

Evaluation and Management of Apparent Life-Threatening Events in Children

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Apparent life-threatening event syndrome predominantly affects children younger than one year. This syndrome is characterized by a frightening constellation of symptoms in which the child exhibits some combination of apnea, change in color, change in muscle tone, coughing, or gagging. Approximately 50 percent of these children are diagnosed with an underlying condition that explains the apparent life-threatening event. Commonly, the problems are digestive (up to 50 percent), neurologic (30 percent), respiratory (20 percent), cardiac (5 percent), and endocrine or metabolic (less than 5 percent). Fifty percent of these events are idiopathic, which causes great concern to parents and physicians. The evaluation of an affected infant involves a thorough description of the event as well as prenatal, birth, medical, social, and family history. The physical examination, including careful neurologic examination and notation of any apparent anatomic abnormalities, helps diagnose congenital problems, infection, and conditions contributing to respiratory compromise. The laboratory evaluation is driven by historical and physical findings. Inpatient evaluation and monitoring are recommended in virtually all cases unless investigations are normal. Should the history reflect a severe episode, or should the child require major interventions such as cardiopulmonary resuscitation, inpatient observation and monitoring are recommended, even if physical examination and laboratory findings are normal. Once a presumptive diagnosis is made, events should cease after appropriate intervention. If not, reviewing the history, performing another physical examination, and reassessing the need for laboratory and imaging studies are the next steps. Although consensus statements by the National Institutes of Health and the American Academy of Pediatrics support home monitoring, the relationship of apparent life-threatening event syndrome to sudden infant death syndrome is controversial. (Am Fam Physician 2005;71:2301-8. Copyright© 2005 American Academy of Family Physicians.)

See page 2237 for strength-of-recommendation labels.

Many physicians have received a frantic call from an anxious parent stating that his or her child stopped breathing, became limp, or turned blue, but then quickly recovered. In 1986, participants in the National Institutes of Health Consensus Development Conference on Infantile Apnea and Home Monitoring defined this event as an “apparent life-threatening event” (ALTE).¹ The underlying impetus for the consensus statement stemmed from questions about the use of home monitoring in preventing morbidity and mortality from apnea-related episodes and sudden infant death syndrome (SIDS). The panel also questioned the relationship of apnea to SIDS. As part of this consensus meeting, the panel defined pathologic apnea, apnea of infancy, apnea of prematurity, ALTE, and SIDS (Table 1).¹ Because review of previous studies failed to establish a clear association between ALTE and SIDS, the panel recommended discarding previously used terms,

including “near-miss SIDS” or “aborted crib death.”^{1,2}

Definition of ALTE

By definition, an ALTE refers to a sudden event, often characterized by apnea or other abrupt changes in the child’s behavior (Table 1).¹ Symptoms of an ALTE include one or more of the following: apnea, change in color or muscle tone, coughing, or gagging.² These episodes may necessitate stimulation or resuscitation to arouse the child and reinitiate regular breathing.

Incidence

Because demographic data are derived from cases in which children are admitted to hospitals or emergency departments, and because not all children are brought in for evaluation, the true incidence of ALTE syndrome is unknown. The reported incidence is 0.05 to 6 percent.^{3,4} Most ALTEs occur in children younger than one year.⁴ In one study⁵ of 65 patients with an ALTE, the peak

Strength of Recommendations

<i>Key clinical recommendation</i>	<i>Label</i>	<i>References</i>
Initial evaluation of the infant with an ALTE should include a careful history of the event, circumstances surrounding the event, and observations of the caregiver.	C	1, 2
Inpatient evaluation and monitoring are recommended for children who required complex resuscitation efforts or have abnormal results on physical examination.	C	1, 2
If an underlying cause is identified, further testing is not indicated unless ALTEs continue despite appropriate intervention and treatment.	C	1, 2
Recommended diagnostic tests with high yield include complete blood count, serum bicarbonate and lactate, urinalysis, chest radiography, pertussis and respiratory syncytial virus samples, and gastroesophageal reflux disease investigations.	C	4
Home monitoring is recommended for children who have experienced a severe ALTE or in whom a diagnosis is unclear.	C	1, 20

ALTE = apparent life-threatening event.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, opinion, or case series. See page 2237 for more information.

incidence occurred between one week and two months of age, with most events occurring in infants younger than 10 weeks.

