

# Apparent life-threatening event: a review

*Evento com aparente risco de morte: uma revisão*

*Evento con aparente riesgo de muerte (alte): una revisión*

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## ABSTRACT

**Objective:** To perform a critical review by gathering all the available information about apparent life-threatening events.

**Data sources:** Bibliographic review of the articles published in Portuguese, English and Spanish from the electronic databases Medline, Lilacs and SciELO, using the key-words: apparent life-threatening events, apparent life-threatening event, infant, apnea, monitoring, and cyanosis.

**Data synthesis:** Apparent life-threatening events define sudden events with, a combination of apnea, color change, and marked change in the muscle tone, that have various underlying causes. The real incidence remains unknown, and it affects infants from 11 to 12 weeks of age. There is no association between apparent life-threatening events and sudden infant death syndrome. There are many possible causes for the events, and they must be investigated even in apparently healthy infants, because the presence of a severe underlying disease associated with the event is possible. If the cause of the apparent life-threatening events is found, it must be treated properly. If there is no explainable cause, the event is considered idiopathic and generally has a benign course.

**Conclusions:** It is necessary to investigate all the infants taken to the pediatric emergency unit after experiencing an apparent life-threatening event, since there is the risk of morbidity caused by an underlying disease or the event itself, as well as subsequent mortality. Consensus guidelines about the investigation in apparently healthy infants who experienced apparent life-threatening events are not available. Most authors recommend that careful observation and hospital monitoring should be performed for at least for 24 hours after the event.

**Key-words:** infantile apparent life-threatening event; infant; death; apnea.

## RESUMO

**Objetivo:** Realizar uma revisão crítica reunindo informações disponíveis a respeito dos eventos com aparente risco de morte.

**Fontes de dados:** Revisão bibliográfica dos artigos (em português, inglês e espanhol) obtidos dos bancos de dados eletrônicos Medline, Lilacs e SciELO, utilizando as palavras-chave: eventos com aparente risco de morte, evento com aparente risco de vida infantil, lactente, apneia, monitorização e cianose.

**Síntese dos dados:** Os eventos com aparente risco de morte são súbitos e caracterizados por uma combinação de apneia, alteração na coloração da pele e tônus muscular, com inúmeras causas subjacentes. Sua incidência verdadeira é desconhecida e a faixa etária mais acometida é de 11 a 12 semanas. Não há correlação entre o evento com aparente risco de morte e a síndrome da morte súbita do lactente, embora já tenham sido consideradas manifestações da mesma doença. Muitas vezes, o lactente tem aparência saudável ao ser avaliado pelo pediatra após apresentar eventos com aparente risco de morte, porém, isso não afasta a possibilidade de existir uma doença grave associada ao evento, que deve ser investigada e tratada. Quando não são encontradas as causas, o evento é idiopático, geralmente com boa evolução.

**Conclusões:** É necessário investigar os lactentes levados ao pronto-socorro após apresentarem eventos com aparente risco de morte, devido ao risco de sequelas e mortalidade. Não há uma padronização das condutas a serem realizadas diante de um lactente com aparência saudável que tenha evento com aparente risco de morte, mas recomenda-se que o paciente seja internado e a causa do evento, investigada. A observação e o monitoramento em ambiente hospitalar devem ocorrer no mínimo 24 horas após o evento.

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**Palavras-chave:** evento com aparente risco de vida infantil; lactente; óbito; apneia.

## RESUMEN

**Objetivo:** Realizar una revisión crítica, reuniendo las informaciones disponibles respecto a los Eventos con Aparente Riesgo de Muerte (*ALTE - Apparent life-threatening event*).

**Fuentes de datos:** Revisión bibliográfica de los artículos (en portugués, inglés y español) obtenidos de las bases de datos electrónicas MEDLINE, LILACS y SCIELO, utilizándose las palabras clave *ALTE*, evento con aparente riesgo de vida infantil, lactante, apnea, monitorización y cianosis.

