Apparent Life-Threatening Event (ALTE) and Sudden Infant Death Syndrome (SIDS): A Selected Annotated Bibliography

Warren J, Biagioli F, Hamilton A.
Evaluation of apparent life-threatening events in infants.

What is the appropriate evaluation for an infant presenting with an apparent life-threatening event (ALTE)? A comprehensive, detailed history and physical examination with pulse oximetry and nondilated funduscopy (to look for traumatic retinal hemorrhage) helps to determine the underlying etiology of an ALTE in 70 percent of infants. (Strength of Recommendation [SOR]: C, based on case series). Initial diagnostic evaluation should include 12-lead electrocardiography (ECG); blood gas analysis; chest radiography; complete blood count (CBC); pertussis and respiratory syncytial virus cultures, if respiratory symptoms are present; serum electrolytes; and urinalysis. (SOR: C, expert opinion and case series). If the initial evaluation does not reveal the underlying etiology of an ALTE, then the following tests should be performed: a barium-contrast upper gastrointestinal series or gastric pH probe to evaluate for reflux; computed tomography of the head or a skeletal survey to evaluate for occult cases of deliberate harm; and electroencephalography (EEG) to help diagnose seizure disorders. (SOR: C, expert opinion and case series).


Shah S, Sharieff GQ.
Update on the approach to apparent life-threatening events.

PURPOSE OF REVIEW: Apparent life-threatening events are an ongoing diagnostic dilemma for clinicians. Since most apparent life-threatening event episodes occur in infants under 6 months of age, they can generate considerable anxiety in parents and providers. This review will discuss issues to consider in the evaluation of infants after an apparent life-threatening event. To ensure proper management, a systematic approach should be taken to attempt to determine the cause of the event. RECENT FINDINGS: More recent literature suggests that infants with apparent life-threatening events frequently present without signs or symptoms of illness. Obtaining a careful history and physical examination is essential in determining the cause of the event. In this article, we will review the most current literature and discuss the American Academy of Pediatrics new recommendations on sudden infant death syndrome prevention. SUMMARY: After a careful review of the literature, prone sleeping is one of the biggest risk factors for sudden infant death syndrome. The association between apparent life-threatening events
and sudden infant death syndrome remains to be explored further, but current evidence suggests minimal risk after an apparent life-threatening event episode. This article will help clinicians prepare for this difficult challenge by providing up-to-date information and identifying problems to be addressed in future research.

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Claudius I, Keens T.

Objective: The goal was to identify criteria that would allow low-risk infants presenting with an apparent life-threatening event to be discharged safely from the emergency department. Methods: We completed data forms prospectively on all previously healthy patients <12 months of age presenting to the emergency department of an urban tertiary care children's hospital with an apparent life-threatening event over a 3-year period. These patients were then observed for subsequent events, significant interventions, or final diagnoses that would have mandated their admission (e.g., sepsis). Results: In our population of 59 infants, all 8 children who met the aforementioned outcome measures, thus requiring admission, either had experienced multiple apparent life-threatening events before presentation or were in their first month of life. In our study group, the high-risk criteria of age of <1 year and multiple apparent life-threatening events yielded a negative predictive value of 100% to identify the need for hospital admission. Conclusions: Our study suggests that >30-day-old infants who have experienced a single apparent life-threatening event may be discharged safely from the hospital, which would decrease admissions by 38%.

Full-text available at: http://www.pediatrics.org (not a U.S. Government site)

Maggio AB, Schappi MG, Benkebil F, Posfay-Barbe KM, Belli DC.

