From ALTE to BRUE: Brief Resolved Unexplained Events

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Objectives and Disclosures

Objective: Become familiar with the AAP guideline on Brief Resolved Unexplained Events

Disclosure of relevant financial relationships in the past 12 months:

- I, James P. McCord, have no commercial interest with any entities producing, marketing, reselling, or distributing health care goods or services consumed by, or used on, patients.
Historical Perspective

▪ “Near-miss Sudden Infant Death Syndrome”
▪ Infant Apnea defined as cessation of breathing for $> 20$ seconds or shorter if associated with bradycardia, cyanosis, pallor, or hypotonia
▪ 1986 NIH Consensus Conference on Infantile Apnea coined “Apparent Life Threatening Event” or ALTE:
  > Frightening to the observer
  > 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
    ▪ Gagging.
  > In some cases, the observer fears that the infant has died
ALTE Characteristics

- True incidence is unknown
- May account for 0.6 to 0.8% of ED visits for infants
- Up to 2% of hospitalized children
- No standardized approach for evaluation exists
- Probably a distinct group from subsequent Sudden Infant Death Syndrome (SIDS) patients
  - SIDS is more common in males; ALTE shows no predominance
  - SIDS more likely premature or SGA; ALTE more likely full term
  - Maternal age < 20 years more common in SIDS
  - Peak SIDS age 2-4 months; ALTE more common under 2 months
  - SIDS less common since “Back (Safe) to Sleep” in 1994; no change for ALTE
  - They may share some risk factors: Maternal smoking
Problems with the ALTE Terminology

- The infant may or may not be asymptomatic on presentation.
- Symptoms are sometimes not intrinsically life-threatening and may be a benign manifestation of normal physiology or a self-limited condition.
- Suggests a potential for recurring events or a serious underlying disorder to caregivers and clinicians.
- Supports over testing and hospital admission, which can increase caregiver anxiety.
- Does not include a risk stratification, to set apart the vast majority who have low risk of recurrence or serious underlying disorder.
New AAP guideline published on-line in April 2016 and in print May 2016:

**Abstract**

The American Academy of Pediatrics has developed a clinical practice guideline on Brief Resolved Unexplained Events (BRUEs). This guideline is intended to improve the care of infants younger than 1 year who present with a BRUE and who have a history and physical examination suggestive of further investigation and treatment. The guideline is based on systematic reviews and meta-analyses of available research evidence. The American Academy of Pediatrics discourages routine evaluation of asymptomatic infants after a BRUE. The guideline is intended to provide guidance for clinicians and families on the identification, evaluation, and management of BRUEs.

**Introduction**

BRUEs are episodes of unexplained crying or fretting, typically lasting less than 20 minutes, that are not accompanied by signs of serious illness. BRUEs are common and are often self-limited. However, they can be distressing to parents and can sometimes lead to unnecessary and costly medical interventions.

**Objective**

This guideline is intended to improve the care of infants younger than 1 year who present with a BRUE and who have a history and physical examination suggestive of further investigation and treatment. The guideline is based on systematic reviews and meta-analyses of available research evidence. The American Academy of Pediatrics discourages routine evaluation of asymptomatic infants after a BRUE. The guideline is intended to provide guidance for clinicians and families on the identification, evaluation, and management of BRUEs.

**Methods**

The guideline was developed by a multidisciplinary team of experts in pediatrics, including pediatricians, pediatric residents, and experts in the field of BRUEs. The team reviewed available research evidence and developed recommendations based on the evidence.

**Recommendations**

1. For infants younger than 1 year who present with a BRUE and who have a history and physical examination suggestive of serious illness, further investigation and treatment are recommended.
2. For infants younger than 1 year who present with a BRUE and who do not have a history and physical examination suggestive of serious illness, further investigation and treatment are not recommended.
3. For infants younger than 1 year who present with a BRUE and who have a history and physical examination suggestive of serious illness, further investigation and treatment are recommended.
4. For infants younger than 1 year who present with a BRUE and who do not have a history and physical examination suggestive of serious illness, further investigation and treatment are not recommended.

