BRIEF RESOLVED UNEXPLAINED EVENT, EMERGENCY DEPARTMENT AND INPATIENT

Updated: April 11, 2023

Clinical Pathway Summary

CLINICAL PATHWAY NAME: Brief Resolved Unexplained Event, Pediatric, ED and Inpatient

PATIENT POPULATION AND DIAGNOSIS: Applies to patients with a primary diagnosis of BRUE. By definition, these are patients younger than 1 year of age.

APPLICABLE TO: All Corewell Health West emergency departments, pediatric inpatient units, and outpatient facilities

BRIEF DESCRIPTION: The goal of this pathway is to provide an evidence-based approach to the diagnosis and management of BRUE in patients who are younger than 1 year of age. This pathway is intended for pediatricians, pediatric hospitalists, emergency department physicians, family medicine physicians, resident physicians, nurse practitioners, and physician assistants who care for these children in the emergency department, clinic, inpatient medicine, and intensive care settings. The definition of BRUE, the goals of evaluation, and inclusion/exclusion factors are defined herein.

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Pathway Information

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EXPERT IMPROVEMENT TEAM (EIT): NA

CLINICAL PRACTICE COUNCIL (CPC): Children's

CPC APPROVAL DATE: May 1, 2023

OTHER TEAM(S) IMPACTED: Nursing, respiratory therapy, speech and language pathology, radiology, Center for Child Protection.

Brief resolved unexplained event

Clinical practice guideline and evidence-based care

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BRUE: for providers

What is a brief resolved unexplained event?
In 2016, the American Academy of Pediatrics defined a BRUE as a brief event in an infant characterized by an abrupt change in tone, breathing, color, or behavior (1) (see formal definition on Page 6). These events are believed to be caused by normal immature physiology, especially of the neurologic and gastrointestinal systems. Since these events are usually not harmful, the AAP outlined criteria for patients who are considered “lower risk” (Page 3). In this document, you may also find an evidence-based framework for patients who are not lower risk (Pages 4-5).

What is the goal of evaluation for a patient with a suspected BRUE?
The goal is to identify underlying diagnoses, especially serious diagnoses, that may mimic a BRUE. This should occur while limiting inappropriate testing. Another key goal is reassuring caregivers of infants with confirmed BRUEs that this is normal infant behavior (see Page 7).

What are serious underlying diagnoses to consider, and how common are they?
Few infants with a BRUE (less than 5%) – regardless of being classified as lower risk or non-low risk – will be diagnosed with a serious condition (2-5). In retrospective studies, the most common serious underlying diagnoses are seizure disorders including infantile spasms; airway abnormalities requiring surgery; child abuse including abusive head trauma and medical child abuse; and severe dysphagia or gastroesophageal reflux disease treated with nasogastric tube feeding. Other serious diagnoses include infections such as bacteremia, sepsis, meningitis, and severe lower respiratory tract infections. See Page 6 for a thorough differential diagnosis.

Is there a risk of death, poor prognosis, or event recurrence after an initial BRUE?
A meta-analysis found no increased risk of death in patients after a BRUE compared with the baseline risk of death in the first year of life (6). Another study that followed patients for five years after hospitalization for a BRUE found they had an excellent prognosis (7). One study showed a recurrent event occurring during the index visit in 14.3% of all (term and preterm) patients. Risk factors for event recurrence include a history of similar events and prematurity; however, prematurity does not appear to be predictive of a serious underlying diagnosis (3,4).

How often does hospitalization and additional testing lead to a diagnosis?
In large multicenter retrospective studies, an explanatory diagnosis was made in 37% of hospitalized patients (5), with only 4% of patients receiving a serious diagnosis (4-5). GER and feeding difficulties (overfeeding, choking, gagging, and laryngospasm) composed over two-thirds of the diagnoses made during the course of admission.

How common is it for patients not to meet "lower risk" criteria?
Perhaps not surprisingly, most infants will not meet lower-risk criteria, with retrospective studies showing only 5% to 21.5% of patients falling in the "lower risk" category (2,4,8-10).

