after an ALTE.

Age

Four studies examined chronological age and subsequent adverse events and/or serious underlying medical conditions after an ALTE. Two of those studies found that an age of < 30 days and a postconceptional age of < 43 weeks have an increased risk for an adverse event. However, in 2 other studies, infants aged < 2 months had a decreased risk of recurrent events. As these studies have conflicting evidence, a larger prospective study needs to be performed specifically addressing risk factors for serious disease presenting as an ALTE, including age. Another retrospective study performed in Germany showed a rate of 2.6% of severe ALTEs and SIDS in the first 24 hours of life, with the majority of the cases occurring in the first 2 hours of life.

Multiple Apparent Life-Threatening Events

Several studies report an increased risk for identification of a serious underlying disorder within 24
hours of presentation in patients with a history of multiple ALTEs. This suggests that patients who present with multiple episodes of ALTEs should be considered at higher risk, and, therefore, require admission for diagnostic workup and observation.

**Suspected Nonaccidental Trauma**
Nonaccidental trauma was reported as a cause for ALTEs in 0.5% to 11% of well-appearing infants presenting to the ED with ALTEs. Common historical and physical examination findings include recurrent ALTEs, historical discrepancies, a previous history of suspicious injuries, unexplained facial bruising or bleeding, vomiting, irritability at the time of presentation, and delayed presentation. Other risk factors identified for abusive head trauma include a call to 911, along with vomiting and irritability. Risk factors for suffocation abuse and Münchausen syndrome by proxy include recurrent ALTEs, the same parent or caregiver as witness to most or all of the ALTEs, the presence of blood in the child’s mouth and/or nose, and bruising inconsistent with the event or resuscitation. Nonaccidental trauma and maltreatment should always be considered in a patient presenting with an ALTE, and if any risk factors are identified, the patient may need formal evaluation for maltreatment, such as cranial imaging, dilated funduscopic examination, and skeletal survey.

**Suspected Seizures**
Up to 10% of ALTEs have a diagnosis of seizure as the potential cause for the ALTE. A recent study showed that out of 471 patients with ALTE, 5.3% had seizures, 3.6% developed chronic epilepsy, and 47% of patients with chronic epilepsy were diagnosed within 1 week of their ALTE presentation. Another study found that central nervous system disorders were diagnosed in 7 out of 46 (15%) study subjects with ALTEs. Of these 7 patients, no neurological disorder was suspected in 4 of the patients; however, electroencephalogram (EEG) studies were abnormal in all 4 patients.

**Upper Respiratory Infection**
In a retrospective study examining 625 infants with ALTEs, it was found that patients presenting with upper respiratory infection symptoms (rhino-

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**Table 2. Standardized Questions For Apparent Life-Threatening Event History**

