

Apparent Life-Threatening Event: A Review

Craig C. DeWolfe, MD

*Department of Pediatrics, Pediatric Hospitalist Division, Children's National Medical Center,
George Washington University School of Medicine and Health Sciences, 111 Michigan Avenue NW,
Washington, DC 20010, USA*

The term “apparent life-threatening event” (ALTE) refers to a complex of symptoms that presents unexpectedly in an infant and is of concern to the caregiver and often cannot be characterized easily by the health care provider. Although in most cases its natural history is benign, there is a risk for subsequent morbidity and mortality. Therefore, when caring for a patient who experiences an ALTE, the provider must stabilize the infant as needed, obtain key history, identify and address any underlying causes, educate the caregivers, and provide a safe disposition. This article summarizes the body about ALTE, with specific attention to the diagnosis and management of these cases.

In September 1986, the National Institutes of Health [1] convened an expert panel to review the literature of ALTE and discuss the relationship among infantile apnea, ALTE, and sudden infant death syndrome (SIDS). The consensus group described 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), a marked change in muscle tone (usually marked limpness), choking, or gagging” [1]. With this definition, the group standardized a previously inconsistent description and offered data on its incidence, pathogenesis, and causes, and provided recommendations regarding the evaluation, treatment, and outcome. They also suggested eliminating the terms “near-miss SIDS” and “aborted crib death” because no causal link could be established between ALTE and SIDS. Moreover, they were responsible for the first consensus recommendations on the use of monitors for the condition and proposed future research directions. In the nearly 20 years since this consensus statement, progress has

E-mail address: cdewolfe@cnmc.org

been made concerning ALTE and its management, but questions persist. This article summarizes the body about ALTE, with specific attention to the diagnosis and management of these cases.

Study of the apparent life-threatening event complex

The study of ALTE is particularly complex and difficult [2]. As a result, many authors and clinicians have felt uncomfortable classifying, managing, and providing anticipatory guidance for the condition [3,4].

There are concerns that the working definition consisting of apnea, change in color, change in tone, choking, and gagging may be too broad. Some practitioners have suggested that an ALTE should not include obvious cases of choking or gagging when they are associated with feeding or upper respiratory infections [5]. Others have suggested limiting the term to infants who have required vigorous stimulation for resuscitation [6] or to patients who have no obvious abnormalities on physical examination [7]. Still others, however, consider the current case definition too restrictive. Some researchers have explicitly included infants with altered mental status in their definition of ALTE [8]. In summary, the debate regarding the ALTE case definition and heterogeneity in selection criteria for various published reports makes it difficult to develop a coherent approach to the literature.

The investigation of ALTE also depends on the descriptions of an inexperienced or medically naïve caregiver involved in a frightening and often brief event. The examination of the patient after the episode also is typically normal. Therefore, practitioners and researchers depend heavily on historical cues rather than measurable data to define ALTE.

Study design also is complex. Some researchers use referral for subspecialty evaluation to enroll patients who have experienced an ALTE, but the resultant selection bias limits the generalizability of findings. Retrospective study methods are difficult in ALTE as well. A chart review is complicated by the fact that the “Disease Index” of the “International Classification of Diseases (ICD.9.CM)” does not list ALTE as a discharge diagnosis. Although dyspnea, respiratory abnormalities, and apnea often are included in retrospective studies, cyanosis, change in tone, and choking and gagging are not. Furthermore, in cases in which a cause is found for an ALTE, there may be no mention of apnea in the discharge coding.

Even basic assumptions regarding events such as “pathologic apnea,” on which many studies have been based, have been called into question. A multicentered, prospectively designed study that monitored healthy children and those with a history of idiopathic ALTE has found no difference in the incidence of 20-second apneic spells. As a result, previous observational studies that characterize the type and frequency of similar apneic spells in preselected populations may prove to be irrelevant [9].

Definitions

Although the definitions of terms associated with ALTE are not always consistent, the following descriptions may provide a reference for future discussion. Apnea refers to a cessation of airflow and may result from central or obstructive causes. Central apnea is defined as the absence of respiratory effort caused by a lack of output from the central respiratory centers or by neuromuscular insufficiency. Chest wall movement will be absent and no breath sounds will be evident on auscultation of the chest. Obstructive apnea is defined as breaths associated with paradoxical inverse movements of the chest wall and abdomen with a corresponding decrease in oxygen saturation by 3%. Significant apnea has been defined as a cessation of air movement for at least 20 seconds. Shorter episodes also are included if they are associated with central cyanosis, bradycardia, pallor, or loss of muscle tone. Pathologic apnea is associated with physiologic compromise, whereas apneic events without these changes are considered normal.

When an unexplained pathologic apnea event occurs for the first time in an infant older than 37 weeks postconceptional age, it is called “apnea of infancy.” It is distinct from “apnea of prematurity,” which resolves by 37 weeks postconceptional age. In rare circumstances, apnea of prematurity may persist beyond term, particularly in infants born at less than 28 weeks of gestation.

Periodic breathing is defined as three or more respiratory pauses of greater than 3 seconds’ duration, with less than 20 seconds of respiration between pauses. It is common and physiologic in preterm infants and may persist beyond term in other infants. Periodic breathing is considered pathologic if it is associated with cardiorespiratory instability. Clinically, the pattern may appear as short periods (eg, 5–10 seconds) of increased rate and rigor of breathing alternating with periods of shallow or undetectable breathing [1].

