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The Crying Infant: Diagnostic Testing and Frequency of Serious Underlying Disease

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What's Known on This Subject	What This Study Adds
Although the differential diagnosis of crying is extensive, the frequency of severe underlying disease is unclear. On the basis of very limited data, it has been recommended that corneal fluorescein staining, eyelid eversion, and rectal examination be performed on crying infants.	This study confirms that the clinical assessment should guide decision-making in children presenting with crying. Afebrile infants in the first few months of life should undergo urine evaluation. Other investigations should be performed on the basis of clinical findings.

ABSTRACT

OBJECTIVE. To determine the proportion of children evaluated in an emergency department because of crying who have a serious underlying etiology. Secondary outcomes included the individual contributions of history, physical examination, and laboratory investigations in determining a diagnosis.

PATIENTS AND METHODS. We performed a retrospective review of all afebrile patients <1 year of age who presented with a chief complaint of crying, irritability, screaming, colic, or fussiness. All children with a serious underlying illness were identified by using a priori defined criteria. Chart review was conducted to determine if history, physical examination, or investigation data contributed to establishing the child's diagnosis.

RESULTS. Enrollment criteria were met by 237 patients, representing 0.6% of all visits. A total of 12 (5.1%) children had serious underlying etiologies with urinary tract infections being most prevalent ($n = 3$). Two (16.7%) of the serious diagnoses were only made on revisit. Of the 574 tests performed, 81 (14.1%) were positive. However, only 8 (1.4%) diagnoses were assigned on the basis of a positive investigation. History and/or examination suggested an etiology in 66.3% of cases. Unwell appearance was associated with serious etiologies. In only 2 (0.8%) children did investigations in the absence of a suggestive clinical picture contribute to the diagnosis. Both of these children were <4 months of age and had urinary tract infections. Among children <1 month of age, the positive rate of urine cultures performed was 10%. Ocular fluorescein staining and rectal examination with occult blood testing were performed infrequently, and results were negative in all cases. Successful follow-up was completed with 60% of caregivers, and no missed diagnoses were found.

CONCLUSIONS. History and physical examination remains the cornerstone of the evaluation of the crying infant and should drive investigation selection. Afebrile infants in the first few months of life should undergo urine evaluation. Other investigations should be performed on the basis of clinical findings. *Pediatrics* 2009;123:841–848

INFANTS COMMUNICATE AND express discomfort by crying. This can be due to a variety of reasons ranging from hunger or a desire for attention to severe life-threatening illness. Healthy children cry on average nearly 3 hours per day at 6 weeks of age with the peak occurring between 3 PM and 11 PM.[1] By the time parents present to the emergency department (ED) with their crying child, caregivers are often anxious, frustrated, and sleep deprived. These emotions contribute to making the evaluation of the nonverbal, crying infant very difficult.

Although the prevalence of excessive crying varies by definition employed,[2] the peak nevertheless occurs during the second month of life with a prevalence of 1.5% to 11.9%.[3] Although the differential diagnosis is extensive and involves every organ system, the frequency of severe underlying disease is unclear. Although it has been stated that organic diseases underlie <5% of cases of infantile colic,[4] the only North American ED study of afebrile infants with acute, unexplained, excessive crying reported a "serious" etiology in 61% of such children.[5] The authors of that study defined a diagnosis as serious if it was deemed "by at least 2 of a panel of 3 pediatricians to require prompt treatment or to have the potential to cause harm if not recognized or left untreated."[5] This definition was very inclusive, as otitis media, herpangina, herpes stomatitis, gastroesophageal reflux, and vaccine reactions were among the diagnoses

represented. Subsequently, this study, which recommends routinely performing corneal fluorescein staining, eyelid eversion, and rectal examination, formed the basis for the establishment of guidelines for the evaluation of crying infants.

In an attempt to develop evidence-based guidelines for the diagnostic evaluation of afebrile children presenting with excessive crying, we reviewed the clinical findings, test results, and diagnoses in a consecutive series of children who presented to the ED with acute, excessive, unexplained crying.

METHODS

Study Site
The Hospital for Sick Children is a tertiary care referral hospital in downtown Toronto. It serves a broad demographic and socioeconomic spectrum of patients and a geographic region that includes urban, suburban, and rural regions. The ED provides care for >50 000 patient visits per year and is staffed by attending physicians 24 hours per day.

Patients
This retrospective report includes data from a consecutive series of afebrile infants <12 months of age who presented to the ED between January 1, 2005, and September 30, 2005, with a chief complaint of crying. Children were identified by searching our electronic database using a chief complaint family word root search for "cry," "irritable," "fuss," "scream," and "colic."