What do we know about risk factors for patients who are not “lower risk”?
The presence of only one risk factor outlined by the AAP (Page 3) has not been found to be significantly associated with a serious diagnosis (2-3), and infants who do not meet lower-risk criteria are not necessarily at risk of an adverse outcome. In a retrospective study using data from 15 children's hospitals, risk factors that were associated with a serious diagnosis included a history of a similar event, a history of event clusters, the need for CPR, and an abnormal medical history (2). Patients with underlying diagnoses were also more likely to exhibit a color change or altered responsiveness and less likely to have an abnormal breathing pattern.

What’s next for research on BRUEs?
At the time of this writing, we need prospective studies since most studies are retrospective in nature. Unanswered questions include defining clear recommendations for admission in non-low-risk patients and improving diagnosis for BRUE mimics. It seems likely that the AAP guideline introduced in 2016 will be revised in the future as additional research is conducted.

About this guideline
The AAP's 2016 BRUE clinical practice guideline was the model for our approach to lower-risk patients (Page 3). We also outlined an evidence-based framework for patients who are not lower risk (Pages 4-5). Throughout, we have sought to emphasize not only the "what" but the "why" when it comes to evaluation.

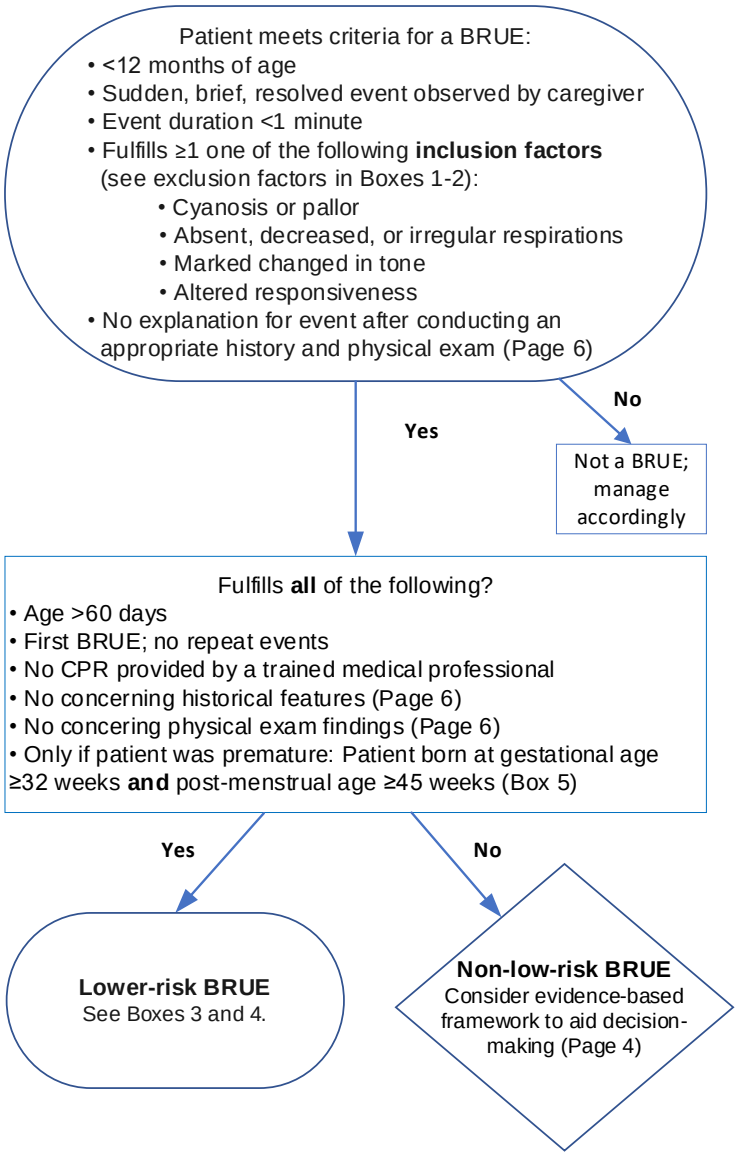
Formally, the AAP's guideline uses the term "higher risk" for patients who are not lower risk. However, studies since 2016 have shown that infants who are not "lower risk" are not necessarily at a high risk of a serious diagnosis. Hence, in this guideline, we have adopted the terms "lower risk" and "non-low risk" to stratify the patient populations by risk. We hope doing so causes less anxiety for caregivers and providers.

