Inconsolable Crying in Infants: Differential Diagnosis in the Pediatric Emergency Department

Nusa Matijasic, MD1 and Zdenka Plesa Premilovac, MD1

Introduction

Crying is a part of the physiological neurodevelopment of an infant, ensuring survival and social interaction. The crying period reaches its peak at 6 to 8 weeks of life, with an average duration of 2.6 hours per day, after which it gradually decreases by the age of 3 to 4 months. Episodes of inconsolable crying typically tend to cluster during the evening, but may occur throughout the day, causing anxiety, fatigue, and concern in the caregiver. Therefore, it is not surprising that excessive crying is one of the most common symptoms in emergency departments, leading to approximately 20% of pediatric consultations of infants up to 3 months old.1,2 According to studies, an organic cause is revealed in only 5% of infants, with urinary tract infections being the most prevalent (in more than 50% of cases), especially in newborns.2,3 Other underlying etiologies are numerous, varying from simple general causes such as hunger or tiredness to severe life-threatening conditions. In most cases, the diagnosis can be set after taking a detailed medical history and performing a thorough clinical examination of the child.

Differential Diagnosis by Organic System

Upon studying extensive literature concerning pathologies in infancy, we herein briefly discuss the most common organic causes leading to inconsolable crying in infants that should be taken into consideration by physicians working in pediatric emergency departments. Throughout the following text, we point out alarming accompanying signs and symptoms requiring further diagnosis or prompt therapeutic intervention. In order to simplify the text and make it easier for the reader, we have listed these conditions according to organic systems.

The Skin

Hair Tourniquet Syndrome

Hair tourniquet syndrome is a circumferential constriction of body appendages by a strand or strands of hair or clothing fibers, causing strangulation, which may subsequently lead to ischemic gangrene and amputation of the affected part. According to a review of 66 cases from the medical literature, the most commonly affected sites are toes (43%), genitalia, and fingers.4 The diagnosis can be delayed, as hair strands are more stretchable when moist, but once they are dried they shrink and wind so tightly around the body part that they even cut through the edematous skin. The surrounding skin may re-epithelialize, and the hair escapes detection. The median age of infants with toe involvement is 4 months, which coincides with excessive hair loss in the postpartum period (telogen effluvium). The optimal therapeutic option is wound exploration under general anesthesia, along with a longitudinal incision on the dorsum, perpendicular to the constricting agent, which allows safe and complete decompression.4,5

Diaper Dermatitis

Diaper dermatitis is a location diagnosis that encompasses a group of dermatoses affecting body parts covered by the diaper (perineum, buttocks, lower abdomen, and thighs). Primary irritant diaper dermatitis, the most prevalent one, is a result of maceration of the skin in the hot and humid, enclosed diaper environment. It is one of the most common skin diseases in the first months of life. Characterized by confluent erythematous lesions in the form of the letter W, it usually spares body folds that are not in direct contact with the diaper. The intensity of skin affection ranges from mild to severe forms, including Jacquet dermatitis with vesiculo-erosive-ulcerative lesions, followed by permanent atrophy and hyperpigmentation of the skin. As the skin’s natural pH is altered and its barrier function reduced, secondary infections, mainly fungal such as those caused by Candida yeasts, occur. Typical findings of candidosis are erythematous

1Children’s Hospital Zagreb, Zagreb, Croatia

Corresponding Author:
Nusa Matijasic, Children’s Hospital Zagreb, Klaićeva 16, Zagreb 10000, Croatia.
Email: nusa.matijasic@gmail.com
plaques that, unlike in primary irritant diaper dermatitis, affect the body folds, peripheral skin desquamation, and satellite pustules. The incidence has increased in recent years with the increased use of broad-spectrum oral antibiotics and subsequent diarrhea. Atopic Dermatitis

Infants affected by atopic dermatitis tend to have behavioral deviations in the form of irritability, fussiness, and increased crying, due to intense pruritus, discomfort, and sleep deprivation. Their caregivers, unable to cope and help their crying child, therefore often search for comfort and advice through numerous emergency department visits. It is interesting that excessive crying in infants with a normal skin status can be a predictive symptom for development of atopic dermatitis later in childhood. A prospective study conducted on 116 healthy but high-risk infants, with a positive family history, demonstrated that those who manifested atopic disease at 2 years had shown significantly more fussing during the 7th week of life and excessive crying during the 12th week of life, compared with those who remained healthy.