Premature infants, premature infants with respiratory syncytial virus (RSV) infections, and premature infants who undergo general anesthesia are at increased risk for an ALTE.⁴

Children who feed rapidly, cough frequently, or choke during feeding also are at increased risk, and more boys than girls experience ALTEs.⁴ One study⁵ indicated that infants older than two months who had an ALTE and those with recurrent episodes of ALTEs were more likely to have significant disorders.

TABLE 1

Definitions from the 1986 National Institutes of Health Consensus Panel on Infantile Apnea and Home Monitoring

Apparent life-threatening event (ALTE): sudden event, frightening to the observer, in which the infant exhibits a combination of symptoms, including apnea, change in color (pallor, redness, cyanosis, plethora), change in muscle tone (floppiness, rigidity), choking, gagging, or coughing

Apnea: cessation of respiratory airflow for any reason; central, obstructive, or mixed

Pathologic apnea: apnea lasting 20 seconds or more and accompanied by bradycardia, cyanosis, hypotonia, or other signs of compromise

Apnea of infancy: unexplained respiratory pauses lasting 20 seconds or more, or pauses of less than 20 seconds that are accompanied by pallor, cyanosis, bradycardia, or hypotonia in the term infant; this term is reserved for infants with ALTE in whom no plausible etiology is identified.

Apnea of prematurity: pathologic apnea associated with preterm delivery; usually resolves by 37 weeks' gestation but may continue several weeks beyond term

Periodic breathing: breathing pattern in which three or more pauses occur, each lasting more than 3 seconds, with less than 20 seconds of normal respiration between pauses

Sudden infant death syndrome: sudden death in a child without historical, physical, laboratory, or thorough postmortem findings that explain the cause of death

Information from reference 1.

TABLE 2
Diagnoses Made in Children with an Apparent Life-Threatening Event

Idiopathic (approximately 50 percent)	Respiratory
GI (most common, up to 50 percent of diagnosed cases)	Vocal cord abnormalities, adenoid vegetations
Gastroesophageal reflux	Laryngotracheomalacia
Gastric volvulus	Airway obstruction resulting from congenital abnormalities
Intussusception	Foreign-body aspiration
Swallowing abnormalities	Cardiac (up to 5 percent)
Other GI abnormalities	Arrhythmia
Neurologic (approximately 30 percent)	Long QT syndrome
Seizure disorder	Wolff-Parkinson-White syndrome
Febrile seizure	Congenital heart disease
CNS bleeding	Myocarditis
Neurologic conditions affecting respiration (Budd-Chiari syndrome, hindbrain malformation, brainstem malformation)	Cardiomyopathy
Vasovagal reflexes	Metabolic abnormalities (less than 5 percent)
Hydrocephalus	Inborn errors of metabolism
CNS infection	Endocrine, electrolyte disorders
Ventriculoperitoneal shunt malfunction	Other infections
Malignancy	Urinary tract infection
Respiratory (approximately 20 percent)	Sepsis
Respiratory compromise from infection, respiratory syncytial virus, pertussis, mycoplasma, croup, other pneumonias	Child abuse (less than 5 percent)
Obstructive sleep apnea	Munchausen syndrome by proxy (suffocation, intentional salt poisoning, medication overdose, physical abuse, head injury)
Breath-holding spells	Smothering (unintentional or intentional)
Conditions affecting respiratory control (prematurity, central hypoventilation)	Other
	Food allergy (uncommon)
	Anaphylaxis
	Medication (prescription, over the counter, herbal remedies)

GI = gastrointestinal; CNS = central nervous system.
 Information from references 1, 2, and 4 through 15.