Central cyanosis represents the arterial circulation of desaturated blood and becomes clinically apparent at 5 g/dL of desaturated hemoglobin. It is best determined by a bluish discoloration of the oral mucus membranes, usually evident in the lips and tongue. Peripheral cyanosis occurs when there is an increased extraction of oxygen by peripheral tissues, as can be seen with sepsis, circulatory shock, hypovolemia, and vasoconstriction.

Acrocyanosis refers to a bluish discoloration of the hands and feet and is a common, normal phenomenon in newborns, believed to be caused by distal vasomotor instability or vasoconstriction from heat-retention efforts. Circumoral cyanosis is another benign entity that often is seen in fair-skinned infants and is characterized by a bluish mustache or circular blue or purple color in the perioral area. It is usually more pronounced with crying, straining, or other Valsalva-like maneuvers. It represents a prominence of the superficial perioral venous plexus. Acrocyanosis and circumoral cyanosis are not signs of a central cyanotic state, unless the overall clinical picture supports sepsis or another shock-like state [10].

Idiopathic ALTE is the term offered for an ALTE that occurs when an underlying cause cannot be found. SIDS is the unexpected death of an infant less than 1 year old that is unexplained by history and in which a thorough autopsy

and death scene investigation fail to demonstrate an adequate explanation of the cause of death. No causal link has been made between these two entities.

Epidemiology

A longitudinal cohort study of monitored children suggests that 43% of healthy term infants have at least one 20-second apneic episode over a 3-month period [9]. Another study suggests that 5.3% of parents recall seeing such events [11]. The rates do not differ among healthy controls, patients with a history of idiopathic ALTE, or patients with a sibling who died of SIDS. Only preterm infants less than 34 weeks postconceptional age have significantly higher rates of apnea; however, these differences resolve when the premature infants reach 43 weeks postconceptional age. Thirty-second apnea occurs in 2.3% of healthy infants and 13.1% of patients with a history of idiopathic ALTE. Although a difference in percentage was found in the study, it did not reach statistical significance [9].

It is reported that 0.2% to 0.9% of infants will have apnea that leads to admission and that 0.05% of infants will have events that occur during sleep and require vigorous stimulation [11–13]. This is likely an underestimation of the ALTE admission rate because changes in color and tone, choking, and gagging exclusive of apnea were not included in the estimate. Moreover, discharge diagnoses may not reflect the true ALTE presentation if an alternative diagnosis was provided during the admission. In these studies of infants admitted for apnea, the researchers found maternal smoking and single-parent households to be risk factors for ALTE. The infants with ALTE had a median age at presentation of approximately 8 weeks and were equally likely to be male or female [11,12].

Presentation

A case series of 243 infants admitted to a tertiary care hospital has characterized the presentation of infants with ALTE [8]. The researchers found that nearly half of admitted patients had experienced more than one ALTE before being admitted to the hospital. The most common individual symptoms included, in order of frequency, apnea, cyanosis, hypotonia, unresponsiveness, labored breathing, and lethargy. Approximately 10% of these patients required supplemental oxygen or assisted ventilation by a caregiver or an emergency medical services provider.

Pathophysiology

The potential underlying abnormalities in ALTE are numerous, thus precluding any discussion of a unifying pathophysiology. Rather, the events common to an ALTE will be related to disease processes and their general pathophysiology. Therefore, the discussion begins with the sign most commonly associated with ALTE: apnea.

Central apnea results from a disruption in the generation or propagation of respiratory signals in the brainstem and descending neuromuscular pathways. Causes include prematurity, head trauma, or even the rare condition of congenital central hypoventilation syndrome (Ondine's curse). These conditions may disturb the respiratory generators, alter the pulmonary vasomotor tone, and disrupt reflexes arising from and around the pulmonary vascular bed that match perfusion to ventilation in the lungs [14]. In apnea of prematurity, studies have demonstrated a delayed and diminished central response to increasing carbon dioxide levels [15]. It is hypothesized that with decreasing respiratory effort, the Hering-Breuer inflation reflex may be disrupted. Normally, activation of these stretch receptors in this reflex terminates the inspiratory effort. During hypopnea or apnea, lung volumes fall, and the afferent input decreases. At this point, the Hering-Breuer reflex is down-regulated, resulting in increased efferent signal to terminate inspiratory effort at low levels of stretch. This causes further compromise of the breathing pattern. When positive-pressure ventilation is provided, it resets the stretch reflex, which helps to normalize breathing. The autonomic nervous system also has been implicated in syndromes associated with central apnea, and it contributes to the heart rate and blood pressure variability [16]. These mechanisms are believed to be manifest in Ondine's curse [17].

Obstructive apnea results from breathing through an occluded airway despite neuromuscular respiratory efforts. It may result from several pathophysiologic mechanisms. The obstruction may be caused by masses that occlude the airway, as seen in infants with Pierre Robin syndrome, in which the poorly anchored tongue is displaced posteriorly when the person is in the supine position. Another common cause is adenotonsillar hypertrophy, in which snoring and apnea are associated with sleep. An aspirated foreign body also can be a barrier to air movement. Functional or dynamic obstruction occurs when the airway collapses due to positive pressure inspiration. This can be seen in infants with laryngomalacia or intraluminal cysts. Finally, vocal cord paralysis, as seen in central compression of the abductor vocal cord nerves from hydrocephalus or Chiari type II malformations, may produce stridor and obstructive apnea [18].