**Conclusion**

The American Academy of Pediatrics recommends that clinicians and families use this guideline to improve the care of infants younger than 1 year who present with a BRUE and who have a history and physical examination suggestive of serious illness. The guideline is intended to provide guidance for clinicians and families on the identification, evaluation, and management of BRUEs.
Objectives of the New Guideline

- Recommends replacement of the term ALTE with BRUE
- Provides an approach to patient evaluation that is based on risk of repeat event or serious underlying disorder
- Allows delineation of patients based on this risk into lower and higher risk groups
- Provides evidence based management recommendations for lower risk patients whose history and physical examination are normal
- Definition of BRUE
  - Occurs in infants less than 1 year of age
  - Observer reports a sudden, brief, now resolved episode with > 1 of these:
    - Cyanosis or Pallor
    - Absent, decreased, or irregular Breathing
    - Marked change in Tone (hyper or hypotonia)
    - Altered level of Consciousness

Diagnosed only when there is no explanation for this event after an appropriate history and physical exam in an infant who has returned to normal.
Changes in definition from ALTE to BRUE

- BRUE has a strict age limit (less than 1 year)
- An event is a BRUE only when there is no other likely explanation
- In BRUE, the infant returns to a normal level of baseline health
- A BRUE diagnosis is based on the clinician’s characterization of features of the event and not on the caregiver’s perception that the event was life threatening
- The clinician should determine whether the infant had episodic cyanosis or pallor rather than just color change (such as redness)
- Respiratory criteria are expanded from apnea to absent breathing, diminished breathing, and other breathing irregularities
- Muscle tone changes are better defined and characterized
- Choking and gagging are left out of the criteria
- “Altered level of responsiveness” is added because it can be an important component of an episodic but serious cardiac, respiratory, metabolic, or neurologic event.
Table 2: Historical Features to be Considered in the Evaluation of a Potential BRUE

- Considerations for possible child abuse
  - Multiple or changing versions of the history/ circumstances
  - History/ circumstances inconsistent with child’s developmental stage
  - History of unexplained bruising
  - Incongruence between caregiver expectations and child’s developmental stage, including assigning negative attributes to the child

- History of the event
  - General description/ who reported the event?
  - Witness of the event (parents, other children, other adults)/ Reliability?
  - Where did it occur? (home, elsewhere, room, crib, floor)
  - Awake or asleep?
  - Position: supine, prone, upright, sitting, moving?
  - Feeding? Anything in the mouth? Availability of items to choke on? Vomiting or spitting up?
  - Objects nearby that could smother or choke?
Table 2: Historical Features to be Considered in the Evaluation of a Potential BRUE

- **State during the event**
  - Choking or gagging noise? Active/moving or quiet/flaccid?
  - Conscious? Able to see you or respond to voice?
  - Muscle tone increased or decreased? Repetitive movements?
  - Appeared distressed or alarmed?
  - Breathing: yes/no? Struggling to breath?
  - Skin color: normal, pale, red, blue?
  - Bleeding from nose or mouth?
  - Color of lips: normal, pale, or blue?

- **End of event**
  - Approximate duration of event? End abruptly or gradually?
  - How did it stop: with no intervention, picking up, positioning, rubbing or clapping back, mouth-to-mouth, chest compressions?
  - Treatment provided by parent/caregiver (Glucose containing drink or food)
  - 911 called by caregiver?
Table 2: Historical Features to be Considered in the Evaluation of a Potential BRUE

- **State after event**
  - Back to normal immediately/ gradually/ still not there?
  - Before back to normal, was quiet, dazed, fussy, irritable, crying?

- **Recent history**
  - Illness in preceding days?
    - If yes, detail signs/symptoms (fussiness, decreased activity, fever, congestion, rhinorrhea, cough, vomiting, diarrhea, decreased intake, poor sleep)
  - Injuries, falls, previous unexplained bruising?

- **Past medical history**
  - Pre-perinatal history, gestational age
  - Newborn screening normal? (for IEMs or congenital heart disease)
  - Previous episodes/ BRUE?
  - GE Reflux? If yes, obtain details, including management
  - Breathing problems? Noisy ever? Snoring?
  - Growth patterns normal?
Table 2: Historical Features to be Considered in the Evaluation of a Potential BRUE

- **Past medical history**
  - Development normal? Assess a few major milestones across categories, any concerns about development or behavior?
  - Illness, injuries, emergencies?
  - Previous hospitalization, surgery?
  - Recent immunization?
  - Use of over-the-counter medications?