Outcomes
Our primary outcome was the proportion of infants who had a potentially serious underlying etiology. To allow us to a priori identify illnesses felt to require prompt diagnosis and therapy, a literature review was performed, followed by a focus group discussion with 6 full-time members of our division. The failure to make the diagnosis of any of the disease entities listed in Table 1 was felt to have the potential to result in an adverse outcome. For illnesses identified during data abstraction that had not previously been considered, a panel of 3 pediatric emergency medicine physicians, blinded to historical and physical examination features, met to determine if the diagnosis constituted a serious underlying disease.

Secondary outcomes included the proportion of children with a serious underlying etiology in whom the diagnosis was not suspected on the basis of the initial history or physical examination and whether there existed high-yield investigations that should routinely be performed.

Data Collection
Data were abstracted from our electronic patient chart system. Medical charts were reviewed employing a standardized data collection instrument to record demographic data, history and physical examination findings, diagnostic tests, final diagnosis, and disposition. The study was approved by the hospital's research ethics board. Subjects were enrolled after a letter was mailed informing caregivers on how to avoid being contacted. Subsequently, attempts were made to obtain informed consent by telephone.

A follow-up telephone call was performed 9 to 18 months after the index visit to inquire about other physician visits, alternative diagnoses made, and tests or treatments required. Calls were attempted a maximum of 3 times. Caregiver report was confirmed via medical chart review. All alternative diagnoses assigned within 1 week of the index visit were considered as potential etiologies of crying at the index visit.

Definitions
The analysis considered historical variables (review of systems, feeding, perinatal, vaccination, and family history), physical examination (vital signs, general description, pertinent findings), tests of blood, urine, and cerebrospinal fluid, imaging studies, stool occult blood testing, eye fluorescein staining, and electrocardiograms. Fever was defined as a documented fever at home or in the ED. Recorded temperatures were adjusted for location of measurement with 1.1°C and 0.6°C added to axillary and oral temperatures, respectively.[6] Children with an adjusted temperature of ≥38.0°C were considered to have a fever.[6] Children with a tactile fever at home but no evidence of fever in the ED were considered to be afebrile. General appearance was classified for all children by the data abstractor (Dr Al-Harthy) as well, unwell, or unclear.

All tests performed in the ED were recorded, and if positive, the data abstractor indicated whether the test

TABLE 1 Serious Underlying Etiologies or Conditions Sorted According to Organ System

Abdominal	Appendicitis, malrotation/midgut volvulus, intussusception, incarcerated/strangulated hernia, peritonitis, choledocholithiasis, pancreatitis, intestinal obstruction
Cardiac	Myocarditis, congestive heart failure, supraventricular tachycardia
Chest	Hypoxia, hypercarbia, pneumonia, bronchiolitis, acute airway obstruction (croup, foreign body, asthma)
General	Bacteremia, sepsis, hypovolemia, hyperbilirubinemia
Genitourinary	Testicular/ovarian torsion, genital tourniquet, urinary tract infection, nephrolithiasis
HEENT	Foreign body
Hematologic	Sickle cell disease, malignancy, neutropenia, thrombocytopenia, anemia
Skin/musculoskeletal	Septic arthritis, osteomyelitis, digital tourniquet, fracture, dislocation, subluxation, nonaccidental trauma, cellulitis
Neurologic	Bacterial meningitis, encephalitis, intracranial hemorrhage, hydrocephalus, cerebral edema, epilepsy, degenerative condition
Toxic-metabolic	Prenatal drug use, toxic ingestion, electrolyte abnormality, inborn error of metabolism, hyperthyroidism

HEENT indicates head, eyes, ears, nose, and throat.

contributed to the diagnosis. Negative tests were not considered as contributing to a diagnosis, because although negative tests can be helpful in ruling out a particular disease, they are generally less diagnostic when evaluating a child with a nonspecific complaint such as crying. All laboratory tests were classified as positive/negative on the basis of age-specific ranges of normal.[7] Cultures that grew a clinically significant pathogen were considered positive. Imaging studies were deemed positive on the basis of the interpretation of the responsible specialist. When a test was ordered more than once, we considered only the results of the initial test. Urine dipstick was considered positive if the testing reagent indicated the presence of any leukocyte esterase or nitrites.

For each child, we classified the role of the initial history and physical examination in guiding subsequent investigations. Historical and examination features considered to be indicative of particular diagnoses were identified in advance to guide the abstractor (Dr Al-Harthy) in classifying the contributory role of these variables (Table 2). As has been previously done, all patients were grouped into 1 of 4 categories according to the source(s) of data that contributed to the diagnosis:[8]

1. Diagnosis was based on the history and/or physical examination alone.

2. Diagnosis was based on positive test results obtained after the history and physical examination failed to suggest a cause.