**Síntesis de los datos:** Los *ALTE* (*apparent life-threatening event*) son eventos súbitos y caracterizados por una combinación de apnea, alteración en la coloración de la piel y tono muscular, con innúmeras causas subyacentes. Su incidencia verdadera es desconocida y la franja de edad más acometida es de 11 a 12 semanas. No hay correlación entre *ALTE* y *SIDS* (Síndrome de la Muerte Súbita del Lactante), aunque ya hayan sido consideradas manifestaciones de la misma enfermedad. Muchas veces, el lactante tiene apariencia sana al ser evaluado por el pediatra después de presentar *ALTE*, pero eso no aleja la posibilidad de que exista una enfermedad grave asociada al evento, la cual se debe investigar y tratar. Cuando no se encuentran causas, el evento es idiopático, generalmente con buena evolución.

**Conclusiones:** Es necesario investigar los lactantes llevados a la emergencia después de presentar *ALTE*, por riesgo de secuelas y de mortalidad. No hay una estandarización de las conductas a tomar frente a un lactante con apariencia sana que presentó *ALTE*, pero se recomienda que se interne el paciente y se investigue la causa del evento. La observación y monitorización en ambiente hospitalaria debe ocurrir por un mínimo de 24 horas después del evento.

**Palabras clave:** evento con aparente riesgo de vida infantil; lactante; óbito; apnea.

## Introduction

The term Apparent Life-Threatening Event (*ALTE*) was first defined in 1986 by the National Institutes of Health in the United States. The definition was the result of a consensus reached at a conference on infantile apnea and home monitoring, which established the term *ALTE* and ended the use of terms such as “aborted crib death”

and “near-miss *SIDS*”. The conference was organized in response to the dilemma caused by the difficulty of defining the differences between *ALTE*, Sudden Infant Death Syndrome (*SIDS*) and apnea of infancy, even though the lack of pathophysiologic correlations means distinctions are obligatory<sup>(1-4)</sup>. In Portuguese, terms that back-translate as “event possibly threatening life” (*episódio de possível ameaça à vida*), “event apparently involving risk to life” (*evento com aparente risco de vida*) and “event apparently involving risk of death” (*evento com aparente risco de morte*) have been used as translations of the English term “apparent life-threatening event”<sup>(5-7)</sup>.

The following definitions were established by the 1986 consensus with certain modifications based on the the results of later studies:

- Apnea: Cessation of respiratory air flow. The cause of the respiratory pause may be central, muscular, obstructive or mixed. Short (15 seconds), central apnea can be normal at all ages<sup>(2)</sup>.
- Apnea of Prematurity: An unexplained episode of cessation of breathing for 20 seconds or longer, or a shorter respiratory pause associated with bradycardia, cyanosis, pallor, and/or marked hypotonia. The term should be reserved for infants up to 37 weeks’ post-conception gestational age. In some cases apnea of prematurity may persist beyond 37 weeks, particularly in newborn infants with less than 28 weeks’ gestational age<sup>(2-3)</sup>.
- *ALTE* (Apparent Life-threatening Event): An episode that is frightening to the observer and that is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking or vomit reflex<sup>(2)</sup>. After an *ALTE*, the infant’s course is often benign, but there is a risk of subsequent morbidity and mortality caused either by the event itself or by the subjacent disease that provoked the event<sup>(3,8-9)</sup>.
- Apnea of Infancy: An unexplained episode of cessation of breathing for 20 seconds or longer, or a shorter respiratory pause associated with bradycardia, cyanosis, pallor, and/or marked hypotonia. The terminology “apnea of infancy” generally refers to infants who are greater than 37 weeks gestational age at onset of pathologic apnea. Apnea of Infancy should be reserved for those infants for whom no specific cause of *ALTE* can be identified. In other words, these are infants whose *ALTE* was idiopathic and believed to be related to apnea<sup>(2-3,10)</sup>.

- SIDS (Sudden Infant Death Syndrome): The sudden death of any infant or young child, which is unexplained by history and in which a thorough postmortem examination fails to demonstrate an adequate explanation of cause of death<sup>(2)</sup>.

The objective of this review article is to identify information on ALTE in the literature and use it to develop an instrument designed to improve the care given to infants who present with ALTE.

## Methods

Searches were run on PUBMED, SCIELO and LILACS databases to identify publications in English, Portuguese or Spanish using the following keywords: ALTE, apparent life-threatening event, infant, apnea, monitoring and cyanosis. A total of 59 articles published between 1984 and 2011 and related to ALTE were identified and 55 of these, covering clinical manifestations, epidemiology, risk factors, admission criteria, clinical course, etiology, treatment, and outpatients follow-up of infants suffering ALTE, were selected for review. These studies included retrospective and prospective designs, case descriptions, review articles, consensus statements and metanalyses (no randomized studies exist) and have a variety of sample sizes and evidence levels.