Mixed apnea has features of both central and obstructive apnea. It may result from an underlying obstructive condition (eg, adenotonsillar hypertrophy) with a superimposed insult (eg, preoperative sedation). Conversely, children with an underlying condition of central apnea (eg, premature infants) with an acquired obstructive burden (nasal congestion from a viral respiratory illness) also may develop a mixed picture. Alternatively, single conditions may present with features of both entities, as seen in gastroesophageal reflux (GER) or infection with respiratory syncytial virus (RSV); in the former, suspected mechanisms of apnea include choking on regurgitated gastric contents, bronchospasm, and laryngeal chemoreceptor reflex central apnea [19]. With RSV infection, the virus has been believed to alter the sensitivity of laryngeal chemoreceptors to regurgitated gastric contents, resulting in reflex central apnea [20,21], and to cause inflammation of the airway that leads to obstructive apnea.

Decreased oxygenation or differential blood flow to a portion of the body may cause cyanosis, erythema, plethora, and pallor. Cyanosis may manifest centrally or peripherally. It is a consequence of hemoglobin desaturation and can result from impaired oxygen exchange or distribution. The former may occur during periods of apnea, whereas the latter may result from conditions such as sepsis. The presence of 5 g/dL desaturated hemoglobin will manifest as cyanosis. Normally, 2 g/dL desaturated hemoglobin is present in the venules, so an additional 3 g/dL reduced hemoglobin in the arterial blood produces clinical cyanosis [52]. A polycythemic infant with a hemoglobin concentration of 20 g/dL will appear cyanotic when oxygen saturations reaches 85% (ie, $[20 \text{ g/dL} - 3 \text{ g/dL}] / 20 \text{ g/dL}$). An anemic infant with a hemoglobin concentration of 6 g/dL will appear cyanotic only at 50% desaturation ($[6 \text{ g/dL} - 3 \text{ g/dL}] / 6 \text{ g/dL}$).

Transient plethora may result from hyperemia and localized vasodilation (often venous), whereas pallor may result from vasoconstriction. Both conditions tend to be mediated by autonomic activity. The practitioner should recognize that pathologic and physiologic states may be difficult for lay people to differentiate. It has been suggested that as many as two of 150 patients presenting on referral after mouth-to-mouth resuscitation had physiologic pallor with normal oxygenation [22].

Altered muscle tone may appear as limpness, hypertonia, and rhythmic movements of the extremities. The source of the defect may originate in the nervous system, as seen in hydrocephalus. However, the defect may result secondary to a systemic process such as crying in a vasovagally mediated breath-holding spell. Other more general neurologic triggers of ALTE may include central or autonomic nervous system disorders.

Choking, coughing, and gagging are normal protective responses to stimulation of the posterior nasopharynx, hypopharynx, larynx, and lower airway. These reflexes result in the temporary interruption of ventilation by two key processes. Mechanical obstruction can occur from the foreign material present or from the reflexive occlusion of soft tissue designed to prevent passage of the material. Also, the forceful effort to expel the offending material prevents effective ventilation. These forceful efforts may cause plethora and erythema of the face and head because the increased intrathoracic pressures that are generated cause increased blood flow and venous congestion superiorly. Sustained efforts may result in hypoxia or limpness caused by the vagal stimulation, but typically, the coughing, gagging, and retching responses are self-limited when the offending stimulus is removed. These responses have been associated with digestive, neurologic, vasovagal, and acute airway obstruction abnormalities [2].

Differential diagnosis

Because ALTE is a description rather than a diagnosis, the hospitalist must consider the broad range of possible underlying causes. Table 1 [23–35] provides a suggested grouping of causes and their relative percentages from a systematic review of the literature that has examined patients on their first presentation to

Table 1
Differential diagnosis of ALTE

Gastrointestinal (33%) ^a	Cardiovascular (1%)
Gastroesophageal reflux [19]	Congenital heart disease
Gastroenteritis	Cardiomyopathy
Esophageal dysfunction	Cardiac arrhythmia/ <i>prolonged QTc</i> [30]
Colic	<i>Myocarditis</i>
Surgical abdomen	Metabolic/endocrine
<i>Dysphagia</i> ^b	Electrolyte disturbance
Neurologic (15%)	Hypoglycemia
Seizure [23]	Inborn error of metabolism [31]
Central apnea/hypoventilation syndromes (apnea of prematurity, Ondine's curse)	Other infections
Head injury (intraventricular hemorrhage, subarachnoid hemorrhage)	<i>Sepsis</i>
Meningitis/encephalitis	Urinary tract infections
Hydrocephalus	<i>Child maltreatment syndrome</i>
Brain Tumor	<i>Shaken baby syndrome</i> [40]
Neuromuscular disorders	<i>Intentional suffocation</i> [22]
Vasovagal reaction [24]	<i>Munchausen-by-proxy syndrome</i> [22]
<i>Congenital malformation of the brainstem</i> [18]	Other diagnoses
Respiratory (11%)	Physiologic event (periodic breathing, <i>acrocyanosis</i>)
Respiratory syncytial virus [25]	Breath-holding spell [14]
Pertussis [26,27]	Choking
Aspiration pneumonia	Drug or <i>toxin reaction</i> [32]
Other lower or upper respiratory tract infection	<i>Unintentional smothering</i> [33]
Reactive airway disease	<i>Anemia</i> [34]
<i>Foreign body</i>	<i>Hypothermia</i> [35]
Otolaryngologic (4%)	Idiopathic/apnea of infancy (23%)
Laryngomalacia [28]	ALTE
Subglottal and/or laryngeal stenosis [28]	
Obstructive sleep apnea [29]	