3. Diagnosis was based on tests ordered to investigate positive findings from the history and/or physical examination that suggested a cause.

4. Neither history, physical examination, nor investigations were diagnostic.

A contributory historical or physical examination variable includes any finding that may be connected to the underlying diagnosis. The principle investigator (Dr Freedman) reviewed the classification of all cases that were unclear to the data abstractor. Consistency and reproducibility of the classification scheme was evaluated by having a third investigator (Dr Thull-Freedman) review 10% of cases identified at random (SPSS 15.0 for Windows [SPSS Inc, Chicago, IL]), blinded to the assessment of the data abstractor. Agreement was excellent with a κ value of 0.90 ($P < .001$).

Analysis

The required sample size was calculated to yield stable estimates ($\pm5\%$) of the primary outcome measure. We estimated that 10% of our sample would have a serious underlying organic etiology. Thus, a minimum sample of 138 subjects would be required. However, we anticipated a follow-up telephone call response rate of only 75%. After sample size adjustment, the final size required was 245.

Frequency counts and percentages are given for discrete variables, and means, medians, SDs, and interquartile ranges are provided for continuous variables. The χ^2

TABLE 2	Features of History and Physical Examination Considered to Be Helpful in Diagnosing Specific Conditions
Atypical colic	Diagnosis of colic assigned by the treating physician but does not meet definition of colic (see below)
Bacterial meningitis	Fever, paroxysmal irritability, lethargy, vomiting, full/bulging fontanelle, meningismus, positive cerebrospinal fluid culture
Bronchiolitis	Cough, fever, wheezing, tachypnea, apnea, poor feeding, respiratory syncytial virus positive, imaging consistent with bronchiolitis
Colic	Paroxysmal crying >3 h/d, >3 d/wk, lasting >3 wk in an otherwise healthy child who is >3 wk and <4 mo of age
Constipation	History of difficult, infrequent, hard stools, palpation of small pellets on abdominal examination
Cow's milk allergy	Resolution of symptoms after dietary manipulation
Crying	No alternative diagnosis made to explain the episode
Gastroesophageal reflux	Visible regurgitation, feeding refusal, Sandifer syndrome
Hernia	Bulging in groin/umbilicus noted on history or examination
Intussusception	Sudden onset of severe intermittent crampy abdominal pain, drawing up legs, well between episodes, vomiting, lethargy, hematochezia, currant jelly stools, occult blood positive stool, sausage-shaped abdominal mass, imaging consistent with intussusception
Otitis media	Fever, ear discharge, pulling/rubbing ear, tympanic membrane erythema, bulging, loss of landmarks, effusion and/or reduced tympanic membrane mobility
Pneumonia	Cough, fever, tachypnea, poor feeding, recent upper respiratory infection, leukocytosis (>20 × 10⁹ WBCs per L), focal auscultatory findings, imaging consistent with pneumonia
Urinary tract infection	Fever, odorous urine, dysuria, frequency, vomiting, positive urinalysis (leukocyte esterase, nitrites), culture with ≥50 000 CFU/mL on catheter specimen
Viral illness[a]	Fever, cough, rhinorrhea, nasal congestion, sneezing, vomiting, diarrhea, skin rash, ill contact

WBCs indicates white blood cells; CFU, colony-forming units.
[a] Viral illness includes herpangina, influenza, nasal congestion, roseola, upper respiratory tract infection, viral exanthem, and viral meningitis.

test was used for discrete variables. When the number of observations in any given cell of the contingency table was <5, Fisher's exact test was used. On the basis of the definitions provided above, the diagnostic yield of tests performed was calculated with the number of patients with positive diagnostic tests divided by the number of tested patients. As the underlying etiology may vary by age, we have performed sub-analyses, with children divided into groups of 0 to 3 months and ≥4 months of age. When the results have been significantly different, we have reported them. All statistical tests were evalu-

TABLE 3 Baseline Features of Study Patients (N = 238)