Finally, note the definition of "post-menstrual age" on Page 3. This is a simpler term and calculation compared with the terms "corrected gestational age" and "post-conceptional age" in the AAP's 2016 article, the latter of which is a term that should be avoided (11).

- Lee Morris and Paige Cassidy, editors

BRUE: low-risk patients

Clinical practice guideline (1)



BOX 5: **Post-menstrual age** = gestational age + chronological age (11). For instance, an infant who was born prematurely at 32 weeks 0 days is now 3 months 1 week in chronological age (13 weeks).

PMA = 32w0d + 3 months 1 week (13 weeks) = 45w0d

In this example, the infant could be considered lower risk. Providers may use the gestational age calculator at *https://peditools.org/dates* (12)

BOX 1: Not a BRUE if any **exclusion factors are present at time of medical evaluation** (not brief or resolved):
- Fever or recent fever
- Persistent vital sign anomalies
- Mental status changes, somnolence, lethargy
- Hypotonia, hypertonia
- Vomiting
- Bruising, petechiae, signs of injury/trauma
- Abnormal weight, growth, head circumference
- Noisy breathing (stridor, stertor, wheezing)
- Repeat event(s)

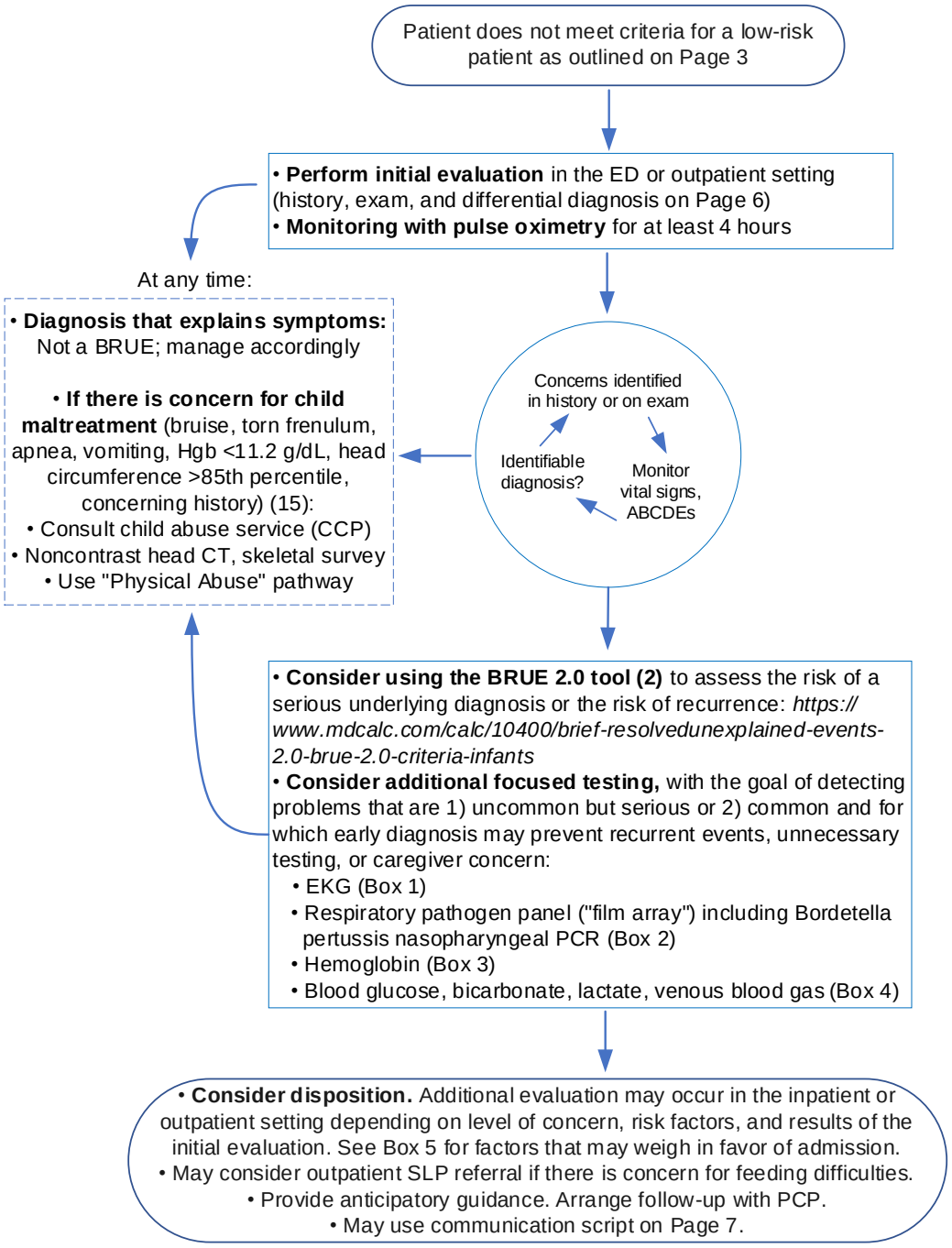
BOX 2: Not a BRUE if the initial event was characterized by any of these **exclusion factors:**
- Acrocyanosis or perioral cyanosis
- Rubor/redness
- Periodic breathing of newborn
- Breath-holding spell
- Tone changes or loss of consciousness from a breath-holding spell
- Hypertonia associated with crying, choking, or gagging due to reflux or feeding problems
- Tonic eye deviation or nystagmus
- Tonic-clonic seizure activity
- Infantile spasms