Eyes

Corneal Abrasion

Corneal abrasion is a superficial lesion of the corneal epithelium, usually caused in infants by fingernail scratching or foreign body trauma. Signs and symptoms include redness of the eye, excessive tearing, blepharospasm, and photophobia. A study conducted on 96 1- to 12-week-old, asymptomatic, healthy infants showed 49% of them had corneal abrasion, diagnosed by a fluorescein dye test. Although the study confirmed a high incidence of corneal abrasions in infants, it also demonstrated that the mean crying times were not significantly different for children with and without abrasions, pointing that pediatricians should be extremely careful when attributing excessive crying to corneal abrasions, potentially missing a more serious condition.

Glaucoma

Most cases of glaucoma in infants are primarily congenital, occurring as a result of an anomalous development of the eye’s aqueous outflow system, leading to increased intraocular pressure. Apart from the infant being irritable, it presents with photophobia, blepharospasm, epiphora, and a strikingly enlarged eye (hydrophthalmus, buphthalmos). The condition is more common in males and is usually bilateral. Although glaucoma is mainly diagnosed immediately at birth (25% to 40% of cases), signs may be noticed at any time during the first few months of life. Considering that it is an organic disorder leading to blindness, with surgery being the only form of effective treatment, early diagnosis is of utmost importance.

Ears and Oropharynx

Ear Infections

Various conditions involving the ears and oropharynx result in excessive crying in infants. They are mainly infections, especially otitis, which is one of the most frequent diagnosis during childhood, with a reported incidence peak between the ages of 6 and 18 months. Although the medical literature suggests that there is a serious problem concerning the overdiagnosing of acute otitis media in children, a large cohort Danish study actually proved that the infection frequently remains undetected in young infants due to their lack of language skills and the small external ear canal. Therefore, many of those examined for inconsolable crying leave the physician with a misdiagnosis of infantile colic. In order to prove the hypothesis, the study investigated whether infants with a diagnosis of infantile colic were more likely to have reported subsequent ear problems during early childhood, compared with infants with normal crying patterns. A “dose-response” pattern was observed as the highest risk of ear infections was in the group of infants who spent the most hours crying and fussing. In conclusion, to avoid these mentioned problems, it is essential to perform a precise otoscopic examination with adequate illumination, after cerumen removal and with the emphasis on the position and mobility (not only redness) of the tympanic membrane.

Stomatitis

Inflammatory conditions of the oral mucous membranes are of great clinical importance in infants, as they often present with erosions and ulcers, which are painful and can lead to decreased oral intake and dehydration. They may be related to relatively harmless conditions, such as acute Herpes simplex and Coxsackie virus infections or candidosis, but may also be associated with severe systemic diseases that need a prompt diagnostic and therapeutic approach. A special entity found in infants is Bednar aphthae. These are infected wounds localized on the hard palate caused by chronic trauma due to an incorrect feeding posture and feeding method. Although Bednar aphthae do not require specific treatment since they regress spontaneously in a few days after correcting the feeding position, if they remain undiagnosed
they may worsen the nursing and cause feeding intolerance.\textsuperscript{12}

**Infant Teething**

A variety of symptoms has long been strongly associated with infant teething by both parents and pediatricians. However, there is little evidence to support these beliefs. Although studies have found that symptoms, such as inconsolable crying and irritability, along with increased biting, sucking, sleep disturbances, facial rash, decreased appetite for solid foods, and mild temperature elevation, were all statistically associated with teething, they did not confirm the expected strong connection. A prospective study conducted on 125 healthy infants showed that none of the above-mentioned symptoms was sensitive enough for teething or could reliably predict the emergence of a tooth, as no symptom occurred in $>35\%$ of teething infants and no symptom occurred $>20\%$ more often in teething than in nonteething infants. Therefore, the strong idea that teething causes excessive discomfort may delay the diagnosis of a more serious underlying pathologic process in a crying infant.\textsuperscript{13}