Male, n (%)	124 (52)
Age, median (25th–75th percentiles), mo	2.3 (1.0–5.4)
Triage time, mean ± SD	13:52 ± 7:44
Duration of crying, median (25th–75th percentiles), h	27 (3–96)
Character of cry[a]	
Constant, n (%)	52 (22)
Intermittent, n (%)	93 (39)
Inconsolable, n (%)	45 (19)
Easily consoled, n (%)	44 (18)
Tactile fever at home, n (%), yes[b]	41 (17)
Taking analgesic/antipyretic, n (%), yes[c]	61 (26)
Adjusted temperature, mean ± SD, °C[d]	37.2 ± 0.4
Heart rate, beats per min ± SD	136 ± 17
Respiratory rate, breaths per min ± SD	34 ± 9
Oxygen saturation, % ± SD	98 ± 3.0
Blood pressure systolic, mean ± SD	94 ± 12
Weight, median (25th–75th percentiles), kg	5.2 (4.2–7.9)
General appearance	
Well, n (%)	226 (95)
Unwell, n (%)	7 (3)
Unclear, n (%)	5 (2)

[a] Not all children had a description of the crying reported.
[b] No children had a documented fever at home or in the ED.
[c] Analgesic/antipyretic use included acetaminophen or ibuprofen.
[d] Adjusted for location of measurement, with 1.1°C and 0.6°C added to axillary and oral temperatures, respectively.[6]

ated at the 5% level of significance. Statistical analysis was conducted with the use of SPSS.

RESULTS

A total of 37 549 ED visits occurred during the 9-month eligibility period. Two hundred thirty-eight children met the inclusion criteria (0.6% of all visits) (Table 3); 55.0% (131 of 238) were firstborn children. Thirteen percent

TABLE 4 Serious Underlying Diagnoses Sorted According to Time of Diagnosis

	Index Visit	Within 1 wk of Index Visit
Acute cholecystitis	1	—
Acute lymphoblastic leukemia	1	—
Clavicle fracture	2	—
Epidural hematoma	1	—
Intussusception	1	—
Nephrolithiasis	—	1
Pulled elbow	1	—
Spinal muscular atrophy type I[a]	1	—
Urinary tract infection	2	1
Total	10	2

[a] This 2-month-old infant presented with increased crying and decreased feeding. On examination, the child was hypotonic with absent deep-tendon reflexes. The diagnosis of spinal muscular atrophy was confirmed via electromyography, nerve conduction studies, and genetic testing.

(30 of 238) revisited the Hospital for Sick Children's ED within 1 week of the index visit. Sixty-three percent (150 of 238) were triaged between 6 PM and 6 AM (Fig 1).

Five percent (12 of 238) of our cohort met our primary outcome definition of serious underlying etiology (Table 4). Eighty-three percent (10 of 12) of these children were correctly diagnosed at the initial visit; 2 (16.7%) of the 12 were diagnosed during the subsequent 7 days. Overall, the most common serious underlying disease was urinary tract infection. A total of 14 children were diagnosed with colic (age range: 1.1–3.6 months) and 11 were diagnosed with atypical colic (age range: 0.5–4.5 months). When comparing patients <4 months of age to those ≥4 months of age, there was a tendency for serious illness to be more common among
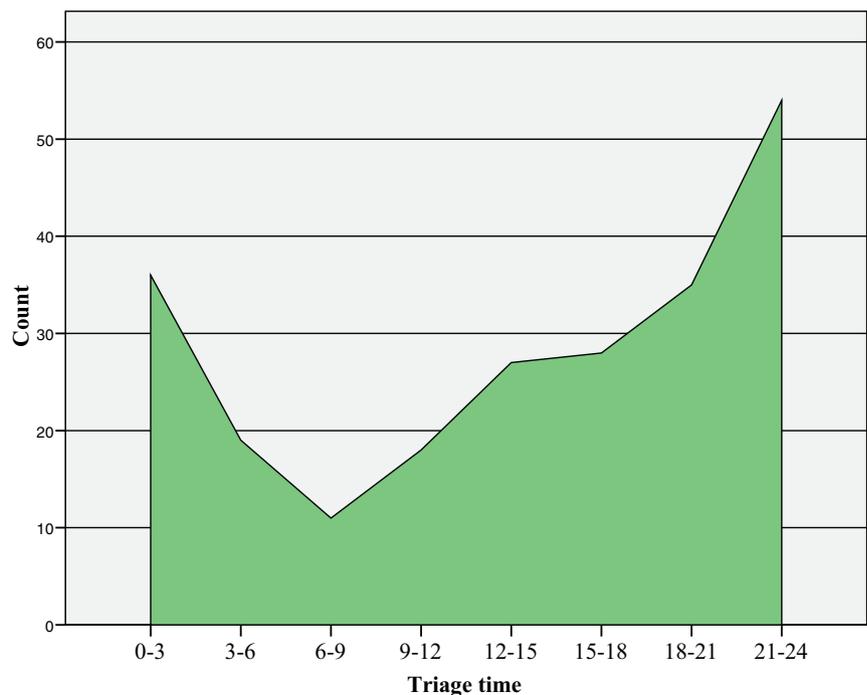
FIGURE 1

Triage time of 238 patients who presented to the ED because of crying. The distribution was nonnormal (P < .001) with the majority of patients presenting between 6 PM and 3 AM.