McGovern and Smith [36] described the relative frequency of specific diagnoses (%)^a across all patients in studies reviewed by them. Using the same methods and studies, these figures are shown with respect to broader diagnostic groupings (eg, gastrointestinal rather than gastroesophageal reflux). The table includes broad categories and potential diagnoses (*italics*)^b not considered by McGovern and Smith based on their inclusion criteria. Thus, the reader is provided a wider range of diagnostic possibilities to consider, with references to additional studies.

a medical system [36]. The data were extrapolated from a large number of case series with varying selection criteria and ALTE definitions, but it provides useful estimates of the relative frequency of a wide range of causes. Diagnoses that were not identified in the study were added (in *italics*) to provide a more complete illustration of the differential diagnosis. "Idiopathic ALTE" is the term used when an underlying cause could not be identified.

Special consideration is given to GER because it may be a coexistent but not necessarily a causative entity. A case series [37] involving a standard battery of tests on all patients presenting with ALTE has found that 89% of a subpopulation of screened infants had radioisotope-labeled milk scan evidence of GER. More than half of these cases also had an alternative diagnosis that the authors con-

sidered more likely than GER as the cause of the ALTE (eg, seizures, pertussis, or urinary tract infection). With the extremely high prevalence of GER in young infants, practitioners should be wary of assigning this condition as the cause for ALTE because it may be detected in most children presenting for ALTE evaluation.

History

A history is the single most important component in the evaluation of infants with ALTE. In many cases, a history may determine the diagnosis and thereby abrogate the need for further diagnostic testing. In other cases, it may suggest a particular diagnosis or diagnoses that direct the work-up. The practitioner, however, may find it difficult to gather or interpret the data from a sudden and irreproducible event in a child who otherwise appears to be well [4]. Some caregivers may not be familiar with the physiologic nature of periodic breathing or acrocyanosis. Others, by contrast, may minimize more serious pathologic events. The entire event may not have been witnessed, and caregivers commonly overlook or distort features during the unexpected and distressing event. Despite these shortcomings, the practitioner should make every attempt to obtain a history of the event from all observers. Important features of the history are included in [Box 1](#).

The chief complaint often clearly illustrates the element of most concern to the parent. It also will allow the practitioner to focus on the same element when explaining potential mechanisms of action in relation to the evaluation and diagnosis or when providing anticipatory guidance and reassurance.

Another important aspect of the history is differentiating between true apnea and central or obstructive symptoms. Sometimes it is difficult to distinguish true apnea from shallow respiratory efforts that are undetectable to the observer. Lighting conditions, proximity to the patient, and the amount of clothes or bedding present may influence the ability to detect breathing motions.

Central apnea will appear as an effortless pause, whereas obstructive apnea in an awake or awakened infant presents as a sudden onset of choking, gasping, coughing, or gagging, with or without an appearance of distress. The appearance of gastric contents (milk, mucus, or gastric secretions) may proceed, accompany, or follow the event and may be a causative or an associated phenomenon. The caregiver should be asked about events leading up to the spell, milk or mucus coming from the nose or mouth, a history of spitting up, relationship to feedings, or any possibility of a foreign body aspiration. Obstructive sleep apnea often is associated with stridor, snoring, or other evidence of partial airway obstruction along with repeated episodes of self-limited apnea. The cause of an obstructive event may be suggested by the recent or past medical history, for example in recent symptoms of upper respiratory tract infection or a past history of endotracheal intubation. Attention to more long-standing symptoms and more recent superimposed symptoms may be key when a mixed apnea picture presents [10].

Box 1. Focused history

Chief complaint
Presence of apnea with attention to obstructive or central symptoms
Type of color change and distribution
Any change in tone, rhythmic shaking, and its distribution
Choking, gagging, coughing, vomiting
Duration
Relationship to feedings
Feeding difficulties such as aversion, choking, fatigue, diaphoresis, sloppiness
Eye deviation
Loss of consciousness
Coryza
Fever
History of trauma: intentional or unintentional
State of alertness prior to ALTE
Location of the infant at the time of the ALTE
Sleep position
Witness to the ALTE
Type of resuscitation needed and who performed it
Review of the prehospital (emergency medical service) record, if available
Current condition of the child in the caretaker's opinion or the amount of time to reach baseline
Presence of a monitor
Medicines taken by the child or by the mother who is breast feeding him/her
History of ALTE in the past and type of evaluation
Medical history, including pregnancy, birth, delivery, diet, and development
Family history of ALTE, SIDS, or unexpected sudden death

Although GER should be considered in the child who has events around the time of feedings, the astute practitioner also will consider any difficulties with feedings. Swallowing difficulty, inability to complete a feeding without respite, diaphoresis, or respiratory distress with feedings may suggest oromotor difficulties, cardiac dysfunction, or an aerodigestive fistula.

A history of fever or hypothermia may be an important harbinger of infection. However, apnea alone may be a presenting sign of serious infections in an infant who appears to be ill with meningitis or sepsis. It also may be the initial symptom of an RSV infection.