- **Family history**
  - Sudden unexplained death (including unexplained car accident or drowning) in first or second degree family members before age 35, and particularly as an infant?
  - Apparent life threatening event in a sibling?
  - Long qT syndrome?
  - Arrhythmia?
  - Inborn error of metabolism or genetic disease?
  - Developmental delay?
Table 2: Historical Features to be Considered in the Evaluation of a Potential BRUE

- Environmental history
  - Housing: general, water damage, or mold problems?
  - Exposure to tobacco smoke, toxic substances, drugs?

- Social history
  - Family structure, individuals living at home?
  - Recent changes, stressors, strife?
  - Exposure to smoke, toxic substances, drugs?
  - Recent exposure to infectious illness, particularly upper respiratory illness, paroxysmal cough, Pertussis?
  - Support systems/ access to needed resources?
  - Current level of concern/ anxiety; how family manages adverse situations?
  - Potential impact of event/ admission on work/ family?
  - Previous child protective services or law enforcement involvement (e.g. domestic violence, animal abuse), alerts/ reports for this child or others in the family (when available)?
  - Exposure of child to adults with history of mental illness/ substance abuse?
Table 3: Physical Examination Features to be Considered in the Evaluation of a Potential BRUE

- General appearance
  - Craniofacial abnormalities (mandible, maxilla, nasal)
  - Age-appropriate response to environment
- Growth variables
  - Length, weight, OFC
- Vital signs
  - Temperature, pulse, respiratory rate, blood pressure, oxygen saturation
- Skin
  - Color, perfusion, evidence of injury (e.g. bruising or erythema)
- Head
  - Shape, fontanelles, bruising or other injury
- Eyes
  - General, extraocular movement, pupillary response
  - Conjunctival hemorrhage
  - Retinal examination, if indicated by other findings
Table 3: Physical Examination Features to be Considered in the Evaluation of a Potential BRUE

- **Ears**
  - Tympanic membranes, bruises on or behind pinna

- **Nose and mouth**
  - Congestion/ coryza
  - Blood in nares or oropharynx
  - Evidence of trauma or obstruction
  - Torn frenulum

- **Neck**
  - Mobility

- **Chest**
  - Auscultation; palpation for rib tenderness, crepitus, irregularities

- **Heart**
  - Rhythm, rate, auscultation

- **Abdomen**
  - Organomegaly, masses, distention, tenderness
Table 3: Physical Examination Features to be Considered in the Evaluation of a Potential BRUE

- **Genitalia**
  - Any abnormalities

- **Extremities**
  - Muscle tone, injuries, limb deformities consistent with fracture

- **Neurologic**
  - Alertness, responsiveness
  - Response to sound and visual stimuli
  - General tone
  - Pupillary constriction in response to light
  - Presence of symmetrical reflexes
  - Symmetry of movement/ tone/ strength
Defining Lower-Risk BRUE

- Those unlikely to have a recurrent event or undiagnosed serious condition (lower risk of adverse outcomes)
- Can be managed safely without extensive diagnostic evaluation or hospitalization
- A standardized diagnostic approach can be applied
- Definition:
  - Age greater than 60 days
  - Prematurity: gestational age $> 32$ wks. and postconceptional age $> 45$ wks.
  - First BRUE (no previous BRUE ever and not occurring in clusters)
  - Duration of event $< 1$ minute
  - No CPR required by trained medical provider
  - No concerning historical features
  - No concerning physical examination features
BRUE Management Algorithm

BRUE Diagnosis

Patient presents for initial medical assessment after a brief, resolved event that was observed by caregiver in a child <1 year of age.

- Patient is well-appearing
- Patient has additional symptoms or abnormal vital signs (e.g., cough, respiratory difficulties, or fever)

Clinician characterizes the event as a sudden, brief, and now resolved episode of one or more of the following:
- Cyanosis or pallor
- Absent, decreased, or irregular breathing
- Marked change in tone (hyper or hypotonia)
- Altered responsiveness

Event criteria present
- Perform appropriate history and PE
- No explanation for event identified

Diagnosis of Brief Resolved Unexplained Event is made

Event criteria absent
- Not a BRUE

Use event characteristics, rather than the term “ALTE,” to describe the event.