Etiology

The underlying etiology of these events varies. An ALTE should be viewed as a manifestation of other conditions rather than a diagnosis in and of itself. Uncovering the cause of the ALTE is important: in one half of patients, an etiology is found, implying that there is a potential for intervention that could eliminate further events. In the remaining patients, a specific diagnosis is never made, placing them in the “idiopathic” category. This may indicate the onset of a serious underlying condition that requires timely evaluation and treatment to reduce the rates of morbidity and mortality (Table 2).^{1,2,4-15}

Evaluation

It is important that physicians who care for children take the history of ALTE seriously and arrange for immediate evaluation. Because these children can be diagnosed with a wide variety of conditions, the work-up may be extensive.

The evaluation of the infant with an ALTE begins with a careful history of the event, the circumstances surrounding the event, and any observations made by the caregiver, as well as the resuscitative measures used.² The history from the caregiver in this frightening and emotional situation may be unreliable; however, there may be important clues to the underlying precipitating event.

TABLE 3

Historical Information to Obtain in Children with Apparent Life-Threatening Events

Description of event (chief complaint)

Condition of child: awake or asleep, position of infant (prone versus supine or on side), location of child (crib, parent's bed, baby seat, other), bedclothes, blankets, pillows

Activity at the time of the event: feeding, coughing, gagging, choking, vomiting

Breathing efforts: none, shallow, gasping, increased

Color: pallor, red, purple, blue, peripheral, whole body, circumoral

Movement and tone: rigid, tonic-clonic, decreased, floppy

Observations of productive cough, vomiting: mucus, blood, or noise (silent, cough, gag, wheeze, stridor, crying)

Duration of the event: Length of time required to reinstate regular breathing and normal behavior or tone or length of time of resuscitation

Interventions (in order)

None

Gentle stimulation

Blowing air in face

Vigorous stimulation

Mouth-to-mouth breathing

Cardiopulmonary resuscitation by medically trained person

History of present illness

Ill in days or hours leading up to event

Fever

Poor feeding

Weight loss

Rash

Irritability, lethargy

Contact with someone who is sick, medications administered, immunization

Medical history

Prenatal history; use of drugs, tobacco, or alcohol during pregnancy

Small for gestational age, prematurity

Birth history: birth trauma, hypoxia, presumed sepsis

Feeding history: gagging, coughing, poor weight gain

Developmental history: appropriate milestones

Previous admissions, surgery, apparent life-threatening event

Accidents (being dropped or tossed; possibility of trauma)

Family history

Congenital problems, neurologic conditions, neonatal and child deaths

Smoking in the home

Cardiac arrhythmia

Sudden infant death syndrome

Information from references 2 through 4.

Table 3²⁻⁴ outlines historical information that is helpful in assessing the event.

After the history is obtained, the physical examination must include a general impression of the child, noting any dysmorphic features or obvious malformations. Height, weight, and head circumference measurements should be plotted on appropriate growth charts. A careful neurologic examination, including assessment of muscle tone and physical findings appropriate for the age of the child (e.g., head lag, posturing, motor abilities, eye tracking, social smile), should be performed. Abdominal findings and any sign of trauma or bruising also should be noted. In one study,⁶ retinal hemorrhages leading to a diagnosis of child abuse were observed during the dilated ophthalmologic examinations of two children. This finding prompted the investigators to include this examination as standard in the work-up at their center.

Laboratory and imaging studies should be performed on the basis of the history and physical examination.² Baseline tests for the underlying causes of ALTEs are listed in Table 4.²⁻⁴ Recommendations for a minimum work-up are difficult because each case is highly individualized.² Because gastrointestinal and infectious causes are common, recommended laboratory studies include complete blood count and appropriate cultures, as well as investigation for gastroesophageal reflux disease (GERD) in children who have a history of gagging, spitting up, vomiting, or coughing, or who have difficulty feeding.²⁻⁴ High-yield tests in patients with an ALTE are complete blood count (infection, anemia), serum bicarbonate and lactate (acidosis), urinalysis (infection), chest radiography (occult respiratory infection), pertussis, and RSV.⁴ In one study,⁵ investigators reported that lower serum bicarbonate and higher serum lactate levels were predictive of more serious conditions. However, not all laboratory, imaging, or other studies need to be performed in all children.³