**Cardiovascular System**

**Congenital Cardiovascular Anomalies**

In 2009, a large Norwegian case-cohort study was the first to reveal increased emotional reactivity (irritability, intense crying, and difficulty soothing) in infants with moderate to severe congenital heart disorders.\textsuperscript{14} These congenital disorders affect about 1\% of all live born children with a wide spectrum of severity. Neonates with critical congenital anomalies requiring prompt intervention usually present during their birth hospitalization with serious and life-threatening manifestations, including shock, cyanosis, tachypnea, and/or symptoms of pulmonary edema. However, some infants with congenital cardiovascular defects may be asymptomatic at birth and develop symptoms after discharge.\textsuperscript{15,16} Examples are congenital coronary artery anomalies, such as the abnormal origin of the left coronary artery from the pulmonary artery (ALCAPA) syndrome, known also as the Bland-White-Garland syndrome. ALCAPA is characterized by episodes of crying, along with pallor, increased sweating, and feeding difficulties. The newborn is discharged as healthy, but as the pulmonary vascular resistance decreases so does the perfusion through the anomalous left coronary artery, causing myocardial ischemia, pain, heart failure, and even sudden death.\textsuperscript{17}

**Paroxysmal Supraventricular Tachycardia (PSVT)**

PSVT is the most frequent form of symptomatic arrhythmia in children. Newborns may have a positive history of fetal tachycardia, possibly with signs of ventricular dysfunction due to tachycardia in fetal age. On the other hand, infants with no known history of fetal tachycardia present with episodes including crying, irritability, poor feeding, pallor, tachycardia, and diaphoresis. Their heart rate is typically in excess of 220 beats per minute, unresponsive to calming measures and fluid resuscitation. Most of them have structurally normal hearts. Only 15\% of infant PSVT cases are associated with heart disease, drug administration, or febrile illnesses. It is crucial to identify the condition as it causes progressive left ventricular dysfunction, especially if the heart rate is higher than 250 beats per minute, which leads to heart failure.\textsuperscript{18}

**Myocarditis**

The main pathophysiological process in myocarditis is the development of myocardial necrosis and interstitial edema, with the consequent impairment in the contractile function of the myocardium. This leads to inadequate cardiac output that worsens in the presence of comorbidities, such as fever and anemia. In addition, acute life-threatening arrhythmias may occur. As compensatory mechanisms are depleted, the heart fails. Newborns and infants are more severely affected because of their limited adaptive possibilities. The common complaints in infants are dyspnea with feeding, vomiting, and irritability, usually with a positive history of flu-like symptoms. Physical examination reveals tachypnea, gallop rhythm, tachycardia, hypotension, pallor, delayed peripheral capillary refill, hepatomegaly, and generalized edema. Cardiomegaly on chest X-ray and small voltages on electrocardiogram are also typical findings.\textsuperscript{19,20} Myocarditis in children is mainly caused by cardiotropic viruses, with infants having a higher rate of blood viral positivity compared with older children.\textsuperscript{21}

**Gastrointestinal System**

**Acute Abdomen**

Acute gastroenteritis, constipation, gastroesophageal reflux (GER), nutritive allergies, lactose intolerance, anal fissures, hernia, appendicitis, and gastrointestinal obstruction are only some of the various gastrointestinal causes of discomfort and crying in young children. A
proper physical examination of the abdomen is always challenging in infants, but crucial, as one should never miss possibly lethal acute conditions, such as bowel obstruction, primarily as a result of volvulus or intussusception. If this is the case, the infant presents with periodic fierce attacks of inconsolable crying, perfuse vomiting, distension, fever, and signs of shock. Intestinal malrotation is a congenital abnormality resulting in shortening of the mesenteric root that is predisposed to midgut volvulus. Its incidence is estimated as 1 in 500 live births.\textsuperscript{19,22} A review performed on 37 cases of intestinal malrotation showed that the most common symptom was bilious vomiting (97%), followed by constipation. Therefore, neonates and infants with persistent bilious vomiting should always be highly suspect for malrotation and preferably undergo ultrasound as the first diagnostic step.\textsuperscript{22} However, 95% of patients appear to be well on initial examination, including a large number of those with an already developed volvulus.\textsuperscript{23} On the other hand, intussusception, which remains the number one cause of intestinal obstruction in infants and young children, is characterized by a classical symptom triad consisting of abdominal pain, vomiting, and currant-jelly stools. Still, this well-known triad is present in less than a quarter of patients, and currant-jelly stools are especially rare in the early stages, as they are a manifestation of an already significantly ischemic gut.\textsuperscript{19,24}