## Results

The results of the major studies are in Table 1 along with the description of the number of patients included, percentage of death, and ALTE recurrence and main etiologies. We highlight a great variation in the prevalence of the main etiologies (respiratory, gastrointestinal, and idiopathic) in the different studies.

## Discussion

### Epidemiological aspects of ALTE

#### Incidence

The true incidence of ALTE in the general population of infants less than 12 months old has not yet been clearly established<sup>(4)</sup>. Different authors present their data in different ways: some as a proportion of the total number of visits to emergency by children under 1 year; others as a proportion of hospital admissions in the same age group; and still others report the

figures with relation to the number of live births at the same place during a given period. Thus, the incidence of ALTE is variously given as 0.2 to 1.9% of infants less than 1 year old<sup>(15-17)</sup>; as 0.6 to 5.0 in every 1000 live births<sup>(4,17-20)</sup>; and as 2.3 to 4.2% of admissions resulting from visits to an emergency service<sup>(6,20)</sup>.

With regard to age at time of ALTE, studies show that the age of peak incidence is from 11 to 12 weeks of life, ranging from events that occur during first hours of life to events occurring up to the end of the first year, since the majority of these authors do not consider events affecting children over 1 year to be ALTE<sup>(6,8,19,21-23)</sup>. Notwithstanding this general trend, some samples had peak ALTE incidence at 7–8.5 weeks of age<sup>(9,24)</sup>.

#### Risk factors

The studies listed the following risk factors for ALTE: age greater than 2 months<sup>(25)</sup>, prior occurrence of ALTE<sup>(9)</sup>, prematurity, late delivery and comorbidities<sup>(19)</sup>. There was not, however, any evidence that apnea of prematurity (which tends to disappear between 34 and 36 weeks' corrected gestational age) is a risk factor for apnea of infancy or, therefore, for ALTE<sup>(2,17,24)</sup>. Notwithstanding, apnea events are more frequent and more symptomatic among infants with post-conceptual ages below 34 weeks and cease after 43 weeks' corrected gestational age<sup>(26)</sup>. On the other hand, late delivery (at gestational ages greater than 42 weeks) is also considered a risk factor associated with occurrence of ALTE<sup>(19)</sup>.

### ALTE and SIDS

Although infants with a history of ALTE used to be considered at increased risk of SIDS and studies show that 7 to 10% of SIDS victims have suffered some type of ALTE previously<sup>(15,16,27,28)</sup>, there does not appear to be any evidence that ALTE and SIDS are facets of the same disease, or even that infants who suffer ALTE are at greater risk of dying from SIDS<sup>(1,3,9,16,19,29,30)</sup>.

Further reinforcing the hypothesis that ALTE and SIDS are different diseases, studies show that ALTE and SIDS have different ages of incidence, with SIDS being more frequent around 3 to 5 months, whereas ALTE's incidence peaks 1 to 3 months earlier<sup>(12-15,18,27,31)</sup>.

Furthermore, the SIDS risk factors that have already been identified (male sex, low birth weight, prematurity, seasonal distribution of cases (winter), mothers smoking while pregnant, poor socioeconomic conditions, adolescent mothers, single mothers, multiple pregnancies and high parity) were not found