Once an underlying etiology is identified, further testing is not indicated unless ALTEs continue despite appropriate intervention and treatment of the presumed

TABLE 4
Baseline Tests to Assess Underlying Causes of Apparent Life-Threatening Events in Children

<i>Evaluation</i>	<i>Diagnosis</i>
Chest radiography*	Infection, cardiomegaly
Complete blood count and differential*	Infection, anemia
Electrocardiography*	Arrhythmias, QT abnormalities
Electrolytes, magnesium, calcium*	Metabolic diseases, dehydration
Serum bicarbonate*	Hypoxia, acidosis
Serum lactate*	Hypoxia, toxins (salicylates, ethylene, glycol, methanol, ethanol) Hereditary enzyme defects (glycogen storage type I, fatty acid oxidation defects, multiple carboxylase deficiency, methylmalonicaciduria)
Urinalysis*	Infection
Ammonia	Inborn errors of metabolism, liver disease
Arterial blood gases	Acidosis
Blood cultures	Sepsis
Brain imaging (computed tomography, magnetic resonance imaging)	Trauma, neoplasm, congenital abnormalities
Liver function studies	Hepatic dysfunction
Lumbar puncture/spinal fluid analysis, culture	Meningitis
Nasal swab for RSV	Respiratory infection, RSV
Nasopharyngeal aspirate	Upper airway infections
Pertussis culture, serology	Pertussis infection
Stool cultures	Infection
Toxicology screen	Accidental or intentional overdose
Urine toxicology screen	Screen for metabolic disorders
Radioisotope milk scan/esophageal pH	Gastroesophageal reflux
Radiologic skeletal survey	Previous or current fractures

*—Those considered by some experts to be minimal diagnostic evaluations.⁴

RSV = respiratory syncytial virus.

Information from references 2 through 4.

cause.² Important points to remember are dual diagnoses in children and the possibility of child abuse. For example, in a group of infants with other gastrointestinal disorders, GERD also was present.⁷ British researchers reported positive pertussis titers in children with RSV.¹⁶ Child abuse also may play a role in children who present with an unexplained ALTE. In a study¹⁷ of children requiring cardiopulmonary resuscitation (CPR), investigators reported that 18 of 77 children in whom a diagnosis was reached had been deliberately suffocated; another

seven were victims of Munchausen syndrome by proxy. If a child presents repeatedly with episodes of ALTEs but has negative work-up results, Munchausen syndrome by proxy should be considered. This is especially true when the caregiver alone has observed the events. Other historical clues may include a caretaker's personal history of odd medical complaints. Events of children in these situations should resolve when they are monitored in a protected setting or when they are removed from the custody of their primary caregiver.

Management

The challenge for the physician is to manage the immediate event, discern the underlying cause of the event when possible, educate parents, and determine the need for further monitoring.

Initial management of the child with an ALTE begins before hospitalization, when the caretaker contacts the physician. The physician or office staff should be able to instruct the family about providing immediate care in the home and determine if the child should be brought in right away for evaluation. At home, if gentle stimulation fails to arouse the child, the caretaker should try more vigorous stimulation and provide CPR if necessary.

In some cases, observation of the infant in the hospital demonstrates a normal pattern of breathing or “startles” that represent normal infant behavior. Physical examination and laboratory data in these children are normal. Generally, these infants may be discharged home with reassurance and usual well-child care.²

For children who present with more complicated resuscitation efforts or with abnormal results on physical examination, many physicians recommend the conservative approach of admission, inpatient work-up, and monitoring.^{2,4,5,8,9,18} Once a diagnosis is made, intervention should resolve further events. If not, the diagnosis should

be revisited. Because reflux is common in infants, ALTEs may recur if GERD had been a confounding rather than a causative factor. Management of GERD includes feeding management (i.e., keeping the child upright after feeding, adequate burping, raising the head of the bed for sleep, placing the child on his or her side for sleep, thickening formula), medical management with histamine H₂-receptor antagonists and, in severe cases, surgical intervention (Nissen fundoplication).¹⁹