Gastro-oesophageal reflux (GOR) has a high prevalence in infancy. The supine position is among numerous aggravating factors. The exact relationship between GOR and apparently life-threatening events (ALTE) is not clear, although it has been repeatedly investigated. In 1992 the worldwide Back to Sleep campaign was implemented, which had a dramatic effect on the incidence of sudden infant death syndrome (SIDS) with a drop of 50%. Although the vast majority of children now sleep on their back, the effect of this position on ALTE has not been studied. In this retrospective study, we aim to define the potential association between GOR and ALTE. We hypothesise that the incidence of ALTE has increased since the 1992 recommendation. No bias in the population's selection was introduced, as our centre is the only one for paediatric emergencies in the county. A total of 107 children presenting with ALTE were identified during the study period (1987-99). A pH study was performed in the 75 patients presenting with ALTE in the last 6 years of the study (1994-99). Neither morbidity nor mortality was noted in a
long-term 4-year follow-up. Our present results show that the frequency of ALTE increased sevenfold (P < 0.005) between 1992 and 1999. The ALTE episodes took place significantly more often in the post-prandial period. The prevalence of GOR was much higher in patients presenting with ALTE (nearly 75%) when compared with the general population. Furthermore, on medical treatment for GOR, very few patients presented with a second episode of ALTE. Consequently it is thought that GOR and ALTE are linked and that ALTE patients would benefit from GOR treatment. The worldwide marked decrease in SIDS since the implementation of the supine position possibly masks the negative effect of an increase in ALTE.


Hunt CE.
**Ontogeny of autonomic regulation in late preterm infants born at 34-37 weeks postmenstrual age.**

Late preterm infants (34-37 weeks postmenstrual age at birth) are intermediate between less mature preterm infants and infants born at 38 weeks or more in regard to autonomic brain stem maturation. Ventilatory responses to CO(2) in preterm infants born at 33 to 36 week are significantly higher than in infants born at 29 to 32 weeks both at 3 to 4 and 10 to 14 days postnatal age, but do not differ from full-term reference levels. The ventilatory response to hypoxia in preterm infants is biphasic; initial transient hyperventilation is followed by a return to baseline and then a decrease below baseline. In infants born at 32 to 37 weeks, parasympathetic maturation appears significantly less than in full-term infants based on diminished increases in high frequency heart rate variability in quiet sleep, suggesting that late preterm infants are still more susceptible to bradycardia than full-term infants. Both the presence and severity of apnea of prematurity progressively decrease the higher the postmenstrual age. Late preterm infants, however, are still at risk, with prevalence rates as high as 10% compared with about 60% in infants born at <1500 g. The incidence of apparent life-threatening events is more common in preterm infants (8-10%) than full-term infants (1% or less). In the Collaborative Home Infant Monitoring Evaluation studies, the frequency of conventional and extreme events in near term infants is intermediate between preterm infants <34 weeks at birth and full-term infants. The relative risk for at least one extreme event in late preterm infants is increased (5.6 and 7.6, respectively, P < 0.008) compared with full-term infants and remains higher until 43 weeks postmenstrual age. The rate for Sudden Infant Death Syndrome in preterm infants born at 33 to 36 weeks is 1.37/1000 live births compared with 0.69 in infants born full term. Affected late preterm infants die at a older mean postmenstrual age compared with less mature infants (48 and 46 weeks, respectively), but die at a younger postmenstrual age than full-term infants (53 weeks, P < 0.05).


Sleep architecture in term and preterm infants beyond the neonatal period: The influence of gestational age, steroids, and ventilatory support.
Sleep. 2005 Nov 1; 28(11):1428-36