TABLE 5 Investigations and Yield of Diagnostic Tests Performed at the Initial Visit (*N* = 238)

	Test Performed	Positive Findings	Finding Contributed to Diagnosis			Diagnoses to Which the Positive Findings Contributed[a]
	a, *n* (%)	b, *n* (b/a%)	c, *n*	c/b, %	c/a, %	
Miscellaneous						
Fluorescein	1	0 (0)	0	0	0	None
Fecal occult blood	8	1 (12.5)	0	0	0	None
Electrocardiogram	6	1 (16.7)	0	0	0	None
Nasopharyngeal aspirate	6	1 (16.7)	1	100.0	16.7	Bronchiolitis
Blood						
White blood cell count	55	12 (21.8)	1	8.3	1.8	Acute lymphoblastic leukemia
Hemoglobin	55	10 (18.2)	1	10.0	1.8	Acute lymphoblastic leukemia
Platelet count	50	25 (50.0)	1	2.0	2.0	Acute lymphoblastic leukemia
Sickle cell screen	4	1 (25.0)	0	0	0	None
Blood gas	31	2 (6.5)	0	0	0	None
Routine electrolytes	44	1 (2.3)	0	0	0	None
Renal function tests	42	1 (2.3)	0	0	0	None
Lactate	2	0 (0)	0	0	0	None
Bilirubin	13	2 (15.4)	0	0	0	None
Liver transaminases	9	1 (11.1)	1	100.0	11.1	Acute cholecystitis
Coagulation profile	8	0 (0)	0	0	0	None
Blood culture	35	1 (2.9)	0	0	0	None
Urine						
Urine analysis	74	5 (6.8)	1	20.0	1.4	Urinary tract infection
culture	68	2 (2.9)	2	100.0	2.9	Urinary tract infection (2)
Cerebrospinal fluid						
Culture	4	0 (0)	0	0	0	None
Cell count	4	2 (50.0)	0	0	0	None
Chemistry	4	2 (50.0)	0	0	0	None
Radiologic investigations						
Chest radiograph	20	8 (40.0)[b]	1	5.0	12.5	Bronchiolitis
Abdominal radiograph	14	0 (0)	0	0	0	None
Skull radiograph	1	1 (100.0)	1	100.0	100.0	Skull fracture
Abdominal ultrasound	16	2 (12.5)	2	100.0	12.5	Intussusception, acute cholecystitis

[a] Patients may have had >1 test that contributed to the diagnosis.
[b] Positive chest radiograph findings as interpreted by the pediatric radiologist included: lower airway inflammation (*n* = 4), hyperinflation (*n* = 2), perihilar thickening (*n* = 1), and mild cardiomegaly (*n* = 1).

the older cohort (10.4% vs 3.4%); however, this did not achieve statistical significance (*P* = .07).

Investigations

In our cohort of 238 children, anterior eye fluorescein staining was performed and documented in 1 (0.4%) child, and fecal occult blood testing was recorded for 8 (3.4%) children. Both of these tests were negative in all cases (Table 5). Of the 574 tests performed on these children (2.4 tests per child), 81 (14.1%) of 574 were positive, but only 8 (1.4%) diagnoses were assigned on the basis of a positive investigation. Among the 238 children evaluated, the most frequently performed tests were urine analysis (31.1%) and culture (28.6%), both of which contributed to the final diagnosis <3% of the times they were performed. All positive urine cultures occurred in the 47 children <4 months of age in whom urine specimens were obtained by urinary catheterization. Of the 60 infants <1 month of age, 19 (32%) had urine cultures performed. These infants had the highest

rate of positivity (10% [95% confidence interval: 0.03–0.30]).