Finally, the practitioner should have a low threshold for consideration of nonaccidental trauma. The American Academy of Pediatrics Committee on Child Abuse and Neglect [38] has suggested that certain circumstances should alert the practitioner to the possibility of abuse, including recurrent ALTE or previous infant death while in the care of the same person, especially if the child and the caregiver are unrelated; previous unexplained deaths or simultaneous symptoms in siblings; or discovery of blood in the infant's mouth or nose in association with ALTE [38,39]. Studies have demonstrated that intentional suffocation, shaken-baby syndrome, and Munchausen-by-proxy may manifest with nonspecific symptoms and few, if any, clinical signs [22,40]. Moreover, these children are at continuing risk if they are returned to an unsafe environment. In one prospective study [8], two of three infants presenting with an ALTE who ultimately died presented secondary to child abuse. Another study [22] has documented deliberate suffocation in over 10% of patients evaluated after active resuscitation. Finally, 3% to 5% of SIDS cases are believed to be a result of infanticide [38].

Examination

Although the event of concern has resolved typically by the time the patient presents for medical evaluation, there are important features on which to focus the physical examination. Aside from residual findings of the event (eg, post-ictal somnolence and dried formula at the nares), the practitioner is looking for any

Box 2. Areas of focus for the physical examination of an ALTE

General condition: arousal, irritability, somnolence
 Vital signs, including the pulse oximetry
 Growth curves, including head circumference
 Examination of the:
 Head for evidence of trauma or fontanelle size and fullness
 Tympanic membrane for hemotympanum
 Eyes for pupil reactivity and conjunctival and retinal hemorrhages
 Nasopharynx for congestion or presence of milk or formula
 Lungs for work of breathing and stridor, wheeze, crackles, rhonchi, or transmitted upper airway sounds
 Heart for rate and rhythm, murmur, and capillary refill
 Abdomen for signs of an acute abdomen
 Musculoskeletal system for range of motion or signs of trauma
 Skin for bruising or other signs of trauma or rash
 Neurologic examination for tone, movement, head control, and reflexes
 Features suggestive of a genetic or metabolic syndrome

evidence of an underlying process that might have caused or contributed to the ALTE (eg, rhinorrhea or micrognathia). [Box 2](#) details some of these important aspects.

Other areas and methods of observation may be informative. Interactions between the caregiver and the child may reveal areas of concern. Observing a feeding may allow the practitioner to confirm or detect previously unrecognized difficulties. Cardiovascular monitoring during the entire intake process would allow detection of subclinical cardiorespiratory events as well as provide valuable data, if an event recurs.

Evaluation

The medical evaluation of an ALTE is directed at uncovering any underlying cause, determining the severity, frequency, and nature of the events, and detecting any progression of symptoms or clinical deterioration. Immediate medical evaluation and referral for cardiorespiratory monitoring may be warranted in many cases and often is accomplished best initially in an emergency department.

The initial assessment includes determining and establishing cardiorespiratory stability. Once this has been achieved, taking the history and performing a physical examination can proceed with cardiorespiratory monitoring and pulse oximetry in place.

The extent and direction of further evaluation will depend on the initial assessment and the clinician's clinical judgment. No medical protocol has ever been tested for ALTE, therefore the practitioner should not be confined to a minimum or maximum number of tests. The enormous number of tests available to the practitioner makes it challenging to embark on an appropriate work-up. Aside from the discomfort, inconvenience, risk, and cost of the various tests, the sheer number performed may affect the reliability of the results. The more tests that are performed, the more likely an abnormality (real or spurious) will be detected, whether related to the ALTE event or not.

An organized approach is helpful, and a flow sheet is provided that is useful as a general guide ([Fig. 1](#)). As indicated in this guide, in some cases the history, physical examination, and initial period of cardiorespiratory monitoring may be sufficiently reassuring to preclude the need for further work-up. This is especially true if the event was promptly reversible, short lived, and self-limited. Some examples might include an unintentional brief smothering event leading to external airway obstruction (eg, from a pillow or stuffed animal over the face); infrequent, isolated choking episodes either during feeding or with vomiting; hypothermia caused by unintentional, unexpected exposure to cold, such as after bathing; or a frank breath-holding spell. Each of these situations mandates counseling, anticipatory guidance, and education to avoid or manage repeat events and to prevent unintentional behaviors that portend subsequent risk.

If the clinical presentation is consistent with central apnea, and the health care provider is unable to elicit any diagnostic clues on initial assessment, a set of screening tests may be warranted. These tests may include a complete blood