<table>
<thead>
<tr>
<th>History of event</th>
<th>Before:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• How was the infant acting the day the episode occurred?</td>
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<tr>
<td></td>
<td>• What was the infant doing right before the episode?</td>
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<td></td>
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<tr>
<td></td>
<td>During:</td>
</tr>
<tr>
<td></td>
<td>• When did the episode occur?</td>
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<td></td>
<td>• How long did the episode last? If the observer is unsure, ask him or her to describe or act out the event.</td>
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<tr>
<td></td>
<td>• Who observed the episode?</td>
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<td></td>
<td>• Did the infant fall or experience any other trauma?</td>
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<td></td>
<td>• If the infant was asleep, where was the baby and in what position?</td>
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<td></td>
<td>• How did the infant look during the episode?</td>
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<td></td>
<td>• Did the infant's body change color and, if so, what part?</td>
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<tr>
<td></td>
<td>• Did the infant gasp, choke, gag, or cough?</td>
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<tr>
<td></td>
<td>• Did the infant vomit?</td>
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<tr>
<td></td>
<td>• Did the infant become weak, floppy, limp, stiff, or start shaking?</td>
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<tr>
<td></td>
<td>• Did the infant lose consciousness?</td>
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<td></td>
<td>• Did the observer notice any unusual eye rolling?</td>
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<tr>
<td></td>
<td>• Did the observer notice any blood, milk, or stomach contents in the infant’s mouth or nose during the episode?</td>
</tr>
<tr>
<td></td>
<td>• Did the episode stop on its own or did someone act to stop it? If someone intervened:</td>
</tr>
<tr>
<td></td>
<td>□ What did that person do?</td>
</tr>
<tr>
<td></td>
<td>□ Were emergency medical services involved?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>History of event</th>
<th>Immediately After:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Does the infant currently have a runny nose, cough, vomiting, diarrhea, or fever?</td>
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<tr>
<td></td>
<td>• How has the infant been acting since the episode occurred?</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>History of event</th>
<th>Past medical history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• What prescription or over-the-counter medications or herbal remedies has the infant received within 24 hours before the episode?</td>
</tr>
<tr>
<td></td>
<td>• Does the infant have any medical problems or conditions?</td>
</tr>
<tr>
<td></td>
<td>• Has the patient recently had a runny nose, cough, vomiting, diarrhea, or fever?</td>
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<tr>
<td></td>
<td>• Has the infant ever experienced a similar episode in the past and, if yes, what was done to evaluate or treat afterward?</td>
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<tr>
<td></td>
<td>• Was the infant full-term, early, or late?</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>History of event</th>
<th>Family history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Has anyone in the infant's family ever experienced a similar episode or died of Sudden Infant Death syndrome?</td>
</tr>
<tr>
<td></td>
<td>• Has anyone in the infant's family been diagnosed with a genetic, metabolic, cardiac, or neurological condition, or died in childhood of unknown causes?</td>
</tr>
</tbody>
</table>
Seizure-like activity, limb-shaking, tremors
Perioral pallor or cyanosis
Change in color, cyanosis, duskiness, red face
History of feeding difficulties, failure to thrive
Alteration of consciousness, not responding to caregiver
Choking, vomiting, milk in the mouth or nose
Hypotonia or hypertonia, stiffness
Lethargy, irritability, jitteriness
Respiratory distress, stridor, tachypnea, cough, rhinorrhea
Diaphoresis, poor activity
Eye deviation or staring into space
Apnea (infant “stopped breathing”)

Underlying Conditions
A variety of underlying conditions may place an infant at increased risk for ALTE; however, there are limited data available in these populations since most studies examining ALTEs exclude patients with known underlying conditions. Some underlying conditions may include infectious (RSV, pertussis), cardiovascular (congenital heart disease), central nervous system (status post ventriculoperitoneal shunt, known seizure disorder), and pulmonary (pneumonia) diseases.

Physical Examination
Infants presenting with an ALTE should undergo a careful physical examination, including evaluations of the cardiac, respiratory, and neurological systems. Examination should include: (1) vital signs with oxygen saturation; (2) measurement of height, weight, and head circumference; (3) examination for signs of trauma (bruising, abrasions, bulging anterior fontanel, funduscopic examination); (4) development assessment; and (5) an observation period, especially while the infant is feeding. Common presentations of an infant with an ALTE are presented in Table 3.

Table 3. Common Presentations Of An Apparent Life-Threatening Event

- Change in color, cyanosis, duskiness, red face
- Perioral pallor or cyanosis
- Apnea (infant “stopped breathing”)
- Respiratory distress, stridor, tachypnea, cough, rhinorrhea
- Alteration of consciousness, not responding to caregiver
- Lethargy, irritability, jitteriness
- Eye deviation or staring into space
- Hypotonia or hypertonia, stiffness
- Seizure-like activity, limb-shaking, tremors
- History of feeding difficulties, failure to thrive
- Diaphoresis, poor activity
- Choking, vomiting, milk in the mouth or nose

Diagnostic Testing

Laboratory Testing
As physical findings are absent in most infants with ALTEs, the emergency clinician is often compelled to perform a wide array of tests to ensure identification of any possible abnormality. This type of poorly focused testing pattern is often low-yield in identifying an etiology for the events. A study by De PIERO et al of 150 patients presenting to the ED with ALTEs found that only 3 out of the 122 (2.5%) infants who underwent diagnostic testing had a positive result with identifiable underlying diagnoses. This retrospective study identified pertussis, hypoglycemia, and anemia as underlying entities. However, these diagnoses were uncovered by a careful history and physical examination and would have enabled targeted testing in this cohort. This study concluded that the rate of identification of underlying entities in patients with ALTEs is low, and that most infants may be best managed with limited diagnostic testing and a period of observation. Focused testing based on history and/or physical findings is recommended.