BOX 3: **For lower-risk BRUE patients:**
- Observe infant for 1-2 hours on pulse oximetry and cardiac monitor; observe during PO trial (13)
- Perform a thorough assessment of social risk factors to screen for child abuse
- Perform a complete, head-to-toe skin examination to assess for bruising
- Review the nature of BRUE with caregivers
- Reassurance and shared decision-making
- Anticipatory guidance per page 8; may offer CPR training; arrange close follow-up with PCP
- May obtain EKG. May identify channelopathy but may lead to false positives.
- May test for pertussis by nasopharyngeal swab. Consider vaccination status. May identify treatable infection; risk of unnecessary cost.

BOX 4: **The following tests should routinely be avoided** in lower-risk BRUE patients: CBC, hemoglobin, blood culture, lactic acid, bicarbonate, electrolytes, ammonia, blood glucose; urinalysis (bag or catheter); lumbar puncture or CSF studies; chest x-ray, respiratory pathogen panel, venous or arterial blood gas; urine organic acids, plasma amino acids, or plasma acylcarnitines; echocardiogram; home cardiorespiratory monitoring, overnight polysomnograph; neuroimaging (CT, MRI, ultrasound) or EEG; GER studies (upper GI series, pH probe, endoscopy, barium study, nuclear scintigraphy, ultrasound). **Do not order** anti-seizure drugs or anti-reflux medications for patients with lower-risk BRUE.

BRUE: non-low-risk patients

This page is an evidence-based framework for **initial evaluation** of non-low-risk patients (14). Due to limited data on non-low-risk patients with BRUE, this framework is not a clinical practice guideline.



Box 1: Obtain **EKG** to screen for arrhythmia and congenital heart disease. Ask about family history of sudden unexplained death in a first- or second-degree relative before age 35, and history of BRUE or arrhythmia in family. EKG should be read by pediatric cardiologist if available.

Box 2: A **respiratory pathogen panel** may be useful because apnea may present before other infectious symptoms. Consider exposures, season. This test includes **pertussis**, which carries a particular risk in underimmunized families and communities.