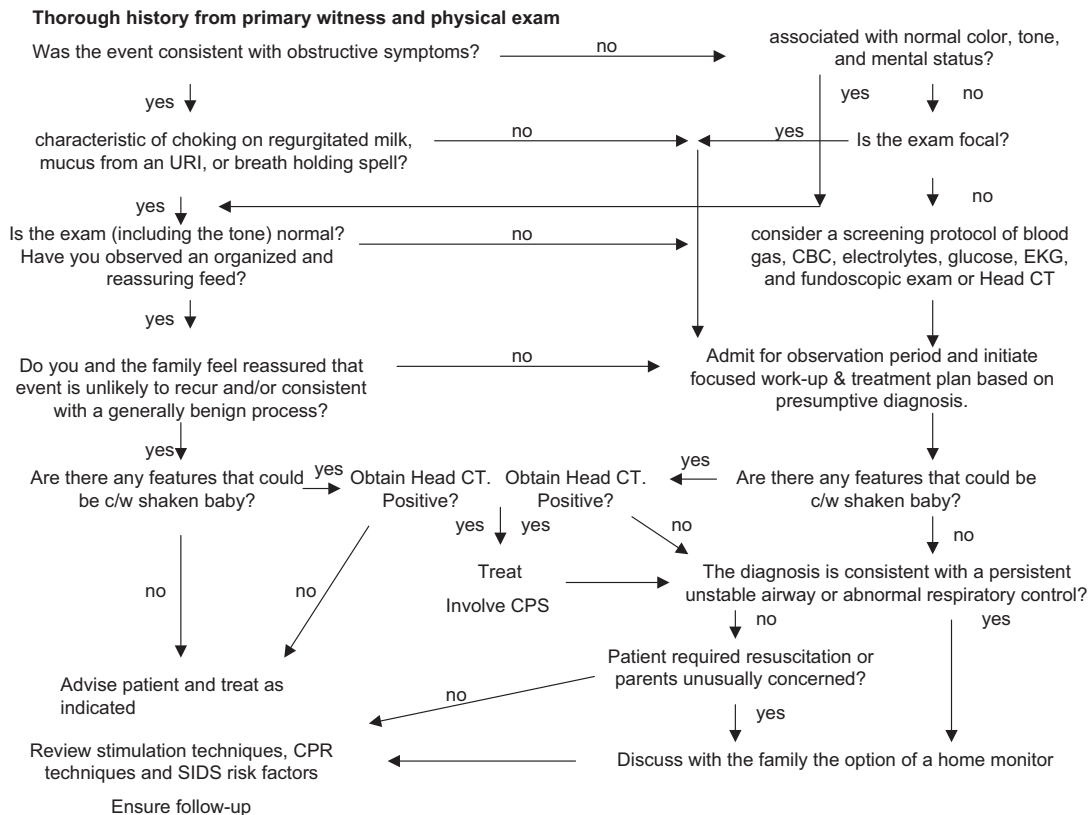


Fig. 1. An untested approach to the evaluation of an ALTE.

count, a basic serum metabolic panel, and a venous blood gas or lactate level. Acidosis with or without an elevated serum lactate level would prompt a more thorough investigation of metabolic disorders and could provide clues about the extent of respiratory compromise. Other electrolyte abnormalities such as hypo- or hypernatremia, hypo- or hypercalcemia, and hypoglycemia in neonates may suggest metabolic disorders manifesting as seizures or lethargy. An elevated white blood count would suggest infection, leading to other microbiologic studies and possibly empiric therapy. Anemia may be, in and of itself, an explanation for an apneic event, or it may be a clue to an underlying hematologic disorder. A screening CT scan of the head is recommended by some experts, especially when the practitioner has any concern for abuse. Studies suggest that the scan may be more sensitive for abuse, with fewer false-positive results than a dilated fundoscopic examination and could detect nontraumatic causes of ALTE such as hydrocephalus [41]. Performing a scan on a patient who is unsedated would likely be more accessible and arguably safer than administering mydriatic and cycloplegic drugs to a patient who requires serial neurologic examinations. If seizure activity or a focal neurologic deficit is suggested by the history or physical examination, electroencephalography should be considered in addition to brain imaging.

If a sudden event with poor perfusion or seizure suggested a possible rhythm disturbance, then an electrocardiogram should be performed, looking for a prolonged QTc interval. If, however, long-standing feeding issues, a failure to thrive, or diaphoresis with feedings accompanies the presentation, a chest radiograph, four-extremity blood pressure measurements, and pre- and postductal oxygen saturation measurements should be included, along with a consultation with cardiology.

If the oxygen saturation was abnormal, arterial blood gas evaluation and chest radiography would be indicated. If oxygen saturation cannot be corrected with the inspiration of 100% oxygen supplementation, a right-to-left vascular shunt becomes another important consideration.

When a patient presents with a history consistent with an obstructive event or physical examination findings reveal features that predispose to such an event, the work-up should be directed at localizing a lesion. The recent onset of upper respiratory tract symptoms with nasal congestion, a barking cough, or hoarseness could reassure the clinician or lead to testing of the nasal secretions for common viral respiratory pathogens. A history of long-standing stridor or hoarseness may direct anatomic or functional assessment of the airway, including radiographs of the neck with or without airway fluoroscopy, chest radiography, contrast esophagram, nasopharyngolaryngoscopy, or occasionally, bronchoscopy. A visible hemangioma, especially in the beard distribution, should raise the concern for airway involvement. Circumstances of concern for foreign body aspiration might lead the clinician to obtain neck and chest radiographs and bilateral decubitus films.

If an event occurred during feeding, it would be prudent to observe another feeding and to refer a child with suspected dysfunction for a modified barium swallow evaluation with a speech, occupational, or feeding specialist. If the

infant's neurologic examination and feeding technique are normal but aspiration (especially chronic) is still a consideration, then evaluation by endoscopy or contrast radiography for the detection of a tracheoesophageal fistula might be prudent. If clinical evidence of GER disease is present (eg, emesis with discomfort or apnea, food aversion, or documented esophagitis) and no other diagnosis seems likely, an evaluation may be pursued, but many clinicians start with a trial of empiric therapy. Finally, in patients who do not have classic symptoms of GERD but do have a history that suggests central apnea in the absence of other pathology, an isotope-labeled milk scan or a pH probe could help identify subtle laryngochemoreceptor reflex apnea. In an infant who presents while on a home cardiorespiratory monitor or because of frequent alarms, an expedited monitor download should be conducted to determine if and to what extent true apnea or bradycardia occurred.