A 2005 prospective study conducted by BRAND et al reported that a thorough history and physical examination enabled the clinicians to identify a diagnosis for ALTE in 70% of study patients, underscoring that a myriad of diagnostic tests may be unnecessary. They reported that certain tests yielded positive findings in the absence of a suggestive history and physical examination, however. These tests (white blood cell count, urinalysis and urine culture, chest radiograph, brain neuroimaging, screening for gastroesophageal reflux, and a pneumogram) identified an occult etiology for ALTEs in 33 of the 243 (13.5%) study subjects. This study supports that broad testing without contributory factors has limited usefulness, though a specific subset of tests performed in the emergency or inpatient setting may yield positive findings.

Imaging
A variety of potential imaging studies can be performed for an infant who has experienced an ALTE. It is well described in the literature that the yield for routine imaging of infants with ALTEs in the emergency setting is low when unsupported by the clinical history or physical examination. The study by BRAND et al showed that 36.2% of chest radiographs performed in the presence of a contributory history and physical examination were supportive of a diagnosis, while only 2.2% were supportive with a noncontributory history and physical examination (P < .0001). Other radiologic studies (such as head computed tomography [CT], brain magnetic resonance imaging [MRI], echocardiogram, and skeletal survey) had similar low
yield when unsupported by history and physical examination; however, this was not statistically significant due to low overall numbers of these studies performed. The potential missed diagnoses in patients with a normal history and physical examination were not reported in this study.

In a study by Tiede et al, head CT was reported to be the most common cranial imaging ordered in the workup of ALTEs. Other modalities include cranial ultrasound and MRI. In patients with ALTEs, cranial imaging may diagnose structural abnormalities responsible for a seizure or aid in the diagnosis of a closed head injury. However, in a study by Bonkowski et al, cranial imaging had a sensitivity of 6.7% in identifying a structural abnormality as a cause of epilepsy in patients with ALTEs. Neuroimaging may be considered in infants with ALTEs who present with seizure-like behavior and/or focal neurologic findings.

Fu and Moon reported that, although head CT is the most common neuroimaging study in the evaluation of ALTEs, in the absence of a history of head trauma, it should be reserved for cases of suspected abuse. Further, the authors of this study stated that, since 1% to 3% of ALTE cases are due to abusive head trauma, a discrepancy in history and physical examination findings or a delay in seeking medical care should prompt neuroimaging to evaluate for head injury.

A Diagnosis-Focused Evaluation

Conditions most often tested for in the ED in infants with ALTEs include anemia, infections, toxic ingestions, cardiac disorders, and neurological abnormalities. Tests to consider when evaluating an infant who has experienced an ALTE are noted in Table 4.

### Table 4. Tests To Consider For The Emergency Evaluation Of Apparent Life-Threatening Events

<table>
<thead>
<tr>
<th>Laboratory Studies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count and culture</td>
<td>Serum electrolytes</td>
</tr>
<tr>
<td>Urinalysis and urine culture</td>
<td>Cerebrospinal fluid studies and culture</td>
</tr>
<tr>
<td>Respiratory syncytial virus and pertussis testing</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Imaging</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest radiograph</td>
<td>Head computed tomography, magnetic resonance imaging, ultrasound</td>
</tr>
<tr>
<td>Skeletal survey</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Other</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrocardiogram</td>
<td>Echocardiogram</td>
</tr>
<tr>
<td>Electroencephalogram</td>
<td></td>
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</tbody>
</table>

### Anemia

Several studies document rates of anemia to be 13% to 24% in patients with ALTEs. In a study by Pitetti et al, the rate of anemia in patients with recurrent ALTEs was 21.6%, 16.9% in patients with a single ALTE, and 9.3% in control patients. None of these studies reported whether or not the anemia had a causal role in the ALTE or whether treatment for anemia was initiated.

**Bottom Line:** A complete blood count (CBC) should be considered for evaluation of these infants.

### Infection

In a study that examined the incidence of serious bacterial infection in 198 patients with ALTEs, 44 patients underwent evaluation for serious bacterial infection, and none were found to have urinary tract infection, bacteremia, or bacterial meningitis. Absence of serious bacterial infection was confirmed by a 4-week follow-up interview. In contrast, another study performed with 182 well-appearing, afebrile infants aged < 60 days presenting to the ED with an ALTE found the incidence of serious bacterial infection to be 2.7%, and it was determined that serious bacterial infection was more likely if a patient was premature. One had pertussis, and none had meningitis. While all infants aged > 60 days may not require routine testing for infection, this study suggests that a full serious bacterial infection workup, including lumbar puncture, may be considered for premature infants aged < 60 days who present with ALTEs. A study by Brand et al reported that, in patients whose history and physical examination were noncontributory, a CBC and urinalysis and urine culture in the ED may be beneficial.