Relative Contributions From History, Physical Examination, and Investigations

Positive findings on the history and/or physical examination alone suggested the final diagnosis to explain the crying in 66.4% (158 of 238) of children (Table 6). In 6 of 238 (2.5%) other children, the etiology was suggested by the history and/or physical examination with confirmation by positive investigations. Four of the 7 (57.1%) children described as appearing unwell had a serious underlying illness (*P* < .001). Investigations performed in the absence of a suggestive clinical picture were crucial in determining a diagnosis in 2 of 238 (0.8%) children including (1) a 3-month-old child whose catheter urine sample was positive for nitrites and trace leukocytes, whose culture grew 2 *Escherichia coli* morphotypes, both with colony-forming unit counts of $\geq 50 \times 10^6$/L (this child's blood culture additionally grew *Enterococ-*

TABLE 6 Final Diagnoses Categorized According to the Data Sources That Most Likely Contributed to the Diagnoses ($N = 238$)

Correct Diagnosis	Date Source[a]				Total
	Category 1	Category 2	Category 3	Category 4	
Atypical Colic	11	0	0	0	11
Bronchiolitis	6	0	2	0	8
Clavicle fracture	1	0	0	1	2
Colic	14	0	0	0	14
Constipation	11	0	0	0	11
Crying	0	0	0	65	65
Feeding problem	7	0	0	0	7
Gastroenteritis	11	0	0	1	12
Gastroesophageal reflux	30	0	0	0	30
Otitis media	7	0	0	0	7
Reducible inguinal hernia	3	0	0	0	3
Urinary tract infection	0	1	0	1	2
Viral illness	45	0	0	4	49
Vaccine adverse event	3	0	0	0	3
Other[b]	9	1	4	0	14
Total, n (%)	158 (66.4)	2 (0.8)	6 (2.5)	72 (30.3)	238

Factors considered to be suggestive or contributory to a diagnosis are listed in Table 2.

[a] Explanation of data source: category 1, positive history and physical examination only; category 2, positive diagnostic investigations only; category 3, positive history and physical examination along with positive diagnostic investigations; category 4, history, physical, and diagnostic investigations (if performed) were negative or noncontributory.

[b] Other includes 1 of each of the following: category 1, cellulitis, dermatitis, gas, infantile spasms, nephrolithiasis, thrush, pulled elbow, toe trauma, and spinal muscular atrophy; category 2, bacteremia plus urinary tract infection; category 3, acute calculous cholecystitis, intussusception, epidural hematoma, and acute lymphoblastic leukemia.

cus faecalis, which was felt to be a contaminant); and (2) an 18-day-old male whose catheter urine culture grew E coli with a colony-forming unit count of $\geq 50 \times 10^6$/L.

Long-term Follow-up

Three caregivers declined consent for our telephone follow-up. Sixty-one percent (143 of 235) of caregivers were successfully contacted after the ED visit. Twenty-nine percent (41 of 143) indicated that they had subsequently brought their child to see another non–ED-based health care provider; 3.5% (5 of 143) reported seeking additional evaluation in an ED. All serious underlying diagnoses reported by the caregivers during follow-up were detected during our chart review.

DISCUSSION

This is the largest sample of children presenting to an ED with crying that has been evaluated. We found that caregivers frequently bring their infants to the ED because of crying, fussiness, screaming, or irritability, and the problem frequently persists after discharge, with 13% of children having a repeat ED visit within 1 week. Our results emphasize the need for a careful evaluation as 5% of children had a serious diagnosis. However, routine investigations in afebrile children with crying seem unwarranted as <1% of children received a diagnosis on the basis of investigations alone. Thus, a selective workup guided by clinical findings seems to be optimal.

Urinary tract infections were the most common serious diagnosis in our cohort, accounting for 25% of all serious etiologies. Crying has previously been reported as the chief complaint in afebrile children with urinary tract infections.[9] The overall yield of urine cultures in our cohort (3%) is similar to that reported in a recent cohort of 200 afebrile crying infants evaluated in Iran.[10] The greatest yield occurred among children <1 month of age. Although asymptomatic bacteriuria has been reported to occur in up to 1% of children <60 days of age,[11] it is unlikely that this explains all of the positive cultures in our cohort, which includes an 18-day-old infant whose catheter urine specimen was positive for nitrites and leukocytes and whose culture grew E coli $\geq 50 \times 10^6$/L. Even among those with normal urine analyses, clinicians should not disregard the culture result, as pyuria is not a sensitive marker among neonates, and <50% of febrile infants <8 weeks of age with positive urine cultures have abnormal urinalysis.[12] Thus, although false-positive urine cultures are possible, even on catheter specimens, we feel that the positive urine cultures in our cohort of patients are important and should not be ignored.

In keeping with other research, we found the most important aspect in the evaluation of the crying infant to be a thorough history and physical examination.[5,10] Investigations were only helpful in 3% of our cohort. Although some tests, such as nasopharyngeal aspirate, liver function tests, abdominal ultrasound, and skull radiographs contributed to the diagnosis >10% of the time they were performed, their use was determined on the basis of findings of history or physical examination. Overall, they were infrequently performed in our cohort and thus would not have the same diagnostic properties if used as screening tests.