Box 3: **Hemoglobin** may evaluate for anemia, especially after recurrent BRUE. Anemia results from many causes including abusive head trauma.

Box 4: **Blood glucose, bicarbonate or lactic acid** may show evidence of an inborn error of metabolism but are not specific for inborn errors. A **venous blood gas** may show metabolic or respiratory acidosis and may be considered especially for recurrent BRUEs.

Box 5: **Considerations for hospitalization** based on concern for serious underlying diagnosis (2):
• History of similar event(s)
• History of event clusters (including repeat events during initial evaluation)
• Need for CPR
• Abnormal medical history
• **Considerations for hospitalization** based on risk of recurrence include prematurity or the factors listed above.

BRUE: secondary evaluation

This page is an evidence-based framework for **secondary evaluation** of non-low risk patients (14). Designed for inpatients, evaluation may occur in outpatient setting. Due to limited data on non-low-risk patients, this framework is not a clinical practice guideline.

At any time: Diagnosis that explains symptoms: Not a BRUE; manage accordingly

Patient is admitted

- **Obtain** thorough history and exam (Page 6)
- **Perform** prolonged continuous pulse oximetry
- **Observe** for repeat events, better characterization of events, or social concerns

If not previously done, consider:

- **SLP consult** for feeding and swallow evaluation
- **EKG** to be read by a pediatric cardiologist
- **Respiratory pathogen panel** including pertussis screen as per Page 4

No repeat events and no explanation within 24 hours

- **Discharge home**
- May use communication script (Page 7)
- May offer CPR education (search "infant CPR" in Discharge Instructions tab in Epic for QR code and video link)
- Arrange close follow-up with PCP

Pursue additional evaluation based on initial event and other data (differential diagnosis: Page 6)

Is there concern for ...

Silent aspiration or feeding problem?
History: Chronic, severe, or recurrent feeding problems

Exam: Coughing, choking, or gagging during or shortly after feeding

Evaluation: After careful feeding history and SLP consult, consider videofluoroscopic swallowing study (VFSS)

GERD?
History: Coughing or choking with feeds; regurgitation or vomiting, irritability, feeding resistance, poor weight gain, odynophagia, poor weight gain

Exam: Milk or formula in mouth, choking/gagging noises

Evaluation: After feeding history and SLP consult, consider gastroenterology consult or VFSS

Seizures?
History: Paroxysmal, sustained, recurrent, stereotyped events

Exam: Abnormal reflexes, tone, or eye movements; neurocutaneous findings; dysmorphic features

Evaluation: Consult neurology; obtain prolonged EEG (12-24 hours)

Abusive head trauma?
History: Period of decreased responsiveness, seizures, trouble breathing, apnea, vomiting. May occur without external trauma. In the care of a nonrelated person, more likely nonrelated man (16).

Exam: Bruising, scalp swelling, subconjunctival hemorrhage, hemoglobin <11.2 g/dL, or head circumference >85th percentile

Evaluation per Page 4

Obstructive apnea?
History: Recurrent events, apnea or periodic breathing, prematurity or recurrent and severe presentations, snoring, noisy respirations

Exam: Micrognathia, tachypnea, abnormal breath sounds

Evaluation: After pulse oximetry, consider hemoglobin, VBG, ENT and pulmonology consults, and polysomnography

Central apnea?
History: Prematurity, history of infection (meningitis), trauma (subdural hematoma), or congenital problems (TORCH infection, brain malformation, congenital hypoventilation syndrome)

Evaluation: Consult pulmonlogy; consider MRI or noncontrast CT of head ("rapid" MRI preferred to avoid sedation)

Arrhythmia or congenital heart disease?
History: Family history of sudden death in first- or second-degree relative before age 35; LQTS; arrhythmia; BRUE in sibling; syncope in neonates, children, young adults

Exam: May be normal

Evaluation: After EKG, consult cardiology

Inborn error of metabolism?
History: Episodic hypoglycemia or acidosis; family history of sudden infant death syndrome in first-degree relatives; recurrent events; abnormal or unknown newborn screen