Explanation for event identified (e.g., GER, feeding difficulties, or airway abnormality)

Out of guideline scope; manage accordingly.
BRUE Management Algorithm

BRUE Risk Classification

No concerns identified from history and PE

Concerns identified from history or PE (e.g., FH of sudden cardiac death or subtle, non-diagnostic social, feeding or respiratory problems)

Apply risk stratification
- Age >60 days
- Born ≥32 wks gestation and corrected gestational age ≥45wks
- No CPR by trained medical provider
- Event lasted <1 minute
- First event

Yes

Lower Risk Patient

No

Higher Risk Patient
FIGURE 1
Diagnosis, risk classification, and recommended management of a BRUE. *See Tables 3 and 4 for the determination of an appropriate and negative FH and PE. **See Fig 2 for the AAP method for rating of evidence and recommendations. CSF, cerebrospinal fluid; FH, family history; PE, physical examination; WBC, white blood cell.
Case # 1

- 3 week old, NSVD at 38 weeks
- GBS neg; no Herpes exposure
- Stuffy nose, no fever
- Found in crib: limp with dusky color
- Improved with stimulation
- Vigorous in ED, with normal O2 saturations
Case # 2

- 2 week old male, term, NSVD, breastfeeding
- Did well in nursery
- Began vomiting at home
- Sleepy with feeds
- Several episodes of pale color
- Lethargic
- Increased RR
Case # 3

- 5 month old term male
- Acting OK
- Dad holding sleeping baby notices pale color
- Limp and maybe not be breathing
- Responds to stimulation
- In ED: Vitals normal
- Exam non-focal, good tone
- Baby feeds vigorously
- Sats 98% on RA
Case # 4

- 3 month old male
- Fussy and spitty the past month
- Mom comes home from work
- Baby doesn’t feed well
- Low tone on exam
- Breathing fast
- AF slightly full
Case # 5

- 7 week old term male
- Failed NB hearing screen, not rechecked yet
- Abrupt onset generalized shaking after crying
- Now seems normal
- Exam shows slightly low tone
- AF soft
- No bruising
THOMAS
BRUE

01.
HEAD OF A PRIVATE GERMAN BANK

02.
HIS FATHER WAS CONNECTED TO
A HIGH-LEVEL MEMBER OF THE
RUSSIAN SECURITY SERVICES;
FATHER OF ISSA KARPOV

03.
HAS CLIENTS THAT ARE OF
HIGH INTEREST TO THE
ANTI-TERROR UNIT

#AMostWantedMan 12/9/14
Case # 6

- 9 month old male
- Twitching movements of arms and legs
- Occurred with sleep when younger
- Now occurring while awake
- Funny eye movements
Case # 7

- 3 month old female
- Spitty with occasional vomiting despite change to soy formula
- Hard to feed
- Trouble gaining weight
- Dusky spell noted at end of a feeding
Potential Risks of Acid Supression

- PPI drug interactions: Phenytoin, Diazepam, Warfarin, Clopidogel
- PPIs may increase risk for respiratory infections
- Impaired calcium (acidity needed to release iCa) and magnesium absorption
- Suppressing of immune function
  - Immune cell migration
  - Cytokine production
  - Lysosomal enzyme function
  - Neutrophil function
- Alteration of lower intestinal flora
- Variability of P450 activity in infants may makes dosing uncertain
  - Tighe M et al. Cochrane Database of Systematic Reviews 2014 Issue 11
Respiratory Events in Infants Presenting with ALTE: Is There an Explanation from Esophageal Motility?

- Study of Pharyngoesophageal manometry in 10 patients with prior ALTE compared to 10 controls examining:
  - Upper esophageal pressures
  - Lower esophageal sphincter pressures
  - Esophageal peristalsis characteristics
  - Evidence of gastroesophageal reflux

- Spontaneous Respiratory Events (SREs) are “apneic” events > 2 sec with at least 2 missed breaths.

- Physiologic apnea occurs with deglutition (swallowing during feeding)

- Infants with ALTE history had
  - Delays in restoring aerodigestive baseline after swallowing
  - More frequent SREs and gasping
  - Dysfunctional Aerodigestive rhythm, suggesting brainstem dysregulation
  - Lower magnitude change in upper esophageal pressures
  - No significant difference in lower esophageal function
Case # 8

- 3 month old female
- 35 week premie, doing well
- Parents return home from first date post partem
- Baby sitter notices: wouldn’t awaken with diaper change and floppy for a few minutes
- No color change noted
- Feeds well for mom and now appears normal
Case # 9

- 3 week old term male
- Constipation since birth
- Feeds OK but takes longer than sib did
- Active and alert, good tone
- Noted to be dusky while sleeping
- No distress
- No cough or choking
References

References


▪ Tighe M et al. Pharmacologic treatment of children with GER. *Cochrane Database of Systematic Reviews.* 2014 Issue 11
Thank you!