Although corneal abrasions commonly present with

photophobia, excessive tearing, and conjunctival injection in addition to pain, it has been suggested that corneal fluorescein staining be performed on all infants with acute, unexplained irritability or excessive crying.[13] This recommendation is based primarily on a case series of 20 infants <1 year of age who presented with crying or irritability and were diagnosed with corneal abrasions.[13] The clinical implications of these findings, however, are unclear, as there was no confirmation by an ophthalmologist, and fluorescein-impregnated papers were employed, which themselves can result in corneal abrasion.[14] Although, in a previous study, 5% of crying infants were reported to have corneal abrasions,[5] in the case series,[13] no prevalence data were provided. Even once diagnosed, the need for patching and antimicrobial therapy has been debated.[14] In 2006, a Cochrane review of 11 eligible trials concluded that patching does not improve the rate of healing or reduce pain.[15]

In our case series, although no children were diagnosed with a corneal abrasion (prevalence 0% [95% confidence interval: 0%–1.9%]), we cannot conclude that clinicians should forgo searching for abrasions. Although it is likely that no child had a significant corneal abrasion as evidenced by our follow-up, less significant abrasions may have been overlooked, as only 1 child had a fluorescein examination documented. Thus, it is possible that a child with an abrasion did not undergo fluorescein examination; it is also possible that many more children had an examination performed but not documented.

Other tests of questionable value are stool occult blood testing and rectal examination. Although constipation is not an uncommon condition, constituting 5% (11 of 237; Table 2) of diagnoses in our cohort, the utility of rectal examination is unclear. In a clinical practice guideline, the North American Society for Pediatric Gastroenterology and Nutrition recommends the routine performance of anorectal examination and occult blood testing.[16] This expert panel states that the amount, consistency, and location of stool within the rectum are all helpful pieces of information. However, a systematic review of the diagnostic value of clinical findings in children with constipation found inconsistent results from rectal examination.[17] The likelihood ratio of finding stool on rectal examination relative to abdominal radiography is close to 1, indicating that stool detected on rectal examination occurs almost as often in children with and without fecal loading on radiography.[17] Thus, greater evidence is required to support the routine performance of rectal examinations in crying children.

A rectal examination may also be performed to obtain stool to test for fecal occult blood. Although of potential importance in children suspected of having intussusception, in a recent review of 83 cases of intussusception, blood was detected on rectal examination in only 16%, with other findings being significantly more common. These included abdominal pain (81%), vomiting (66%), bloody stools (57%), pallor (47%), lethargy (46%), and abdominal mass (36%).[18] Given the prevalence of intussusception of only 0.4% in our cohort, it seems unjustified to routinely perform rectal examinations on all

children who present with crying and should be reserved for those with other signs of intussusception.

Missing a serious diagnosis is always a concern when evaluating a crying infant. In our cohort, the most concerning diagnosis not initially detected was urinary tract infection in an infant <1 month of age. This highlights the need to rule out such infections in very young children.[5] The other diagnosis made on revisit, nephrolithiasis, occurred in an 8-month-old male who represented with a stone that was found at the urethral meatus.

Gastroesophageal reflux disease was diagnosed on the basis of clinical presentation in 13% of our sample. This did not vary significantly by age (14% among those <4 months of age versus 8% among those ≥4 months of age). Previous research employing pH monitoring, however, has shown that clinical findings, such as backarching and sleep disturbance, are poorly associated with pathologic reflux.[19,20] Results regarding high-risk groups have been contradictory with 1 study finding pathologic reflux to be more common in children ≥3 months of age,[20] whereas another found it to be more common in infants <3 months of age.[19] Both studies found that reflux was almost always associated with frequent vomiting or regurgitation and that "silent" pathologic reflux was uncommon.[19,20]

LIMITATIONS
This study was a retrospective chart review. Therefore, the data abstracted may be limited in terms of accuracy and completeness. The absence of a uniform testing protocol, with tests performed instead on the basis of individual physician clinical judgment, means that abnormalities related to the underlying etiology may have been missed. Because physicians preferentially perform tests on patients with higher pretest probabilities, it is most likely that contributory rates would be lower in untested patients. In addition, because some tests were infrequently performed, we are unable to make firm conclusions regarding their utility in other settings where utilization patterns may be different.