Exam: May be normal; tachypnea, tachycardia

Evaluation: Consider serum electrolytes, lactate, ammonia, biochemical genetics consult

BRUE: history, exam, differential

Definition (1): A diagnosis of exclusion, a BRUE is an event occurring in infants younger than 12 months described by the observer as brief (lasting less than 1 minute, but typically <20-30 seconds), resolved (meaning the patient returned to baseline state of health after the event), and with a reassuring history, physical exam, and vital signs at the time of evaluation by trained medical providers. During a BRUE, the observer reports one or more of the following: cyanosis or pallor; absent, decreased, or irregular breathing; marked change in tone (hypertonia or hypotonia); or altered level of responsiveness.

Historical features to consider (1)

- **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 of historians?
- **Immediately before the event:** Where did it occur (home/elsewhere, room, crib/floor, etc.)? Awake or asleep? Position: supine, prone, upright, sitting, moving? Feeding? Anything in the mouth? Availability of item to choke on? Vomiting or spitting up? Objects that could smother or choke?
- **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 breathe? Skin color: normal, pale, red, or blue? Bleeding from nose or mouth? Color of lips: normal, pale, blue?
- **End of event:** Approximate duration of the event? How did it stop: with no intervention, picking up, positioning, rubbing or clapping back, mouth-to-mouth, chest compressions, etc? End abruptly or gradually? Treatment provided by parent/caregiver (eg, glucose-containing drink or food)? 911 called by caregiver?
- **After event:** Back to normal immediately, gradually, still not there? Before back to normal: quiet, dazed, fussy, 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, unexplained bruising?
- **Past medical history:** Pre-/perinatal history, gestational age, newborn screen (IEMs, congenital heart disease), previous BRUE episode. Reflux (if yes, obtain details including management)? Breathing problems? Noisy? Snoring? Growth patterns normal? Development normal? Assess a few major milestones across categories: any concerns about development or behavior? Illnesses, injuries, emergencies? Previous hospitalization, surgery? Recent immunization? 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 sibling? Long QT syndrome? Arrhythmia? Inborn error of metabolism or genetic disease? Developmental delay?
- **Environmental history:** Housing (general, water damage, mold problems)? Exposure to tobacco smoke, toxic substances, drugs?
- **Social history:** Family structure, individuals living in home? Housing: general, mold? Recent changes, stressors, or strife? Exposure to smoke, toxic substances, drugs? Recent exposure to infectious illness, particularly upper respiratory illness, paroxysmal cough, pertussis? Support system(s)/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 (eg, 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 or substance abuse?

Physical exam (1)

General: Craniofacial anomalies (mandible, maxilla, nasal), age-appropriate responsiveness to environment
Growth variables: Length, weight, occipitofrontal circumference
Vital signs: Temperature, pulse, respiratory rate, blood pressure, oxygen saturation
Skin: Color, perfusion, evidence of injury (eg, bruising, erythema)
Head: Shape, fontanelles, bruising, other injury
Eyes: General, extraocular movement, pupillary response, conjunctival hemorrhage, retinal examination (if indicated)
Ears: Tympanic membranes
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, anomalies
Heart: Rhythm, rate, auscultation
Abdomen: Organomegaly, masses, distention, tenderness
Genitalia: Any abnormalities
Extremities: Muscle tone, injuries, limb deformities, fracture
Neurologic: Alertness; responsiveness; response to sound and visual stimuli; general tone; pupillary response to light; symmetric reflexes; symmetry of movement, tone, strength

Differential diagnosis by system (14)