Gastroesophageal Reflux

GER is the retrograde passage of the gastric contents into the esophagus. When associated with esophagitis and persistent symptoms such as excessive vomiting, regurgitation, failure to thrive, or respiratory disorders, the condition is referred to as gastroesophageal reflux disease (GERD). GER is a physiological phenomenon in infancy with most infants having complete resolution by the end of the first year of life. In a study of 948 healthy infants, 50% of those aged 0 to 3 months, 67% of those 4 months old, and 21% of those aged 6 to 7 months regurgitated at least once a day, while the incidence declined to only 5% in those 10 to 12 old.\textsuperscript{25} Although there is a widespread opinion that children who cry excessively have GER more often, a study of 151 babies with persistent crying who were admitted to hospital for 24-hour pH monitoring and cry/sleep pattern recording demonstrated that crying was related neither to the duration of reflux nor to the number of reflux episodes.\textsuperscript{26} In addition, the use of proton pump inhibitors in the management of infants with excessive crying, based on the presumptive diagnosis of GERD, remains a common practice, despite the fact that there is a lack of any evidence-based treatment efficacy or utility in these patients. A randomized, double-blind, placebo-controlled crossover trial showed that, compared with a placebo, omeprazole significantly reduced esophageal acid exposure, but not irritability or crying.\textsuperscript{27}

Genitourinary Tract

Besides urinary tract infections, which are the leading organic cause of excessive crying in infants and the reason why crying infants should undergo urinalysis, especially when febrile, other genitourinary conditions are discussed below which may cause discomfort, pain, and inconsolable crying in babies.

Ovarian Torsion

Pediatric ovarian torsion is a rare finding, especially in infants. It is a result of the rotation of the ovary and its vasculature along its axis, leading to the obstruction of venous outflow, infarction, necrosis, and even peritonitis. Most cases are reported in ovaries containing benign masses, predominantly cysts, but if torsion occurs a malign neoplasm should also be suspected. Torsions are more common on the right side, which is probably either due to the hypermobile caecum on the right or the sigmoid colon on the left, which restricts the movements of the ovary. Sterile pyuria is documented in a substantial proportion of patients, although no single laboratory finding is consistently suggestive of torsion. The most useful initial diagnostic modality is ultrasound. Infants usually present with excessive crying and a painful abdomen, but due to its rarity and nonspecific signs and symptoms, which mimic other acute abdominal conditions, the entity frequently goes unrecognized and surgical intervention is unfortunately often delayed. In a study of 13 pediatric patients with ovarian torsions, only one was a 7-month-old infant. Although in her case she underwent prompt surgical intervention, the ovary was found to be necrotic, which raised the question whether the disease process is accelerated in infants, or the more severe findings are due to torsions being initially asymptomatic in that age group.\textsuperscript{28}

Acute Scrotum

Acute scrotum is a pediatric emergency defined by scrotal pain, swelling, and redness, of acute onset. The differential diagnosis encompasses torsion of the appendix of the testis, testicular torsion, acute orchitis and/or epididymitis, trauma, incarcerated inguinal hernia, tumor, or idiopathic scrotal edema.\textsuperscript{29} Testicular torsion accounts for about one quarter of all acute scrotum cases in children, with a much higher incidence in those younger than 1 year of life, and it is usually supravaginal. It is a
sudden rotation of the testis around its axis, resulting in blocked venous drainage, reduced arterial perfusion, and hemorrhagic infarction of the parenchyma. The diagnosis needs to be set rapidly since testicular ischemia may lead to infertility later in life. Special anatomical variants predispose to torsion, such as the bell-clapper anomaly, in which the gubernaculum, testis, and epididymis are not anchored as they normally are, attached to tunica vaginalis.