**Bottom Line:** In cases of suspected infection, CBC with blood culture and urinalysis with urine culture are recommended.

### Toxic Ingestions

Studies have examined the role of urine toxicology screening in the setting of an ALTE. One study demonstrated that intentional poisoning can present as an ALTE and that a urine toxicology screen detected most of the substances. Patients in this study tested positive for acetaminophen, amphetamines, benzodiazepines, cocaine, codeine, meperidine, methadone, phenobarbital, and phenothiazines. A prospective cohort of 274 patients with ALTEs found positive urine toxicology screenings in 8.4% of patients. This was an expanded toxicology screen that identified some infants who were positive for over-the-counter cough and cold preparations, 1 patient who was positive for cocaine, and 1 who was positive for barbiturate. This study suggested that urine toxicology screening should be considered in all patients presenting with ALTEs, particularly if history and/or physical findings are suggestive.
Clinical Pathway For Management Of Apparent Life-Threatening Events

Patient presents with ALTE

Stable cardiopulmonary status?

- Assess ABCs
- Resuscitate patient
- Consider serious pathology
- Initial proper evaluation (Class II)

Admit to pediatric floor or PICU (Class II)

Detailed history consistent with definition of ALTE? One or more of the following:
- Apnea
- Color change
- Muscle tone change
- Choking/gagging (Class II)

History unclear

Risk factors for ALTE present? One or more of the following:
- Prematurity (< 37 weeks)
- > 1 ALTE in the last 24 hours
- Multiple ALTEs
- Suspected nonaccidental trauma
- Suspected seizures
- Comorbid conditions (Class II)

- Perform physical examination
- Admit for observation and monitoring (Class II)

- Perform physical examination
- Observe
- Perform targeted testing, if etiology presents
- Consider admission (Class II)

- Targeted testing based on physical examination
- Admit for treatment and observation (Class II)

- Reassess patient
- Evaluate and manage as indicated
- Discharge with recommendation for close follow-up (Class II)

Abbreviations: ABCs, airway, breathing, and circulation; ALTE, apparent life-threatening event; PICU, pediatric intensive care unit.

Class Of Evidence Definitions

Each action in the clinical pathway section of Pediatric Emergency Medicine Practice receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness
Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful
Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments
Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research
Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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author's of the study commented, however, that this study is limited since not all of the infants presenting to their ED underwent urine toxicology screening and, without a control group, it was unclear whether the study was suggestive of the incidence of positive findings for cough and cold preparations in infants in the general population.

**Bottom Line:** Consider urine toxicology screening if there is clinical suspicion of toxic ingestion, based on history and physical examination.

### Cardiac Disorders

Emergency testing for underlying cardiac disease in infants with ALTEs may include electrocardiogram (ECG), echocardiogram, and a Holter and event monitor. In a retrospective longitudinal study of 485 patients with ALTEs, 219 were tested for cardiac disease (43% with ECG, 8% with echocardiogram, and 1% with rhythm testing). Among the entire cohort, 20 patients (4%) were identified with cardiac abnormalities, and < 1% had significant cardiac disease (Wolff-Parkinson-White syndrome, dilated cardiomyopathy, frequent ventricular ectopy, and moderate aortic stenosis). The decision of clinicians to obtain cardiac testing had a sensitivity of 60% and a positive predictive value of < 1%. The only significant predictor for positive cardiac pathology was prematurity (infants born at < 37 weeks gestation) with a P value of .002. Another study examined 100 patients with ALTEs and found that 62% had 1 or more dysrhythmias on a 24-hour Holter monitor, but only 2% of these required a therapeutic intervention.

**Bottom Line:** Routine ECG screening in infants with ALTEs is a sensitive, inexpensive, noninvasive, and readily available test, and, therefore, may be a worthwhile screening tool for dysrhythmias and structural heart disease.

### Neurologic Abnormalities

Over a 5-year period, Bonkowsky et al studied 471 infants who presented to the ED with ALTEs, and they identified 17 who developed chronic epilepsy. Of these, only 6 (1.3%) were found to have an abnormal EEG at presentation, and 11 had a normal EEG. The EEG at ALTE presentation had a sensitivity of 15% in identifying patients with seizure disorder. Of the 17 patients who developed chronic epilepsy, more than 70% returned within 1 month with a second ALTE event. This signifies that seizures can be a main etiology of an ALTE and must be kept on the differential.