Abuse: Head trauma, poisoning, suffocation, medical child abuse
GI: Reflux (for instance, reflux leading to aspiration causing a vagal response or laryngospasm), laryngospasm, oropharyngeal dysphagia, tracheoesophageal fistula, esophageal stricture, vascular sling, cricopharyngeal achalasia
Pulmonary: Obstructive apnea due to upper or lower structural airway anomalies (laryngomalacia, laryngeal cleft); central apnea due to abuse, meningitis, congenital central hypoventilation syndrome, or structural brain anomalies; parenchymal lung disease due to infection or pneumonitis from "microaspiration"; anemia; periodic breathing
Neurologic: Epilepsy or seizures, infantile spasms, neuromuscular disorder, tuberous sclerosis, benign neonatal epilepsy syndrome
Cardiology: Arrhythmia, long QT syndrome, congenital heart disease, cardiomyopathy
Infection: Bacteremia, sepsis, bacterial or viral meningitis, lower respiratory tract infection (e.g., pneumonia), pertussis, upper respiratory viral infection, UTI
Inborn errors of metabolism: Urea cycle or fatty acid oxidation disorders, organic or lactic acidemias
Congenital: BRUE (a diagnosis of exclusion; caused by normal immature physiology in an infant)

BRUE: communication script

Providers commonly experience apprehension when talking with caregivers about brief resolved unexplained events (17). Uncertainty owes to discomfort with the underlying pathophysiology, the fact that BRUE is a clinical diagnosis without a confirmatory test, and the difficulty in explaining the nature of a frightening event. Indeed, some caregivers continue to feel uncomfortable after discharge (18), which speaks to the challenge of reassurance.

The following communication script was created after soliciting feedback from Helen DeVos Children's Hospital pediatricians. It may be used to assist with communication about BRUE with families, bearing in mind that all conversations should be personalized as needed. Use the phrases that feel natural for you as a provider, and remember that not all of them may be necessary in every situation.

Before evaluation

Express empathy, explore concerns, establish connection with caregivers.

► Acknowledge the frightening nature of the event.
• "This was scary."
• "I'm sorry to hear how stressful it was."
• "We are going to keep your baby safe."
• May say to caregiver, "Tell me what you're worried about" as a way to personalize the conversation.

Explain what a BRUE is and the goals of evaluation.

• "It's common for infants younger than 1 year old to experience changes in breathing, tone, or color."
• "After our evaluation, we can often assign the cause of these events to normal immature physiology. This is called a brief resolved unexplained event."
• "Occasionally, this behavior raises concern for an underlying diagnosis. One of our goals with today's visit will be to make a definitive diagnosis if possible."
• "Sometimes the evaluation does not require a lot of testing from the start, but time and observation. We appreciate your patience."

After completed evaluation

Provide a differential diagnosis as well as diagnoses that "don't fit."

► May provide a short differential of possible diagnoses based on the history and exam; explain why scary or bad diagnoses "don't fit."
• "After hearing your story and doing a physical exam, we have considered several diagnoses."
• "At this time, we have a low concern for a feeding issue, a heart arrhythmia, a problem in the lungs, an infection such as meningitis or pneumonia, or a seizure" (list will vary depending on situation).
► If expressing uncertainty, do so in terms of a differential diagnosis rather than saying, "I don't know" (19).

Offer reassurance; consider using BRUE 2.0 calculator for non-low-risk infants (link on Page 4).

• "Your child is not in imminent danger."
• "The low risk of a serious diagnosis for your infant is supported by their score on the BRUE 2.0 calculator" (after calculating the patient's score and verifying this is true and remembering that risk tolerance varies among families and providers).

If patient will be discharged to home, **describe next steps** and **provide clear reasons for return to care**. Offer to **arrange appointment with PCP** whenever possible.

• "Let's talk about things you can do to keep your baby safe" (20):
- Always place your baby on their back to sleep.
- Your baby should sleep on a flat, firm surface in a crib or bassinet.
- Never co-sleep or share a bed with your baby.
- Keep your baby away from cigarette smoke, including secondhand smoke. Change your clothes and wash your hands after smoking.
- The use of home oxygen monitors is not recommended.

• "Bring your baby back to the doctor if there is":
- fever (defined as 100.4 degrees Fahrenheit or higher)
- vomiting, diarrhea, or rash
- decreased oral intake or decreased urine output
- or if your baby isn't acting like themselves for any other reason

► Offer to arrange appointment with pediatrician to ensure things continue to go well

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