Sleep studies may be indicated in the case of a history suggestive of apnea of infancy or prematurity, when the practitioner wishes to further characterize hospital cardiorespiratory (CR) monitor or home apnea monitor alarms, or when no physiologic mechanism can be found to explain repeated ALTE during sleep. The sleep study can record and characterize the extent of desaturation, the breathing pattern, and changes in heart rate. It also can differentiate between central apnea and obstructive apnea by means of a nasal thermistor and sensors that detect chest wall movement. Additionally, sleep studies may identify seizures and cardiac arrhythmias. In special circumstances, a sleep study can be performed with an esophageal pH probe to characterize the role of GER. Despite these impressive capabilities, there are significant limitations to the sleep study. If an event occurs when the patient is not on a monitor, the event will not be recorded, which may give a false sense that the event has resolved, especially if it has not been witnessed. The hope is that the sleep study detects an event that is similar to the presentation, but a normal test does not rule out future ALTE. Moreover, the sleep study is time and labor intensive, with results that often take days to process. It may be best to reserve the sleep study for events that are consistently and repeatedly found during sleep, after a period of observation in the hospital on a CR monitor or when a home monitor suggests concern.

Treatment and discharge planning

Although hospitalization is not required for all infants who present with an ALTE, there are several benefits to this approach. Prolonged cardiovascular monitoring will allow further evaluation of any recurrences and possibly provide information regarding severity, progression, sequelae, or cause. During this time, diagnostic testing can be more judiciously and expeditiously performed, and subspecialty consultation can be enlisted. Hospitalization also allows for the reassurance and education of caregivers regarding the events, and it allows them to receive specific training in cardiopulmonary resuscitation and modifiable SIDS risk factors.

Practitioners and researchers have advocated observation periods of 23 to 72 hours [4,6,42]. In a case series of 65 infants admitted for a 72-hour period of monitoring after an ALTE, only four patients had a subsequent event. Three of these infants had apnea within the first 24 hours, and the fourth patient manifested the subsequent event by 48 hours [43]. The authors made no mention of the severity of the episodes or the intervention provided during the hospitalization for these four patients, but they did state that all 65 patients were followed for 1 year and experienced no further ALTE or deaths.

Treatment is directed at the underlying pathology that is amenable to therapy, whether it consists of simple techniques that the caregivers can institute at home (eg, upright positioning for GER or suctioning for RSV infection), medical therapy (eg, the use of antacids with or without prokinetic agents for GER disease), or surgical intervention (eg, a tracheostomy for critical subglottal stenosis).

Patients with apnea of prematurity or infancy may benefit from treatment with methylxanthine therapy that is coordinated with a pulmonologist. The best choice is caffeine, which has the best safety-efficacy profile of this group of agents but also exacerbates reflux symptoms.

Infants who demonstrate cardiorespiratory instability during hospitalization need to complete the necessary intervention and demonstrate subsequent stability before discharge. Appropriate home environment and medical support must be established. Communication with the primary care clinician and any subspecialists needs to be ensured to create a safe transition to the home and for outpatient follow-up.

Ultimately, parents should be counseled on appropriate resuscitation techniques in the event of a future ALTE. Specifically, they should be instructed on appropriate stimulation techniques (reinforcing the fact that an infant should never be shaken) and provided with cardiopulmonary resuscitation (CPR) instruction. Moreover, they should be counseled on ways to minimize the risk of SIDS, including the proper supine sleep position, use of a firm crib mattress while avoiding excessive blankets, and avoidance of exposure to environmental tobacco smoke.

Natural history and relationship to sudden infant death syndrome

Although the literature on the natural history of infants who present with ALTE is incomplete, most infants will never experience another event and will develop normally. A study of 65 infants presenting to an emergency room with an ALTE found that none of the infants less than 2 months of age with a normal clinical examination and a lactate level less than 2 mmol/L had experienced a subsequent ALTE or were diagnosed with an underlying disorder. Moreover, none of the larger population of patients died within 3 years after presentation, although eight infants were readmitted and were diagnosed ultimately with a "significant underlying disorder." Any delay in diagnosis did not have a lasting impact on the natural history of the underlying disease [37].

The relationship between ALTE and SIDS also is unknown. Studies have reported a mortality rate of 0% to 6% in infants who presented with ALTE and a 13% mortality rate in subpopulations of infants who presented with idiopathic apnea discovered during sleep that required mouth-to-mouth resuscitation [9,44–47]. These studies had significant methodological differences and were not designed to illustrate causation, but they do illustrate the major concern for families and practitioners.

By contrast, there are striking epidemiologic and clinical differences between ALTE and SIDS. First, the incidence of SIDS peaks at 3 to 5 months of life, whereas ALTE peaks 1 to 3 months earlier [12]. Second, only 4% to 13% of SIDS cases had a history of apnea, a percentage only slightly higher than healthy controls [11,13,48]. Moreover, there is no statistical difference between parental reports of apneic episodes in the 2 weeks preceding a SIDS episode and the frequency reported in healthy controls. Finally, after extensive research, most researchers believe that apnea of prematurity is not a risk factor for SIDS [9,48].