**Bottom Line:** EEG testing may be of benefit for assessment of ALTE patients in whom seizure activity is suspected as the cause of the ALTEs.

### Gastrointestinal Disorders

Although in most patients with ALTEs, the gastrointestinal evaluation is not performed in the emergen-
Monitoring

The 2001 Collaborative Home Infant Monitoring Evaluation study examined home monitoring for apnea in > 1000 infants divided into 7 groups: healthy term infants, preterm patients with idiopathic ALTEs, term patients with idiopathic ALTEs, preterm infants who were siblings of an infant who died of SIDS, term infants who were siblings of an infant who died of SIDS, and symptomatic or asymptomatic preterm infants. The study defined an extreme event as apnea (> 30 sec) and/or bradycardia (heart rate < 60 beats/min for infants aged < 44 wk postconception and heart rate < 50 beats/min for infants aged > 44 wk postconception). Extreme events occurred in 10% of all infants, with 2.3% in healthy term infants. This report suggested that extreme events were more common in preterm infants, though these events are unlikely to be immediate precursors to SIDS. There was no summative comment on home monitoring for any infants, including those presenting with ALTE. The 2003 AAP recommendations state that epidemiologic studies have failed to document any impact of home cardiorespiratory monitoring on the incidence of SIDS, but note that monitoring may be warranted in premature infants who are at high risk for recurrent episodes of apnea, bradycardia, and hypoxemia after hospital discharge. This recommendation also states that home monitoring may be justified in infants who have had ALTEs in order to allow rapid recognition of apnea, airway obstruction, or respiratory failure.

Time-And Cost-Effective Strategies

1. It is essential to obtain a detailed history from the caretaker or witness to the ALTE in order to both make a diagnosis of ALTE and to determine management strategies and the need for admission. Risk Management Caveat: In the setting of an unclear history, it is recommended to admit the infant with a suspected ALTE for further observation and monitoring.

2. Patients with ALTEs may not require extensive and expensive diagnostic testing in the ED without supportive history and physical examination findings. Some diagnostic studies that should be considered as part of a standard approach in the emergency setting are CBC, urinalysis and urine culture, chest radiograph, and brain neuroimaging. Risk Management Caveat: If there is uncertainty regarding the management of an ALTE and extensive testing is unsupported, admit the patient for further observation and monitoring.

Controversies And Cutting Edge

In the emergency setting, the goal in evaluating infants with ALTEs is to identify patients who are at risk for serious underlying conditions and/or recurrent ALTEs requiring intervention. Identifying the high-risk infant with an ALTE allows the emergency clinician to perform a targeted evaluation and determine the most appropriate disposition.

Two clinical decision rules for ALTE patients have been developed recently with the goal of identifying the low-risk infant who may safely be discharged from the ED. In 2012, Mittal et al examined 300 infants with ALTEs presenting to the ED, noting a 76% admission rate. Of these patients, 37 (12%) required significant intervention during their hospitalization. Predictors of the need for significant intervention included prematurity, abnormal physical examination, color change to cyanosis, and, interestingly, the absence of upper respiratory infection symptoms and the absence of choking. The interventions performed in this study included prescription of antibiotics for serious bacterial infection, admission to the intensive care unit, administration of supplemental oxygen for hypoxia, recurrent airway suctioning, tracheal intubation, discharge with an apnea monitor after an abnormal pneumogram, cardiology consultation and echocardiogram, and prescription of antiepileptic medication after an abnormal EEG.

Using these predictors, the clinical decision rule identified 184 patients that could have been discharged home safely from the ED, reducing the hospitalization rate from 76% to 36%. However, the clinical decision rule incorrectly classified 7 out of the 184 (3.8%) patients as being safe to discharge. Those patients ultimately required significant intervention (including 2 patients who required a cardiology evaluation and an echocardiogram, 1 patient with an abnormal pneumogram who was ultimately discharged home with an apnea monitor, 2 patients with repeat ALTEs in the hospital requiring stimulation, and 2 patients requiring intensive care unit admission for hypoxia and cardiac monitoring). This rule has a negative predictive value of 96% (95% CI, 92%-98.3%) and a specificity of 70.5% (95% CI, 64.4%-76%). This study requires external validation and is limited by having been performed in a single institution.