Table 1 - Results dos principal studies analyzed

Author	Type of study	n	Mean age (weeks)	Deaths (%)	Recurrent ALTE (%)	ALTE etiologies (%)	Idiopathic ALTE (%)
Anjos <sup>(6)</sup>	prospective	30	15.4	3.3	73.0	Respiratory: 6.6; Neurological: 13.3; Gastrointestinal: 23.3; Others: 6.8	50.0
Romaneli <sup>(7)</sup>	retrospective	145	15.0	7.6	44.1	Respiratory: 37.3; Neurological: 4.2; Gastrointestinal: 4.9; Cardiocirculatory: 4.2; Others: 14.2	35.2
Davies <sup>(9)</sup>	prospective	65	7.0	0	12.0	Respiratory: 26.5; Neurological: 9; Gastrointestinal: 26.0; Cardiocirculatory: 3.0; Others: 12.5	23.0
Etzaniz <sup>(17)</sup>	prospective	50	8.4	2.0	8	Respiratory: 22.0; Neurological: 4.0; Gastrointestinal: 10.0; Cardiocirculatory: 2; Others: 4.0	58
Kiechl-Kohlendorfer <sup>(18)</sup>	prospective	164	8.0	-	37.8	Respiratory: 29.0; Neurological: 1.0; Gastrointestinal: 22.0; Cardiocirculatory: 2.0; Others: 1.5	44.5
Semmekrot <sup>(19)</sup>	prospective	110	11.4	0	10.0	Respiratory: 24.6; Neurological: 0; Gastrointestinal: 37.3; Cardiocirculatory: 2.7; Others: 7.4	28.0
Samuels <sup>(21)</sup>	prospective	157	12.0	1.9	70.7	Neurological: 6.3; Others: 42.8	50.9
Altman <sup>(22)</sup>	prospective	243	12.0	1.2	46.5	Respiratory: 35.3; Neurological: 10.6; Gastrointestinal: 29.6; Cardiocirculatory: 0.8; Others: 23.7	16
Brand <sup>(25)</sup>	retrospective	243	11.7	-	2.0	Respiratory: 33.3; Neurological: 8.2; Gastrointestinal: 29.2; Others: 13.3	16
Bonkowsky <sup>(32)</sup>	retrospective	471	9.4	0.4	-	Respiratory: 28.2; Neurological: 9.7; Gastrointestinal: 40.3; Others: 8.6	13.2

ALTE: Apparent life-threatening event.

among infants who suffered ALTE<sup>(13,29)</sup>. The “back to sleep” campaign to persuade carers to put infants to bed in the supine position achieved a 30 to 50% reduction in SIDS mortality, but did not impact on the incidence of ALTE during the same period, indicating that ALTE and SIDS are distinct entities<sup>(3,13,31)</sup>.

### ALTE and acquired morbidity

Infants who suffer ALTE episodes generally enjoy a benign course, with no sequelae related either to the event or to its cause and with little chance of the symptoms recurring<sup>(3,8-10,27)</sup>. However, around 5% of ALTE cases are severe events involving prolonged periods of apnea and bradycardia and lead to neurological sequelae, such as non-progressive chronic encephalopathy, delayed neuropsychomotor development, epilepsy and behavioral problems, although it cannot be proven that these sequelae are exclusively caused by the event itself, since they could be associated with the subjacent disease that triggered the ALTE<sup>(2,30,32-34)</sup>.

The rate of recurrence of ALTE can be higher than the incidence of ALTE in the general population, even among infants who did not suffer sequelae from previous episodes<sup>(20)</sup>.

### ALTE and mortality

The mortality rate linked with ALTE is unknown, but it is known that it is not safe to assume that an infant is not at risk of a subsequent fatal event once the cause of the original episode has been identified<sup>(2,3,17,34)</sup>.

Rates of death during follow-up among infants monitored after suffering ALTE vary greatly in the studies analyzed, ranging from zero to 7.6%<sup>(7,17-19-21,32)</sup>.

### Pathophysiology of ALTE

The mechanisms that lead to the manifestations of ALTE can be explained by some of the phenomena shown to be causes of consequences of the subjacent disease, such as apnea. Apnea (whether it has a neurological cause or is due to airway obstruction, or both) causes a reduction in oxygenation and diverted blood flow, leading to other manifestations of ALTE, such as cyanosis, pallor, flushing and muscle hypotonia<sup>(3)</sup>.

Muscle tone effects like hypotonia, hypertonia and rhythmic movements of the extremities may originate in the central nervous system (CNS) or may be secondary to other processes, such as crying that triggers the vasovagal reflex, or even convulsive crises<sup>(3)</sup>. One study has shown that initially there are electroencephalographic abnormalities which are then followed by one or more pauses in respiratory movements, culminating in a fall in peripheral oxygen

saturation below 60%, leading to clinical cyanosis with sinus tachycardia, lasting 40 seconds on average<sup>(35)</sup>.