Study objective: To examine (1) sleep architecture of infants at varied risk for sudden infant death syndrome, (2) delays or advances in preterm infants at term postmenstrual age, (3) whether ventilatory support and gestational age alter sleep, (4) whether steroids alter sleep, (5) confounding influences of sex, small for gestational age, and maternal smoking. Design: Overnight polysomnography. Dependent variables: Percentage of active sleep, quiet sleep, indeterminate, and awake time per total recording time; mean and longest duration of state epochs; number of episodes ≥ 10 minutes; and sleep efficiency. Setting: Collaborative Home Infant Monitoring Evaluation (CHIME). Participants: Two hundred one preterm and 198 term infants between 33 and 58 weeks postmenstrual age during polysomnography. Fifty-one term infants with an apparent life-threatening event without known etiology (apnea of infancy), 59 subsequent siblings of babies who died of sudden infant death syndrome, and 88 healthy term infants. Results: Tracings of infants with apnea of infancy and healthy term infants were similar. Subsequent siblings of babies who died of sudden infant death syndrome spent less time in quiet sleep. Preterm infants (< or = 37 weeks postmenstrual age) exhibited immature architecture compared with infants of term postmenstrual age. The latter exhibited similar sleep except that they had a lower percentage of quiet sleep and longer mean indeterminate and longest indeterminate episodes. Preterm infants with the youngest gestational age lagged behind older preterm infants. Neither sex nor use of steroids affected sleep. Assisted ventilation was associated with a delay in maturation, small-for-gestational age status with increased active sleep, and smoking with increased awake time. Conclusion: With few exceptions, asymptomatic premature infants do not exhibit significant delays in sleep architecture compared with term infants at comparable postmenstrual age. The preterm infant with an early gestational age and morbidity exhibited delayed sleep architecture.

Full-text available at: http://www.journalsleep.org/ (not a U.S. Government site)

Dewolfe CC.
Apparent life-threatening event: A review.

An "apparent life-threatening event" (ALTE) refers to an episode that is of concern to the caregiver and is associated with a combination of apnea, color change, change in tone, choking, or gagging. Although the natural history of ALTE is most often benign, there is a risk for subsequent morbidity and mortality. 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 of literature concerning ALTE, with specific attention to the diagnosis and management of these cases.

Tirosh E, Avengulov I, Jaffe M.  
**Idiopathic apparent life-threatening event in Northern Israel.**  
J Paediatr Child Health. 2006 Jan-Feb; 42(1-2):33-6

Objective: To note whether the incidence of idiopathic apparent life-threatening event (IALTE) has decreased since 1993 in parallel to the decline in the incidence of sudden unexpected death in infancy (SUDI) 2. To compare their epidemiological profile to infants with acute unrelated illness.  

Methods: The discharge diagnoses of each infant investigated for apparent life-threatening event or apnea in the five major hospitals in Northern Israel were reviewed over the period 1991-2000. Infants with identified aetiology or apnea only were excluded. Each infant was matched with two other infants admitted for an acute respiratory illness unrelated to apnea. IALTE rates were compared to the national rates of SUDI.  

Results: Two hundred and forty-three infants were diagnosed with IALTE. No evidence for a decline in incidence was noted over the period of the study, while a consistent decline in the incidence of SUDI was observed. Only few differences in the epidemiological profile were noted between the study and the comparison group, that is, increased rate of prematurity and first-born infants.  

Conclusions: (i) The two conditions probably do not share a common aetiology in the majority of cases; and (ii) the epidemiological profile of IALTE is predominantly similar to that of infants hospitalized for respiratory illness.


Hall KL, Zalman B.  
**Evaluation and management of apparent life-threatening events in children.**  
Am Fam Physician. 2005 Jun 15; 71(12):2301-8

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.


Brand DA, Altman RL, Purtill K, Edwards KS.
Yield of diagnostic testing in infants who have had an apparent life-threatening event.