The 90 patients who were discharged with a diagnosis of colic, atypical colic, or crying may have included some patients with serious undetected pathology. However, this is unlikely given that we were able to perform follow-up using our hospital's database. Data previously collected suggests that 80% of caregivers would bring their child back to our ED should another visit be required.[21] In addition to chart review, we were able to contact 61% of caregivers to confirm the diagnosis. Lastly, the presence of a diagnosed condition does not guarantee causality in individual cases. For example, it cannot be proven that the presence of rhinorrhea and a diagnosis of viral illness, or decreased stooling and a diagnosis of constipation, were the true etiologies of crying. For the purposes of clinical management, in the absence of evidence to the contrary or a more likely explanation, it seems reasonable to accept that such diagnoses are correct and that a causal relationship may exist.

CONCLUSIONS
The etiology of crying ranges from benign to life-threatening. A thorough history and physical examination

remains the cornerstone of the evaluation of crying infants and should drive the selection of investigations to be performed. Afebrile infants in the first month of life should undergo urine evaluation. Other investigations such as rectal examination and fluorescein staining should be performed on the basis of the findings from the history and physical examination.

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REFERENCES

1. Brazelton TB. Crying in infancy. *Pediatrics.* 1962;29:579–588
2. Reijneveld SA, Brugman E, Hirasing RA. Excessive infant crying: definitions determine risk groups. *Arch Dis Child.* 2002; 87(1):43–44
3. Reijneveld SA, Brugman E, Hirasing RA. Excessive infant crying: the impact of varying definitions. *Pediatrics.* 2001; 108(4):893–897
4. Barr RG. Colic and crying syndromes in infants. *Pediatrics.* 1998;102(5 suppl E):1282–1286
5. Poole SR. The infant with acute, unexplained, excessive crying. *Pediatrics.* 1991;88(3):450–455
6. Alpern ER, Henretig FM. Fever. In: Fleisher GR, Ludwig S, Henretig FM, eds. *Textbook of Pediatric Emergency Medicine.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006
7. Cheng A, Williams BA, Sivarajan VB. *The Hospital for Sick Children Handbook of Pediatrics.* 10th ed. Toronto, Ontario, Canada: Saunders Canada; 2003
8. Brand DA, Altman RL, Purtill K, Edwards KS. Yield of diagnostic testing in infants who have had an apparent life-threatening event [published correction appears in *Pediatrics.* 2005;116(3):802–803]. *Pediatrics.* 2005;115(4):885–893
9. Du JN. Colic as the sole symptom of urinary tract infection in infants. *CMAJ.* 1976;115:334–335
10. Fahimi D, Shamsollahi B, Salamati P, Sotoudeh K. Excessive crying of infancy: a report of 200 cases. *Iran J Pediatr.* 2007; 17(3):222–226
11. Wettergren B, Jodal U, Jonasson G. Epidemiology of bacteriuria during the first year of life. *Acta Paediatr Scand.* 1985;74(6): 925–933
12. Crain EF, Gershel JC. Urinary tract infections in febrile infants younger than 8 weeks of age. *Pediatrics.* 1990;86(3):363–367
13. Poole SR. Corneal abrasion in infants. *Pediatr Emerg Care.* 1995; 11(1):25–26
14. Levin AV. Eye trauma. In: Fleisher GR, Ludwig S, Henretig FM, eds. *Textbook of Pediatric Emergency Medicine.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006
15. Turner A, Rabiu M. Patching for corneal abrasion. *Cochrane Database Syst Rev.* 2006;(2):CD004764
16. Baker SS, Liptak GS, Colletti RB, et al. Constipation in infants and children: evaluation and treatment. A medical position statement of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr.* 1999; 29(5):612–626
17. Reuchlin-Vroklage LM, Bierma-Zeinstra S, Benninga MA, Berger MY. Diagnostic value of abdominal radiography in constipated children: a systematic review. *Arch Pediatr Adolesc Med.* 2005;159(7):671–678
18. Buettcher M, Baer G, Bonhoeffer J, Schaad UB, Heininger U. Three-year surveillance of intussusception in children in Switzerland. *Pediatrics.* 2007;120(3):473–480
19. Heine RG, Jordan B, Lubitz L, Meehan M, Catto-Smith AG. Clinical predictors of pathological gastro-oesophageal reflux in infants with persistent distress. *J Paediatr Child Health.* 2006; 42(3):134–139
20. Heine RG, Jaquiery A, Lubitz L, Cameron DJ, Catto-Smith AG. Role of gastro-oesophageal reflux in infant irritability. *Arch Dis Child.* 1995;73(2):121–125
21. Freedman SB, Thakkar VA. Easing the strain on a pediatric tertiary care center: use of a redistribution system. *Arch Pediatr Adolesc Med.* 2007;161(9):870–876

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