The second clinical decision rule, developed by Kaji et al, sought to identify patients with ALTEs who required hospital admission. They enrolled 832 patients from 4 different study sites, with a 79.2% admission rate. The authors identified 3 major categorical predictors for patients who required hospital admission: (1) obvious need for admission; (2) significant past medical history; and (3) > 1 ALTE in 24 hours. Predictors that indicated an obvious need for hospital admission included: patients requir-
ing supplemental oxygen, incubation, ventilation, cardiopulmonary resuscitation, intravenous antibiotics for a confirmed serious bacterial infection, or antiepileptic medications; hemodynamic instability requiring intravenous fluids or vasopressors; or a positive test result for RSV or pertussis in patients with a history of apnea. Significant past medical history included congenital heart disease, Down syndrome or other chromosomal abnormalities, craniofacial disorders, chronic lung disease, previous intubation, hydrocephalus, seizure disorder, history of dysrhythmias, and neuromuscular disorders.

Applying this decision rule to their study population would have reduced the admission rate from 79.2% to 51.5%. However, this clinical decision rule incorrectly classified 14 (2%) patients as being safe to discharge who would have required admission. This rule has a sensitivity of 89% (95% CI, 83.5%-92.9%), a specificity of 61.9% (95% CI, 58.0%-65.7%), and a calculated negative predictive value of 96.5% (95% CI, 94.2%-98.1%). This clinical decision rule also requires external validation and reliability assessment before implementation, but may be considered as a reference for future guidelines in determining admission of infants with ALTEs.

**Disposition**

Determining disposition in patients who present with ALTEs remains a challenge to the emergency clinician. Clinical decision rules may provide guidance in identifying low-risk patients who may be discharged home. When determining disposition, clinicians may take into consideration the risk of mortality in these patients. However, rates of mortality in infants who present with ALTEs are low, and are reported to vary from approximately 0% to 1%, according to a retrospective study examining mortality rates in infants with ALTEs. This study reported that 2 out of 176 patients (1.1%) died within 15 days of admission to the hospital. Both infants who died had a normal physical examination, negative laboratory evaluation, and no additional ALTE episodes. Both infants had been admitted to the hospital for observation; with a 5-day admission and a diagnosis of GERD in the first infant, and a 1-day admission and a history of prematurity in the second infant. Both infants returned to the hospital in cardiac arrest and had a postmortem diagnosis of pneumonia. This study illustrates that there is somewhat of a low risk for mortality in infants with ALTEs, even with admission to the hospital.

Several studies support the practice of admission of ALTE patients for observation. A retrospective study by De Piero et al reported an admission rate of 76%, with 7% of subjects requiring significant intervention. Claudius et al reported an admission rate of 93%, with 13.5% requiring significant intervention. Many etiologies may present after an ALTE occurs, and observation is suggested to allow time for serial examinations and any required diagnostic tests. The risk factors discussed in this issue should be taken into consideration, as well, when determining the need for admission.

Hospital resources and cost have been studied in relation to patients with ALTEs and may be a consideration in determining the diagnostic evaluation and plan for admission to the hospital. In a study by Tieder et al, the cost of admission for infants with ALTEs was estimated at $15,567 per admission, with an average length of stay of 4.4 days.

**Summary**

Infants presenting with ALTEs continue to be an evaluation and management challenge to emergency clinicians. Underlying the lack of consensus on the standard approach to these infants is the subjective nature of the definition of an ALTE used in most studies. This definition lacks a definitive age range, does not address the clinical presentation following the ALTE, and does not exclude patients with a clear diagnosis (such as RSV or seizure-like activity). This, and the absence of any large prospective study examining these infants, has resulted in a wide and varied approach to the evaluation and disposition of the infant presenting to the ED with an ALTE. Many of the studies on ALTEs are limited by small cohort size, single institution sites, and subjective and varied inclusion criteria.