Other clinical manifestations of ALTE, such as choking, coughing and the vomit reflex are protective reflexes triggered by stimuli to the nasopharynx, hypopharynx, larynx and lower respiratory tract. These reflexes temporarily interrupt ventilation, leading to further manifestations of ALTE such as facial flushing, caused by the increase intrathoracic pressure, and hypotonia, which may be caused by hypoxia, vagus reflex or both<sup>(3,10)</sup>. When choking occurs, the contraction of the larynx caused by irritation to the glottis may spread to the upper airways, causing upper respiratory obstruction, and to the lower airways, causing bronchial obstruction. Prolonged hypoxia provokes ischemia and generalized endothelial damage, leading to hemorrhagic phenomena, coagulopathy, breakdown of the blood brain barrier and cerebral edema<sup>(10)</sup>. It is therefore possible that ALTE that last 30 seconds or more and recurrent ALTE may cause venous pressure in the retina to rise, leading to hemorrhage. However, it has not yet proved possible to demonstrate the occurrence of retinal hemorrhage solely as a result of these events<sup>(36)</sup>.

### Number and duration of ALTE episodes before seeking care

In general, ALTE episodes are of short duration, lasting less than 5 minutes, and recovery is complete and spontaneous<sup>(17,19,27)</sup>. The majority of infants are taken to emergency services by their carers immediately after their first event<sup>(7,19,22)</sup>. Notwithstanding, many (44 to 46.5%) are only taken to health services after two or more episodes<sup>(7,22)</sup>.

### Infant activity prior to occurrence of ALTE

Generally, ALTE take place at home without warning and during any type of activity, especially when sleeping, waking up or feeding, but it has been reported that some infants exhibit signs such as vomiting, diarrhea and refusal of food during the 24 hours preceding an ALTE<sup>(2,7,9,18,19,23,27,33)</sup>.

### Admission of infants at emergency services

The first physician to see the child should search for evidence for any type of subjacent disease that could have provoked the ALTE, carefully asking about symptoms presented by the infant and interventions needed for recovery, before conducting a detailed clinical assessment<sup>(3,8,13,20,25,27)</sup>.

Frequently, infants recover rapidly and completely from their ALTE and clinical examinations are typically normal. This does not, however, rule out the possibility of a severe

subjacent disease<sup>(3,7,9,17,22,27,29)</sup>. The severity of symptoms described by observers should be considered important information in these cases<sup>(9,17,19,20,29)</sup>. In around 10% of cases, emergency procedures such as chest compressions, ventilation with bag-valve-mask, oral endotracheal intubation and adrenaline infusions are needed during the first examination<sup>(7,8,22)</sup>.

## Investigation

It is not consensus that all infants suffering ALTE should be admitted for investigation. There are authors who believe that only infants less than 30 days old or repeat ALTE sufferers should be admitted if the first clinical assessment is normal<sup>(3,20,37)</sup>. However, the majority agree that admission for a minimum of 24 hours can provide data that is of great value to determining the event's etiology, severity, clinical course and risk of sequelae<sup>(3,5,26-27,30,32,33)</sup>. Furthermore, observation and monitoring of infants in a hospital environment makes their carers feel more secure and provides an opportunity to train them in cardiorespiratory resuscitation. Some authors consider that such training is a precondition for discharging infants from hospital after ALTE<sup>(3,5,8,27)</sup>.

The physician responsible for the first consultation after an infant suffers an ALTE is therefore faced with a major dilemma, since with the exception of certain minor details of the event's history (coughing, choking, stridor, fever, physical effort or vomiting preceding the ALTE), they will not have any clues to indicate where to start to investigate an apparently healthy infant<sup>(3-5,8,25,27,33,38)</sup>. Some authors consider that the decision to admit to hospital should be based on the severity of the event described, the findings of the initial physical examination and the experience of the first physician to see the infant<sup>(8,27)</sup>. Pediatricians who have had previous experience with cases of ALTE that had unfavorable outcomes are more likely to admit infants, even those who appear healthy. Those who have not, tend to request fewer work-up tests and tend to ignore the majority of the entities in the differential diagnosis of ALTE<sup>(39)</sup>.

The objective when investigating an infant who has suffered an ALTE is to determine whether the event has an underlying cause. Although there are countless proposals for protocols, there is no consensus on which tests should be requested or even what the order of investigations should be. In general, the larger the number of tests that are requested, the greater the likelihood of detecting an abnormality, which in turn may or may not be the cause of the ALTE<sup>(3,5,20,25)</sup>.

