Title
Brief Resolved Unexplained Event (BRUE) in a Low-Risk Infant

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Preface
Some infants (less than 1 year) have transient events involving some combination of altered consciousness, muscle tone, respiration, and/or skin coloration that is frightening to the caregiver and prompts urgent evaluation by a clinician. These events can be a presenting symptom of underlying, undiagnosed pathology, but more often than not, there is no underlying cause identified with no recurrence or complication. The challenge to the clinician is to navigate the broad differential diagnosis with consideration of both the benefit and harm of the work-up.

This guideline offers the clinician guidance on:
- Diagnosis of Brief Resolve Unexplained Event (BRUE)
- Identifying low vs high-risk infants
- Evaluation and management of low-risk infants

Definitions/Name Change
The term Apparent Life-Threatening Event (ALTE) was defined at the National Institutes of Health Consensus Conference in 1986 to replace the term “near-miss SIDS”. An ALTE is defined as an episode that is frightening to the observer (often fearing the infant has died) and is characterized by some combination of:
- Apnea--central or obstructive
- Color change--usually cyanotic or pallid but occasionally erythematous or plethoric
- Marked change in muscle tone--usually marked limpness
- Choking or gagging

The previous terminology of ALTE has been replaced by a new, more precise term: Brief Resolved Unexplained Event (BRUE). This new term is intended to better reflect the transient nature of the event, the lack of clear cause, and removes the “life-threatening” label. It is based on the clinician’s characterization of the event rather than the caregivers’ perception and is given a strict age limit of 1 year. There is more specificity in the color, tone, and respiratory changes and removes the “choking/gagging” criteria. Most notably, the diagnosis of BRUE is intended to only be ascribed to an event that has no other likely explanation after a thorough history and physical.

Brief Resolved Unexplained Event (BRUE)
- An event that occurs in infants less than 1 year of age
- The Event is characterized by the observer as
  - Brief--lasting <1 minute, but typically <20-30 seconds
  - Resolved--the patient returned to baseline state of health after the event with normal vital signs and clinical appearance.
Unexplained—a clinician is unable to explain the cause of the event after an appropriate history and physical examination.

Event includes ≥1 of the following:

- Cyanosis or pallor
- Absent, decreased, or irregular breathing
- Marked change in tone (hyper- or hypotonia)
- Altered level of responsiveness

**Diagnosis**
The diagnosis of BRUE is made clinically with a thorough history and physical exam. The interview should include a detailed history of the event itself, a review of the baby’s recent and past medical history, as well as family and social history. This information can cover an extensive differential diagnosis and lead the clinician to pursue other diagnoses if a concern is elicited. Additionally, the physical examination can direct clinical suspicion of any underlying cause of the event. The exam should include a review of vital signs, an assessment of overall general appearance or signs of distress, and a head-to-toe exam looking for anatomic or functional abnormalities as well as signs of trauma or injury.

If the patient remains symptomatic or there is an element of the history or physical exam that points to a source of the event, then the event is not considered resolved or unexplained and the diagnosis of BRUE cannot be made.

The diagnosis of BRUE can be made if a patient less than 1 year of age presents for evaluation following a **brief** (less than 1 minute) event that was observed by a caregiver and all three of the following criteria are met.

1. The patient is well-appearing, asymptomatic, with normal vital signs at the time of evaluation (resolved)
2. There is no explanation identified with a thorough history and physical exam (unexplained).
3. The event includes ≥1 of the following:
   - cyanosis or pallor
   - Absent, decreased, or irregular breathing
   - Marked change in tone
   - Altered responsiveness

**Risk Stratification**
Once the diagnosis of BRUE is made, the evaluation of the infant is guided by their risk stratification. Risk stratification aims to determine if the patient is at risk to have recurrent events or an undiagnosed serious condition that could lead to poor outcomes.

- Low-Risk
  - Age
    - For term infants: Age >60 days
For premature infants: gestational age $\geq$ 32 weeks and post-conceptual age $\geq$ 45 weeks
- Only one event, not occurring in clusters or multiple events
- Duration of $< 1$ minute
- No CPR required by a trained medical provider
- No concerning historical features
- No concerning physical exam findings.

High-Risk
- Any patient who does not meet the low-risk criteria is considered high-risk.
- High-risk infants may be more likely to have a serious underlying condition, a recurrent event, or an adverse outcome.\(^1,5\)
- See the Pediatric Guideline for an approach to evaluation and management of High-Risk BRUE.