Despite these limitations, review of the literature on ALTEs enables the emergency clinician to identify several meaningful conclusions. The need for a detailed history and physical examination remains paramount. Risk factors for identifying a serious underlying pathology are consistently reported to include prematurity, suspicion for child abuse, possible seizure activity, and recurrent ALTE episodes within 24 hours prior to presentation. Age remains a controversial risk factor as there are conflicting data in the literature. Further investigation is warranted to better define the impact of age on ALTEs. Other risk factors that have been identified include abnormal physical examination findings, color change to cyanosis, absence of upper respiratory infection symptoms, absence of choking, and significant past medical history. Targeted testing supported by history and physical examination findings is warranted in infants presenting with ALTEs. In the absence of suggestive history or physical examination findings, tests that should be considered in the emergency setting include a CBC, urinalysis and urine culture, chest radiograph, and brain neuroimaging. An ALTE in an afebrile infant aged < 60 days may represent a serious bacterial infection, and a full sepsis evaluation is recommended if infection...
1. “The mother’s history of the event is unclear. She isn’t even sure that her baby stopped breathing or changed color. The patient appears well with a normal physical examination, so I am going to discharge them home to follow up with their pediatrician.” The observer’s description of the episode is often skewed due to the frightening nature of ALTEs. If the history is unclear, emergency clinicians should be calming and reassuring, and take the event seriously. Emergency clinicians will need to spend more time with the observer to obtain as much detail as possible about the event. A thorough physical examination is essential in evaluating the infant. Infants may also need to be observed in the ED to provide reassurance to the caregiver if it is felt that this was likely not an ALTE.

2. “The patient has been having upper respiratory infection symptoms for the past several days, so this episode is most likely part of the upper respiratory infection, and he can be discharged.” Recent data conflict with regard to the risk of upper respiratory infection in patients with ALTEs. Some studies have reported that upper respiratory infection symptoms may put a patient at increased risk for extreme apnea or bradycardia. However, a recent clinical decision rule showed that the absence of upper respiratory infection was associated with an increased risk of an infant with an ALTE requiring an intervention. The presence of upper respiratory infection remains an unclarified risk factor and should not influence the evaluation of an infant with an ALTE.

3. “This 4-month-old patient had an ALTE, but she has a normal history and physical examination in the ED. She has no risk factors for an underlying condition. I ordered a screening basal metabolic panel and blood culture, just to be sure.” Recent studies have shown that screening tests without a history and physical examination that is contributory to a diagnosis are of low yield, and do not always add to the evaluation of an ALTE.

4. “The patient has a small bruise on his arm, and his mother said he must have rolled against the bar in his crib. The injury is minor, so I am not really worried about nonaccidental trauma.” It is important for the emergency clinician to decide whether the injury is consistent with the mechanism reported. Nonaccidental trauma can be a cause for an ALTE, and the clinician needs to have a high index of suspicion in these cases. When nonaccidental trauma is suspected, cranial imaging and skeletal survey may need to be obtained.

5. “This patient was reported as having 3 episodes of color change today, but she is completely well-appearing now. We observed her in the ED and decided to discharge her.” Patients who experience recurrent ALTEs within 24 hours prior to presentation are at increased risk for having serious underlying pathology. Patients presenting with multiple episodes should be admitted to the hospital for observation and possible diagnostic testing.

6. “This patient had an episode of limpness and facial cyanosis, but he is 6 months old, so this cannot be an ALTE.” The definition of an ALTE does not include an age range. ALTEs have been found predominantly in infants aged < 3 months, but there is no set upper limit. ALTEs should be considered in any patient aged < 1 year.

7. “The infant seems to be having reflux, so I am sending her home with reflux precautions.” Although GERD may be a cause of an ALTE, there are reports of notable underlying etiologies even in the presence of GERD. Infants with ALTEs and GERD-like symptoms should still be considered for further diagnostic evaluation and monitoring.

8. “I decided to admit the patient for an ALTE, but suggested to the hospitalist that the infant should be discharged with a home monitor for safety.” Home monitoring has been recommended for only a select group of patients, and discussions regarding whether or not a patient needs home monitoring should be initiated by the inpatient team and the clinicians providing follow-up.

9. “The patient has a cough, but appears to be stable, so I planned for discharge.” RSV and pertussis infection can present with minimal symptoms, especially in young infants. Testing for these pathogens should be performed when seasonally appropriate.

10. “The patient looked very well after the event, witnessed at home by the mother. The physical examination was normal, so I discharged her with a plan for follow-up with her pediatrician.” Patients often appear well after an ALTE; however, a normal examination does not rule out all serious pathology. Infants with ALTEs should be considered for admission to the hospital for further monitoring and targeted diagnostic evaluation.
is suspected. Child abuse or nonaccidental trauma should be included in the differential for ALTEs, and imaging is necessary if the suspicion is high.