In view of this, tests are suggested that should at least be capable of identifying the most common and most serious causes. Initially, heart monitoring and continuous transcutaneous oximetry can be set up in the emergency room<sup>(3,8,13)</sup>. Initial laboratory tests should include a full blood count and venous blood gas analysis and serum lactate, glycemia and electrolytes should be assayed<sup>(3-5,9,13,20,21,27)</sup>. Urine should be tested for signs of urinary infection, urine organic acids or reducing substances; and toxicology for drugs and psychoactive substances is also suggested<sup>(5,8,9,40)</sup>. Chest X-rays can also be taken on admission<sup>(4,9)</sup>.

In cases where infants have respiratory symptoms, consideration should be given to taking a nasopharynx swab to test for pertussis and respiratory syncytial virus. Where laryngeal stridor has been present for a prolonged period, cervical and thoracic X-rays, contrast esophagram, nasopharyngeal laryngoscopy and bronchoscopy can be considered, although the last two are not recommended for initial work up<sup>(3,41)</sup>.

Cranial tomography, transfontanelar ultrasound and ophthalmoscopy to rule out bleeding in the CNS are recommended by some specialists (especially if violence is suspected), while an electroencephalogram and polysomnography can complement imaging exams for neurological investigation<sup>(3,9,13,28)</sup>.

An electrocardiogram should be requested if arrhythmia is suspected, especially if peripheral perfusion is poor. If there is a possibility that the long QT syndrome is present then continuous monitoring with a Holter may be indicated. If there is a history of tiring while suckling and frequent flushing, a chest X-ray should be taken and arterial blood pressure and peripheral oxygen saturation should be measured in all four limbs to rule out aortic coarctation<sup>(3,5,9,21)</sup>.

If the event occurred during feeding, the possibility of a disorder of deglutition should initially be investigated by video swallow study, followed by neurological assessment and tests for gastroesophageal reflux disease (GERD) using esophageal pH monitoring, barium contrast swallow, esophageal manometry or scintigraphy with isotope-labeled milk (milk scan)<sup>(3,9,20)</sup>.

Infants who are suspected of suffering from primary or secondary apnea should be put on cardiorespiratory monitoring, which may reveal trigger factors such as sleeping/feeding and the presence of arrhythmia<sup>(5)</sup>.

## Etiologies of ALTE

An apparent life-threatening event can be a symptom of countless diseases<sup>(5,6,27)</sup>. The underlying etiologies may

be digestive, neurological, cardiocirculatory, metabolic, endocrine or infectious<sup>(13,19,22)</sup>. Other causes have also been described, including parental mental disease and negligence or violence<sup>(10,19,22)</sup>.

Although a large number of diseases can manifest with ALTE, the causes of around a half of cases remain unidentified, even after careful investigation of patients who have been admitted to hospital<sup>(2,7-9,15,20,27)</sup>. When no clinical or surgical causes are found to explain the occurrence of an ALTE, the episode is defined as idiopathic, with percentages varying from 16 to 44% of cases<sup>(3,6,7,17,18,22,27)</sup>.

Studies have demonstrated that a wide range of diagnoses are associated with ALTE in apparently healthy infants, such upper airway infections, croup, choking, foreign body aspiration, whooping cough, acute viral bronchiolitis, bacterial pneumonia, bacterial or aseptic meningitis, apnea of prematurity, upper digestive hemorrhage, patent ductus arteriosus, double aortic arch, supraventricular tachycardia, viral or bacterial sepsis, epilepsy, febrile convulsions, birth injury, neonatal jaundice, inborn errors of metabolism, opioid intoxication, urinary tract infection, gastroesophageal reflux disease, Münchausen syndrome by proxy, drug intoxication, ischemic cerebrovascular accident, ventriculoperitoneal shunt dysfunction, CNS neoplasm, acute gastroenteritis and laryngomalacia<sup>(6,7,9,18,20,22)</sup>. Of these, the most commonly identified causes are acute viral bronchiolitis and gastroesophageal reflux disease<sup>(4,7,9,18,20,31)</sup>.

### Diseases of the gastrointestinal tract

Certain diseases of the gastrointestinal tract, such as intussusception, volvulus, infectious gastroenteritis and strangulated hernia can manifest with ALTE, but the most common is gastroesophageal reflux disease – GERD, with incidence rates as high as 40% among infants with ALTE in some studies<sup>(4,20,31,42)</sup>.