Objective: Many infants who have experienced an apparent life-threatening event (ALTE) seem normal by the time they reach the hospital. Nevertheless, they typically undergo an extensive evaluation to rule out serious underlying conditions. The purpose of the present investigation was to determine the yield of different diagnostic tests in helping to identify the cause of the ALTE. Methods: We reviewed test results from a consecutive series of infants who were younger than 12 months and admitted to a tertiary care academic medical center between November 1996 and June 1999 after having experienced a sudden breathing irregularity, color change, or alteration in mental status or muscle tone. For each patient, we noted whether a given test was performed, whether the result was positive, and, if so, whether the test contributed to the diagnosis, that is, suggested or helped establish the cause. We also noted whether the initial history and physical examination contributed information that eventually led to the final diagnosis. Results: A total of 243 patients met the enrollment criteria. Of the 3776 tests ordered, 669 (17.7%) were positive and 224 (5.9%) contributed to the diagnosis. Prompted by findings from the initial clinical assessment, the following tests proved useful in patients who had a contributory history and physical examination: blood counts, chemistries, and cultures; cerebrospinal fluid analysis and cultures; metabolic screening; screening for respiratory pathogens; screening for gastroesophageal reflux; chest radiograph; brain neuroimaging; skeletal survey; electroencephalogram; echocardiogram; and pneumogram. In the remaining patients, who had a noncontributory history and physical examination, only the following tests proved useful: screening for gastroesophageal reflux, urine analysis and culture, brain neuroimaging, chest radiograph, pneumogram, and white blood cell count. Broad evaluations for systemic infections, metabolic diseases, and blood chemistry abnormalities were not productive in these patients. Conclusions: For many tests used in the evaluation of an ALTE, the likelihood of a positive result is low and the likelihood of a contributory result is even lower. Estimates of diagnostic yield derived from the present investigation can help clinicians maximize the productivity and efficiency of their evaluation.

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Aims: To investigate the epidemiology and risk factors of apparent life threatening events (ALTE). Methods: A prospective study enrolled all live-born infants in the Tyrol (1993-2001). Information on pregnancy, sociodemographic characteristics, child care practices, and infant's behavior in the first four to six weeks of life was collected with a standardized questionnaire, and was available for 44,184 infants. ALTE was identified from hospital admission records. Results: During the study period 164 ALTE cases were identified, corresponding to an incidence of 2.46/1000 live births. In 73 of these infants no cause for the event and no comorbidity could be found (idiopathic ALTE). On average ALTE manifested ten weeks earlier than SIDS. Of various SIDS risk factors in the survey area, the prone sleeping position, smoking during pregnancy, low gestational age, profuse night sweating, and family history of infant death showed a moderate relation to the risk of overall ALTE, but only smoking maintained significance in the multivariate risk model. None of these variables was associated with idiopathic ALTE. In contrast to SIDS the frequency of ALTE did not change during the study period. None of the ALTE infants experienced SIDS later in life. Behavioral abnormalities such as feeding difficulties, episodes of pallor, cyanotic episodes, and repeated apnoea episodes were strongly associated with an increased risk of overall and idiopathic ALTE. Conclusions: Although there are some similarities in the clinical presentation and epidemiology of SIDS and ALTE, differences clearly redominate. Accordingly, ALTE and SIDS should not be considered different manifestations of the same disease process.

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Parmigiani S, Bevilacqua G, Leali L, Pisani F.
The web survey network of sudden infant death syndrome and apparent life-threatening events in the Emilia-Romagna region.

To survey epidemiology and to study the etiology of sudden infant death syndrome (SIDS) and apparent life threatening events (ALTE) in Emilia-Romagna, a web network was constituted. A regional supervisor and a steering committee plan the action of district and local coordinators. They keep contact with the Regional Office of Health Services. District and local coordinators collect clinical and laboratory and, in case of SIDS, also autopsy data. Records are communicated to the Regional Supervising Center by on-line software. From these data, future planning of care and of mass information as well as auditing of their efficacy can be carried out. The characteristics of the network that has just started to collect data, as well its future developmental aspects, are discussed.