The CR monitor, an intervention designed to target at-risk infants, has not affected significantly the rate of SIDS. Instead, the “Back to Sleep” campaign has been the most important factor in the 30% to 50% decline in the SIDS rate, since its inception [39]. During this same period of time, admissions for ALTE have not significantly changed. Furthermore, beyond maternal smoking, which is a shared risk factor for SIDS and ALTE, environmental factors for SIDS such as prone sleeping position and co-sleeping have not been found to be statistically associated with ALTE.

Apnea monitors

The role of home CR monitors designed to detect central apnea and bradycardia in patients with ALTE remains an area of debate in the medical literature and among practitioners. The original 1986 National Institutes of Health consensus statement [1], in the absence of definitive literature, has suggested that monitors are indicated in cases of ALTE that require vigorous stimulation or resuscitation. A subsequent policy statement offered in 2003 by the Committee on the Fetus and Newborn of the American Academy of Pediatrics [49] offered more specific indications. The committee suggested that monitors might be used to alert the family of a patient with a known unstable airway, abnormal respiratory control, or symptomatic and technologically dependent chronic lung disease [49]. Although the committee did not differentiate the source of ALTE, one might suggest that if it were a result of the above criteria, a monitor may be justified.

The provider should be aware that obstructive apnea often is not identified by conventional monitors because chest wall motion is maintained despite a lack of airflow [9]. These monitors have devices to detect only chest wall motion and heart rate. Without a device that detects ribcage and abdominal movements, nasal airflow or oxygen saturation, the only detectable abnormality of an obstructive event would be bradycardia if the event were sufficiently severe or prolonged.

Moreover, the parents should be counseled that monitoring has not been shown to prevent SIDS. A multicenter study conducted by the Collaborative Home Infant Monitoring Evaluation (CHIME) Study Group [9] has suggested that apneic events are common to both normal infants and those who are diagnosed with idiopathic ALTE who had previously required CPR or vigorous stimulation. Moreover, the number of extreme apneic events (lasting 30 seconds or more) did not significantly differ between the groups (although the sample size may not have been large enough to detect a difference) [9].

Practitioners must also be familiar with the possible adverse effects of the monitor technology. First, monitors often cannot differentiate between true cardiorespiratory events and disrupted connections, with resultant frequent false alarms. Second, monitors generally increase caregiver anxiety, depression, and hostility, especially during the first few months of use, compared with matched controls [50]. Finally, and perhaps most debatably, infants who were monitored over the course of a year may have worse developmental consequences, and some authors speculate that increased parental stress levels and perceptions of infant vulnerability may be to blame [51].

In appropriate situations, the parents should be empowered to participate in the decision regarding the use of a monitor. Some parents will feel more comfortable with an alarm, whereas others will find it intrusive or potentially more worrisome. Because false alarms are a clinical reality, the parents should be counseled to use the assessment techniques that they have learned in the event of an alarm and should have ready access to medical personnel who can answer immediate questions and refer for follow-up.

If it is prescribed, the CR monitor should have an event recorder and be set with age-appropriate physiologic parameters (Table 2). Most experts agree that the CR monitoring may be discontinued once it is clear of apnea for 2 consecutive months. Furthermore, no subsequent sleep study may be needed if an event recorder is used and sufficient data is gathered.

A home monitor with an oxygen event recorder has been studied and used in rare circumstances. These monitors record the date, time, oxygen saturation, plethysmographic waveforms, partial pressure of oxygen of the skin, breathing

Table 2
Suggested age-appropriate cardiorespiratory monitor settings

Premature infants		Full-term infants	
Age (PCA in weeks)	Bradycardia threshold (beats per minute)	Age (months)	Bradycardia threshold (beats per minute)
≤40	100	≤1	80
40–44	80	1–3	70
≥44	Use corrected age in months with full-term limits	3–12	60
		≥12	50

Apnea, 15 seconds for preterm infants; 20 seconds for term infants.

Abbreviation: PCA, postconceptional age.

movements, and electrocardiograms. With these additional features, researchers have been able to assess features of altered skin perfusion, suffocation, and fabricated illness [22].

Future directions

Because of its prevalence, its potential to consume significant medical resources, and its unpredictable natural history, further research interest and funding are needed to clarify ALTE. The following study designs and objectives suggest immediate research strategies in the field but are not intended to be exhaustive.

First, prospective observational cohort studies are needed to describe the epidemiology and risk factors for ALTE in the United States population. Other epidemiologic studies should follow up on the evidence that 20- or 30-second apneic episodes may be common events in the lives of infants and help to identify which patients may be at risk for adverse outcomes. Second, bench and translational research protocols should continue to describe the pathophysiology of apnea and other neurocardiorespiratory events to describe potential causative mechanisms. Finally, trials are needed to compare the natural history of patients who present with an ALTE based on an intervention such as a diagnostic algorithm, GER treatment, or monitor use. Ultimately, the intention of future study should be to predict and intervene before an ALTE occurs, while limiting the morbidity and mortality associated with it.

Summary

ALTE is a common, nonspecific, and primarily benign disorder that also may be potentially serious. A firm understanding of the definition and differential diagnosis is crucial to allow the practitioner to swiftly differentiate between events that may require minimal intervention and those that demand immediate investigation and therapy. Providing education and anticipatory guidance to concerned parents and caregivers also is critical to the effective management and discharge planning for these infants.

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