While GERD is often detected in infants who have suffered an ALTE, it is still necessary to consider whether it is merely a co-existing condition, since it may or may not be the primary cause of the event<sup>(8,27)</sup>. It is believed that up to 89% of infants with ALTE have GERD that can be detected by esophageal pH monitoring and milk scans, but generally confirmed episodes of reflux do not correlate with manifestations of ALTE<sup>(9,19,20)</sup>. Furthermore, other causes of ALTE can be mistaken for GERD, such as overfeeding by volume, which causes gastric hyperdistension and frequent regurgitations, leading to choking and episodes of aspiration<sup>(27)</sup>.

### Child abuse

It is believed that between 3 and 15.8% of ALTE episodes are related to child abuse<sup>(4,19,31,43)</sup>. Abused infants generally do not exhibit clinical evidence of abuse on initial examination and so this does not rule out a hypothesis of abuse<sup>(3,8,13,19-22,31,43)</sup>. Studies have demonstrated that cases of ALTE have been associated with intentional poisoning, intentional suffocation, shaken baby syndrome and Münchausen syndrome by proxy<sup>(3,8,13,20-22,43)</sup>. Therefore, signs of possible violence, such as bruising and hematoma, burns, fractures, retinal hemorrhage, subdural hematoma, diffuse axonal injury and cerebral edema must always be followed-up, although there are generally no signs of violence on initial examination<sup>(30,42-44)</sup>.

When signs suggestive of violence are present, it is important that the medical team takes care to correlate findings with the carers' accounts of what happened and establish the sequence of events. For example, it should be determined whether the infant was shaken in response to the ALTE, in an attempt at resuscitation, or if the infant had been healthy, was shaken and then suffered an ALTE as a result of injuries provoked by this aggression<sup>(10,19,22)</sup>. It is also important to inquire whether any medications had been administered to infants the active ingredients of which could be identifiable in urine tests<sup>(39,45,46)</sup>.

The American Academy of Pediatrics' Committee on Child Abuse and Neglect directs physicians to be alert to the possibility of abuse if ALTE are recurrent, if they always takes place under supervision by the same carer, if there is a history of other infants dying in the care of the same person or if the initial clinical examination finds blood from the infant's mouth or nose, which is suggestive of an attempt at suffocation<sup>(3,13,14,27)</sup>.

### Infections and epilepsy

Infections should also be considered as possible causes of ALTE, and tests should be conducted to rule out infections even if the infant is apparently healthy on initial clinical examination<sup>(37,47)</sup>. Respiratory infections are the most common, in particular respiratory syncytial virus infections<sup>(17,26,47-50)</sup>.

Disorders of a neurological nature are also found in infants after ALTE. Epilepsy is the principal etiology described, but central nervous system malformations have also been reported<sup>(21,27-28,51)</sup>.

### Home monitoring

It was hoped that home-use cardiorespiratory monitors would be of great utility for infants who had had ALTE,

as long as the infant's carers understood how they worked and were able to take the correct action if the monitor's alarm sounded<sup>(2)</sup>. However, while such monitors are effective instruments for detecting episodes of oxygen desaturation and arrhythmia, it was demonstrated that they did not affect morbidity or mortality from ALTE or SIDS<sup>(3,13,27,52)</sup>. Additionally, it was found that the monitors identified episodes of asymptomatic apnea not requiring intervention, which are common both among healthy infants and among those who have suffered an ALTE previously<sup>(26)</sup>. It was also found that lay people using these monitors were susceptible to confusing true ALTE with false alarms caused by incorrect connections, thereby generating additional anxiety, particularly during the first months of use, and making it necessary

to provide the families involved with psychological support<sup>(5,52-54)</sup>. As a result, the American Academy of Pediatrics recommends that home-use cardiorespiratory monitors should not be used to try to prevent ALTE or SIDS and that their use be restricted to preterm newborns with recurrent episodes of apnea, bradycardia and hypoxemia; infants with tracheostomies dependent on mechanical ventilation; and to infants with unstable airways, abnormal respiratory rhythms and symptomatic chronic lung disease<sup>(55)</sup>.