Full-text available at: http://www.tandf.co.uk (not a U.S. Government site)

Gleeson M, Clancy RL, Cox AJ, Gulliver SA, Hall ST, Cooper DM.
Mucosal immune responses to infections in infants with acute life threatening
This study examined the hypothesis that dysregulation of mucosal immune responses to respiratory infections is a critical event, which could be causal in respiratory arrest of some previously healthy infants. To examine this in hypothesis, a prospective study was undertaken of infants presenting to the emergency department of a major teaching hospital with acute life threatening events (ALTE) of unknown cause and classified as "near-miss" SIDS. Salivary immunoglobulin concentrations were measured on admission and again after 14 days. The salivary immunoglobulins were compared with three control groups: infants with a mild upper respiratory tract infection (URTI); bronchiolitis; and healthy age-matched infants. The salivary IgA and IgM concentrations in the ALTE infants at presentation to hospital indicated a significant mucosal immune response had already occurred, with nearly 60% of the IgA concentrations significantly above the population-based reference ranges. The hyper-immune response was most evident in the ALTE infants with pathology evidence of an infection; 87% of these infants had salivary IgA concentrations on average 10 times higher that the age-related median concentration. The most prevalent pathogen identified in the ALTE infants was respiratory syncytial virus (RSV) (64%). RSV was also identified in all subjects with bronchiolitis. Risk factors for SIDS were assessed in each group. The data indicated that the ALTE infants diagnosed as 'near-miss' SIDS were a relatively homogeneous group, and most likely these ALTE infants and SIDS represent associated clinical outcomes. The study identified exposure to cigarette smoke and elevated salivary IgA concentrations as predictors of an ALTE. The study findings support the hypothesis of mucosal immune dysregulation in response to a respiratory infection in some infants with an ALTE. They provide a plausible explanation for certain SIDS risk factors. The underlying pathophysiological mechanism of proinflammatory responses to infections during a critical developmental period might be a critical factor in infants who have life-threatening apnoea or succumb to SIDS. The study raises the possibility of using salivary IgA to test infants who present with mild respiratory infections to identify a substantial number of infants at risk of developing an ALTE or SIDS, thus enabling intervention management to prevent such outcomes.


Poets CF.

Apparent life-threatening events and sudden infant death on a monitor.

This review summarizes recent data on mechanisms for apparent life-threatening events (ALTE) and sudden infant death (SID) which show that (i). Recordings obtained during ALTE allow the detection of previously unrecognised but preventable mechanisms in a significant proportion of infants and should thus be performed routinely in infants with such a history, (ii).in recordings obtained during SID and idiopathic ALTE, prolonged apnoea was found in only a minority, while severe hypoxaemia appeared to the common mechanism, (iii).it remains yet unclear by which mechanism this hypoxaemia develops,
with upper and/or lower airway obstruction, rebreathing of expired air and intrapulmonary shunting being potential candidates, (iv) there is evidence that arousal fails during SID, which could be related to known risk factors such as tobacco smoke exposure, whereas (v) gasping occurred during the majority of SID cases where respiratory patterns have been analyzed, but it remains unclear why gasping remains ineffective in resuscitating the infant from hypoxaemia.


Kahn A.


Infants with an apparent life-threatening event (ALTE) should not be treated nor monitored without a detailed medical evaluation, as different medical causes may be responsible for the initial clinical presentation. Standard and specific evaluation procedures are listed to help identify a cause for the ALTE. The most frequent problems associated with an ALTE are digestive (about 50%), neurological (30%), respiratory (20%), cardiovascular (5%), metabolic and endocrine (under 5%), or diverse other problems, including child abuse. Up to 50% of ALTEs remain unexplained. The finding of medical or surgical anomalies leads to specific treatments. Surveillance programmes with the use of home monitoring devices may be undertaken, preferably with cardiorespiratory monitors, and when possible, with event monitors, although no currently available home monitoring device is free of false alarms or offers complete protection. Long-term follow-up programmes of infants with an apparent life-threatening event contribute to adapt medical attitudes to the child's needs and to confirm the medical diagnosis. Conclusion a systematic diagnostic evaluation, together with a comprehensive treatment programme, increases survival and quality of life for most affected infants.

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