**Evaluation and Management of Low-Risk Infants**
Infants who are determined to be low-risk can be managed without extensive diagnostic evaluation or hospitalization.\(^3\) The following recommendations are made by the American Academy of Pediatrics based on an extensive review of the ALTE literature.\(^1\) Interventions are listed by system and contain a recommendation of “should”, “may”, “need not”, and “should not” based on the balance of benefit versus harm in the evaluation of these infants.

**Cardiopulmonary Evaluation/Management**
- **May** briefly monitor infants with continuous pulse-ox and serial observations for a period of 1-4 hours.
- **May** obtain a 12-lead EKG.
- **Need not** admit infants presenting with low-risk BRUE to the hospital solely for cardiorespiratory monitoring.
- **Should not** obtain a chest radiograph.
- **Should not** obtain blood gases.
- **Should not** obtain a sleep-study.
- **Should not** obtain an echocardiogram.
- **Should not** initiate home cardiorespiratory monitoring.

**Child Abuse Evaluation/Management**
- **Should** obtain an assessment of social risk factors.
- **Need not** obtain neuroimaging.

**Neurology**
- **Should not** obtain neuroimaging (CT, MRI, ultrasound).
- **Should not** obtain an EEG.
- **Should not** prescribe antiepileptic medications for potential neurologic disorders.
Infectious Disease
- **May** obtain testing for pertussis.
- **Need not** obtain respiratory viral testing.
- **Need not** obtain a urinalysis (bag or catheter).
- **Should not** obtain a white blood cell (WBC) count, blood culture, or cerebrospinal fluid (CSF) analysis or culture to detect an occult bacterial infection.
- **Should not** obtain a chest radiograph to assess for pulmonary infection.

Gastroenterology
- **Should not** obtain investigations for GER (Upper GI series, pH probe, endoscopy, barium contrast study, nuclear scintigraphy, ultrasound).
- **Should not** prescribe acid suppression therapy.

Inborn Errors of Metabolism (IEM)
- **Need not** obtain serum lactic acid or serum bicarbonate.
- **Need not** obtain blood glucose.
- **Should not** obtain serum sodium, potassium, chloride, blood urea nitrogen (BUN), creatinine, calcium or ammonia.
- **Should not** obtain venous or arterial blood gases.
- **Should not** obtain urine organic acids, plasma amino acids, or plasma acylcarnitines.

Anemia
- **Should not** obtain lab evaluation for anemia.

Patient- and Family-centered Care
- **Should** offer resources for CPR training to caregivers.
- **Should** educate caregivers about BRUEs.
- **Should** use shared decision-making.

**Summary**
When an infant less than 1 year presents for evaluation following a frightening event, the clinician should conduct a thorough history and physical exam to determine if the event meets the clinical criteria and is indeed Brief, Resolved, and Unexplained.

If the infant is well-appearing with no concerning history, the clinician should conduct a risk stratification based on the patient and event characteristics described above to gauge clinical suspicion of an undiagnosed serious condition or risk of recurrent events.

If the infant and event is determined to be low-risk, the following evidence-based recommendations will guide the clinician on the appropriate evaluation:
- **Should**
o Educate caregivers about BRUEs and engage in shared decision-making to guide evaluation, disposition, and follow-up.
  o Offer resources for CPR training to caregiver.

- **May**
  o Obtain pertussis testing
  o Obtain 12-lead EKG
  o Briefly monitor patients with continuous pulse ox and serial observations (1-4 hours)

- **Need Not**
  o Obtain labs: blood glucose, bicarbonate, lactic acid, viral testing, urinalysis
  o Obtain neuroimaging
  o Admit the patient to the hospital *solely* for cardiorespiratory monitoring

- **Should Not**
  o Obtain Labs
    ▪ blood: WBC count, hemoglobin/hematocrit, blood culture, sodium, potassium, chloride, blood urea nitrogen, creatinine, calcium, ammonia, blood gas, plasma amino acids, acylcarnitines
    ▪ CSF analysis or culture
    ▪ urine organic acids
  o Obtain imaging:
    ▪ Chest radiograph
    ▪ Echocardiogram
    ▪ Electroencephalogram
    ▪ studies for GER
  o Initiate home cardio-respiratory monitoring
  o Prescribe medications
    ▪ acid suppression
    ▪ anti-epileptic medications

**References**
1. Tieder JS, Bonkowsky JL, Etzel RA, et al. Brief Resolved Unexplained Events (Formerly Apparent Life-Threatening Events) and Evaluation of Lower-Risk Infants. *Pediatrics*. 2016;137(5);e20160590