### Comments

The huge range of diseases that can be associated with ALTE cases means that there is no consensus on best

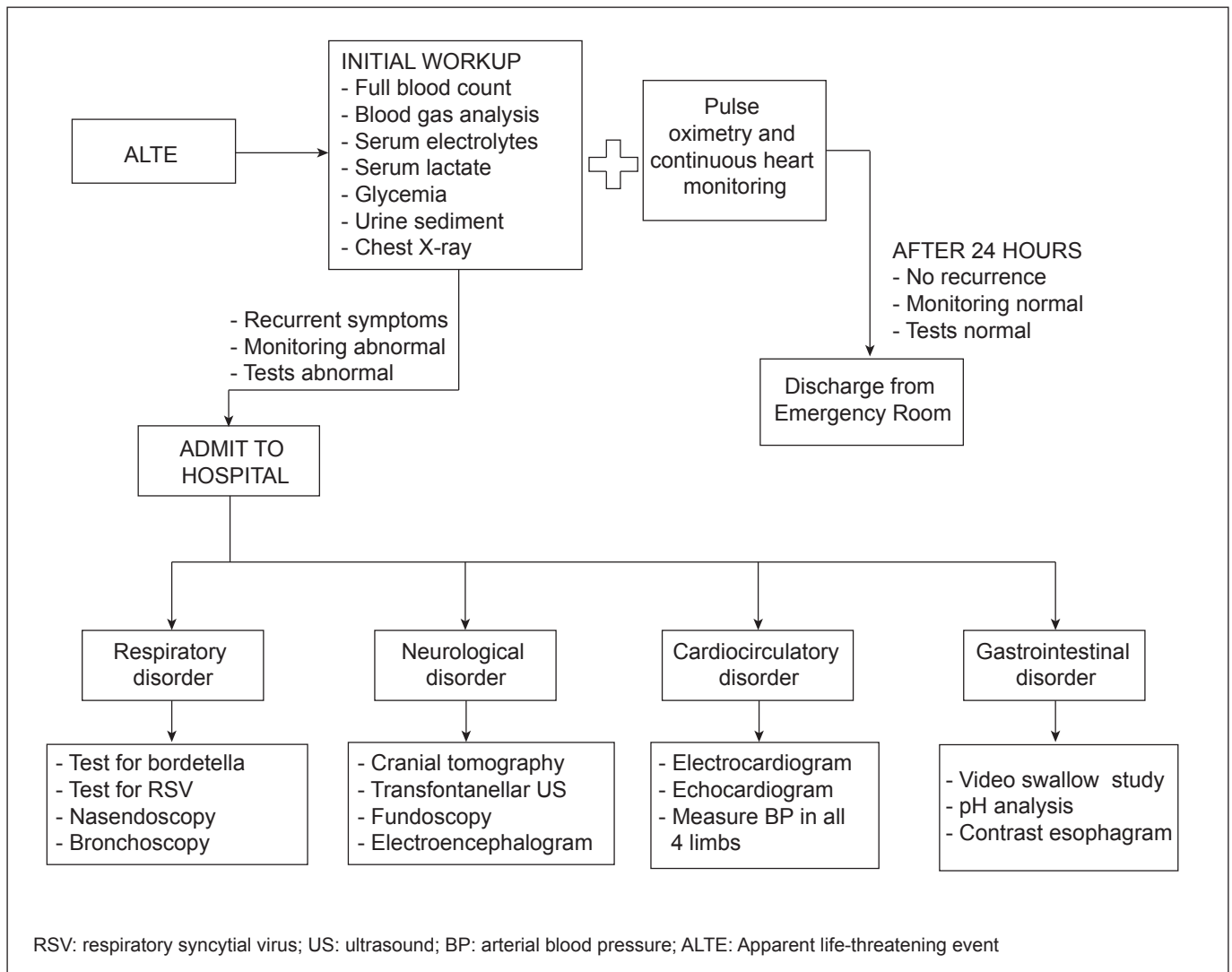


Figure 1 - Suggested conduct for ALTE cases



practice when the infant is seen for the first time after suffering an event. The majority of authors agree that initial laboratory work up should be conducted and recommend heart monitoring and pulse oximetry for a minimum of 24 hours<sup>(1,3-5,8,20,25,26,29,30,32,33,37,38)</sup>. A majority of them also recommend hospital admission for investigation of any

abnormality detected<sup>(1,3,5,8,25,26,29-30,32,33,38)</sup>. Prospective studies have provided further support for the position that history, physical examination and initial laboratory test results should guide further investigation and a rational selection of further tests aimed at confirming initial diagnostic candidates<sup>(9,17,22)</sup>, as illustrated by the flow diagram in Figure 1.

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