Despite work-up and inpatient monitoring, 50 percent of children remain undiagnosed. Consensus guidelines recommend home monitoring in children who have experienced a severe ALTE or children with an unclear diagnosis.^{1,3,20}

If home monitoring is considered, cardiorespiratory monitors should come equipped with event monitor recording capabilities.²⁰ Parents require supportive care and education for situations in which monitoring is used in the home. Physicians should inquire about parental expectations of home monitoring, and parents need to be advised that home monitoring has never been demonstrated to reduce the rate of mortality caused by SIDS.²⁰

Outcome

The overall outcome of children who experience an ALTE depends on the subgroup into which they fall. Children with an ALTE as a heralding event for a serious underlying medical condition, such as seizure disorder or other neurologic condition, have a higher mortality rate and a less optimal outcome.⁴ A review of mortality data from studies performed between 1972 and 1989 showed an overall mortality rate of zero to 4 percent in childhood.⁴ In terms of the risk for SIDS, ALTEs are observed in a small number of children who eventually die of SIDS. Various studies report the percentage of children who died of SIDS with a previous ALTE to be between 4 and 10 percent, although one study that focused on children of nurses reported that 27 percent of SIDS victims exhibited previous ALTEs.^{1,4} The risk of SIDS in children with an ALTE increases

Munchausen syndrome by proxy should be considered if the work-up is negative but apparent life-threatening events continue to occur.

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when the event is linked to central hypoventilation syndrome, seizure disorders, and cardiac arrhythmias including sinus bradycardia, Wolff-Parkinson-White syndrome, and prolonged QT syndrome.²¹

In terms of morbidity, although short-term follow-up studies in patients with an ALTE indicate some deficiencies in development, long-term neurodevelopmental, cognitive, and gross motor developmental skills appear to be the same as in control patients.²²⁻²⁶ In a study²³ of children with an idiopathic ALTE only, no neurodevelopmental delays were noted. In another study,²⁵ researchers followed a group of children with ALTEs who were evaluated at two years of age and again at six to 10 years of age. Children initially showed more aggressiveness, temper tantrums, and social isolation compared with control patients. However, these effects resolved at follow-up. Long-term cognitive, gross motor, or fine motor deficits were not identified.

Controversy in ALTE

Controversy still surrounds the relationship between ALTE syndrome and SIDS. ALTE was once thought to be “near-miss SIDS.” In an extensive review of historical data of children who experienced SIDS and ALTEs, of more than 300 variables, only 15 pointed to differences between the two groups.²⁷ This seems to support the notion that SIDS and ALTEs have much in common. On the other hand, in the majority of patients SIDS occurs without warning and without previous ALTEs. Approximately 7 percent of infants who die from SIDS have a history of ALTEs.¹ Unlike SIDS, there has been no drop in the incidence of ALTEs paralleling the Back to Sleep campaign.²⁸ Regardless, children with ALTEs do have a greater likelihood of sudden death. Further studies are needed to clarify this relationship.

Home monitoring is controversial as well. False alarms, parental anxiety, inappropriate use of monitors, and inadequate training and understanding by caregivers make home monitoring difficult. The National Institutes of Health Consensus document of 1986 recommended home monitoring for

children with severe idiopathic ALTEs, those who require vigorous stimulation or CPR, children with two or more siblings who died from SIDS, and symptomatic premature babies.¹ Follow-up recommendations for monitoring described by the American Academy of Pediatrics indicated that home monitoring may be appropriate for children with ALTEs.²⁰ This document reiterated the lack of efficacy of home monitoring in the prevention of death and the absolute need to counsel parents in this regard.

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The majority of cases of sudden infant death syndrome occur in children without a history of apparent life-threatening events.

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