Although the outcome in most infants with ALTEs is good, a period of inpatient observation is beneficial for infants who have clearly met the definition of an ALTE. Inpatient observation will facilitate determining the need for additional studies. Time in the hospital will also enable the parents to gain reassurance and an opportunity to become educated on managing future episodes.

Case Conclusions

Your first patient appeared to meet some of the criteria for an ALTE in that there was an uncertain period of time that the mother describes the infant to have “stopped breathing.” It is unclear to you whether this meets the definition for apnea, however. Utilizing the clinical decision rules as guides for disposition, you noted that this patient did have a color change to “red,” but there was no reported cyanosis. You determined that this infant had no risk factors for an ALTE and you decided that he did not need any diagnostic workup. However, you did observe him in the ED for a period of time to reassure the mother that the baby was well. You discharged him home with a recommendation for close follow-up with the baby’s primary care provider.

Based on the history as reported by the baby’s mother, you determined that your second patient had indeed experienced an ALTE, as she had several characteristics that met the definition criteria for ALTEs. You recalled the factors that placed this patient at higher risk for an ALTE to include prematurity, age < 2 months, and a recurrent episode of ALTE. Although there were no pertinent findings on her physical examination, you were very concerned about the risk of a serious underlying condition and the possible need for intervention if the ALTE were to recur. You decided to place the patient on continuous cardiorespiratory monitoring, checked bedside glucose level, initiated intravenous fluids, and performed a serious bacterial infection workup, including a CBC and blood culture, urinalysis and urine culture, lumbar puncture, electrolyte panel, and chest radiograph. You initiated empiric broad-spectrum antibiotics and reassured the mother that the baby was now stable. The patient was admitted to the ICU and referred for inpatient evaluation by neurology and gastroenterology specialists.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.


5.* Mittal MK, Sun G, Baren JM. A clinical decision rule to identify infants with apparent life-threatening event who can be safely discharged from the emergency department. Pediatr Emerg Care. 2012;28(7): 599-605. (Prospective; 300 patients)


5. A premature 9-week-old girl presents with 2 episodes of turning blue and becoming motionless while resting in her mother’s arms. After stimulation, the patient returned to normal color and activity level. Her mother denied any recent illness and is the sole caregiver. What in this patient’s history places her at higher risk for having a serious underlying disorder?
   a. Prematurity
   b. Color change
   c. Multiple ALTEs
   d. All of the above
   e. None of the above

6. What risk factor is not associated with possible nonaccidental trauma as a cause for an ALTE?
   a. Historical discrepancies
   b. Unexplained facial bruising
   c. Delayed presentation
   d. Ongoing infant crying after initial assessment

7. In addition to obtaining vital signs, measurement of height, weight, and head circumference, and performing a development assessment, which of the following should be included in the initial physical examination of an infant presenting with an ALTE?
   a. Examination for signs of trauma (bruising, abrasions, bulging anterior fontanel, funduscopic examination
   b. Head CT
   c. An observation period, especially while the infant is feeding
   d. A and B
   e. A and C

8. A previously healthy 3-month-old boy has had a cough and rhinorrhea for the past 3 days. He had a brief episode of turning pale and appeared to stop breathing briefly, according to his mother. She stated that she blew in his mouth, and he started to breathe again. Given his history, what test in the ED would be most high-yield?
   a. CBC
   b. Urinalysis
   c. Blood culture
   d. RSV antigen

9. Which of the following diagnostic tests is recommended for suspected abuse, even in the absence of head trauma?
   a. Cranial ultrasound
   b. Head CT
   c. Brain MRI
   d. EEG

1. Which of the following is not included in the National Institutes of Health Consensus Development Conference on Infantile Apnea and Home Monitoring’s definition of an ALTE?
   a. Change in muscle tone
   b. Apnea
   c. Color change
   d. Vomiting

2. A 16-month-old infant is reported to have stopped talking, and turned red while crying for a toy truck. His mother ran to his side and he became verbal again and back to baseline. She brought him to the ED where he had a normal physical examination. What about the patient’s history makes an ALTE an unlikely diagnosis?
   a. Patient’s age
   b. Lack of apneic period
   c. Lack of change in muscle tone
   d. All of the above

3. Which of the following is considered to be a risk factor in both ALTE and SIDS?
   a. Male gender
   b. Maternal smoking
   c. Age < 2 months
   d. Previous upper respiratory infection

4. The most common underlying disorder found in ALTE patients upon discharge is:
   a. Pneumonia
   b. GERD
   c. Seizure
   d. Urinary tract infection

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