**Neurological System**

**Meningitis**

Meningitis in young children has a nonspecific clinical presentation. Infants are often initially examined in emergency departments due to minor variations in their behavior noticed by caregivers. Bacterial meningitis is a medical emergency, requiring prompt recognition and urgent antibacterial therapy. While overall mortality has declined over the past several decades, morbidity associated with meningitis remains practically unchanged, especially in the neonatal group. Early signs and symptoms are subtle. Positive meningitic signs are usually late findings associated with a poor outcome. According to Mercier, there are 2 distinct clinical forms observed in infants. The first is characterized by irritability, abnormal crying, bulging fontanel, unusual generalized seizures, fever usually greater than 39°C, and poorly specific gastrointestinal signs, such as anorexia and/or vomiting. The second comes in the form of severe sepsis with tachycardia, cold and/or mottled limbs, skin hemorrhage, and suggests a meningococcal disease. Viral central nervous system infections frequently occur as a complication of systemic viral infections, and may be as severe as bacterial. Over 100 viruses are implicated as causative agents, including Herpes simplex virus type 1, which is the most common and neurologically devastating, causing death or permanent disability in 90% of infants affected. Performing lumbar puncture to collect cerebrospinal fluid is necessary to confirm the diagnosis, determine the causative pathogen, and adjust antimicrobial therapy.

**Musculoskeletal System**

**Bone Fractures**

Symptoms and signs suggesting bone fractures in children younger than 12 months of age include reduced movement of the affected body part, localized swelling, crepitus, screaming and withdrawal on palpation of the fractured limb bone, or an asymmetrical Moro reflex. The two most frequently recognized underlying diseases causing bone fragility in infancy are metabolic bone disease of prematurity and osteogenesis imperfecta. The first one, also referred to as osteopenia of prematurity and preterm rickets, is caused by a reduction in bone mineral content due to deprivation of a period of intrauterine minerals supply, inadequate postnatal intake of vitamin D, calcium, and phosphorus, an extended period of total parenteral nutrition, lengthy duration of immobilization, and the use of diuretics and corticosteroids. It is seen mainly in infants born at <28 weeks of gestation, who had necrotizing enterocolitis, late (>30 days) establishment of full enteral feeds, conjugated hyperbilirubinemia, and chronic lung disease. Fractures usually occur at the age of at least 10 weeks and stop before the age of 6 months.

Another important thing to consider is the possibility of physical abuse, which is the underlying etiology of 12% to 20% of fractures in infants and toddlers. The presence of multiple fractures or other injuries (coexisting bruises, injuries of the internal organs or central nervous system), fractures of different stages of healing, and a delay in obtaining medical treatment are all warning signs of possible child abuse.

**Septic Arthritis**

Septic arthritis in infants is a rare and challenging diagnosis. It usually involves the knees, hips, and shoulders. The most common causative microorganisms are Group B Streptococcus, methicillin-sensitive Staphylococcus aureus, Haemophilus influenzae, Streptococcus pneumoniae, Salmonella enterica, and Candida albicans. In a study conducted on 14 infants aged up to 3 months, the leading findings on physical examination were decreased range of motion (100%), tenderness (100%), and swelling (71.4%). Their mean temperature was 38.5°C. White blood cell count, erythrocyte sedimentation rate, and C-reactive protein levels were likely to be slightly elevated, but nonspecific, and the diagnosis was made only in combination with physical status and imaging studies.

Table 1 summarizes some of the most common causes of inconsolable crying in infants, listed by organic systems.

**Conclusion**

Inconsolable crying in infants is one of the most common diagnosis in pediatric emergency departments. Underlying etiologies are numerous and it is practically impossible to list them all; they may be anything from simple general causes, such as hunger or tiredness, to severe life-threatening conditions. However, a thorough medical history and a detailed physical examination of an undressed child are usually
sufficient to set the preliminary diagnosis. If the child is in a good general condition, with stable vital signs, afebrile, and with unremarkable somatic and neurological findings, no further laboratory or imaging studies are recommended. The exception is urinalysis, as urinary tract infections are the most common organic cause of inconsolable crying. Once all the organic causes have been excluded, and the crying continues, the pediatrician should consider the diagnosis of infantile colic, defined as episodes of unexplained fussiness, fulfilling Wessel’s criteria.39

**Author Contributions**

NM: designed the work, made acquisition, analysis and interpretation of data for the work, and made final approval of the version to be published. ZPP: made conception of the work, revised it critically for important intellectual content and made final approval of the version to be published.

**Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

**ORCID iD**

Nusa Matijasic [https://orcid.org/0000-0002-1568-5095](https://orcid.org/0000-0002-1568-5095)

**References**


