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Does This Child Have Appendicitis?

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CLINICAL SCENARIOS

Case 1

A previously healthy 6-year-old boy presents to his physician with a 1-day history of abdominal pain. The pain started in his periumbilical area and is now localized in his right lower quadrant (RLQ). His father states that the child has complained of anorexia and has had 1 episode of nonbilious emesis and a fever of 38.3°C. Diarrhea and dysuria are absent. He appears uncomfortable and has a measured temperature of 38.8°C orally; there is no tachycardia or tachypnea. His abdomen is focally tender in the RLQ, with mild distention and rebound tenderness. His white blood cell (WBC) count is 14 200/μL (67% neutrophils; absolute neutrophil count, 9500/μL). A urinalysis is notable for absence of signs of urinary tract infection.

Case 2

A 9-year-old girl presents to the emergency department with a 1-day history of lower abdominal pain and anorexia. She denies fever, chills, nausea, vomiting, diarrhea, or dysuria. She is premenarchal. On examination, she is

See also Patient Page.

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Context Evaluation of abdominal pain in children can be difficult. Rapid, accurate diagnosis of appendicitis in children reduces the morbidity of this common cause of pediatric abdominal pain. Clinical evaluation may help identify (1) which children with abdominal pain and a likely diagnosis of appendicitis should undergo immediate surgical consultation for potential appendectomy and (2) which children with equivocal presentations of appendicitis should undergo further diagnostic evaluation.

Objective To systematically assess the precision and accuracy of symptoms, signs, and basic laboratory test results for evaluating children with possible appendicitis.

Data Sources We searched English-language articles in MEDLINE (January 1966–March 2007) and the Cochrane Database, as well as physical examination textbooks and bibliographies of retrieved articles, yielding 2521 potentially relevant articles.

Study Selection Studies were included if they (1) provided primary data on children aged 18 years or younger in whom the diagnosis of appendicitis was considered; (2) presented medical history data, physical examination findings, or basic laboratory data; and (3) confirmed or excluded appendicitis by surgical pathologic findings, clinical observation, or follow-up. Of 256 full-text articles examined, 42 met inclusion criteria.

Data Extraction Twenty-five of 42 studies were assigned a quality level of 3 or better. Data from these studies were independently extracted by 2 reviewers.

Results In children with abdominal pain, fever was the single most useful sign associated with appendicitis; a fever increases the likelihood of appendicitis (likelihood ratio [LR], 3.4; 95% confidence interval [CI], 2.4-4.8) and conversely, its absence decreases the chance of appendicitis (LR, 0.32; 95% CI, 0.16-0.64). In select groups of children, in whom the diagnosis of appendicitis is suspected and evaluation undertaken, rebound tenderness triples the odds of appendicitis (summary LR, 3.0; 95% CI, 2.3-3.9), while its absence reduces the likelihood (summary LR, 0.28; 95% CI, 0.14-0.55). Midabdominal pain migrating to the right lower quadrant (LR range, 1.9-3.1) increases the risk of appendicitis more than right lower quadrant pain itself (summary LR, 1.2; 95% CI, 1.0-1.5). A white blood cell count of less than 10 000/μL decreases the likelihood of appendicitis (summary LR, 0.22; 95% CI, 0.17-0.30), as does an absolute neutrophil count of 6750/μL or lower (LR, 0.06; 95% CI, 0.03-0.16). Symptoms and signs are most useful in combination, particularly for identifying children who do not require further evaluation or intervention.

Conclusions Although the clinical examination does not establish a diagnosis of appendicitis with certainty, it is useful in determining which children with abdominal pain warrant immediate surgical evaluation for consideration of appendectomy and which children may warrant further diagnostic evaluation. More child-specific, age-stratified data are needed to improve the utility of the clinical examination for diagnosing appendicitis in children.

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afebrile and has diffuse tenderness to palpation and voluntary guarding but no rebound in both lower quadrants. Her WBC count is 11 000/μL (50% neutrophils; absolute neutrophil count, 5500/μL) and urinalysis is positive only for 1+ leukocyte esterase and 3 WBCs per high-power field. Ultrasonography of the abdomen and pelvis is performed and is unremarkable; however, the appendix is not clearly visualized.

WHY IS THIS QUESTION IMPORTANT?

Abdominal pain is one of the most common presenting symptoms of children brought to medical attention. Etiologies of abdominal pain in children range from simple causes (eg, constipation) to potentially catastrophic ones (eg, malrotation with midgut volvulus). Distinguishing appendicitis from other disorders is difficult, particularly in young, preverbal children. Diagnostic imaging has been used with increasing frequency but has limitations, including exposure to ionizing radiation (eg, computed tomography),[1] limited availability of skilled technicians at all hours (eg, ultrasound), and cost. In addition, these tools may delay definitive treatment (ie, appendectomy) in children with appendicitis. Therefore, evaluation of abdominal pain in children should aim to identify which children with abdominal pain and likely appendicitis should undergo immediate surgical evaluation for potential appendectomy and which children with equivocal presentations of possible appendicitis may benefit from further diagnostic evaluation, including the use of diagnostic imaging, observation, and/or surgical consultation.

Among children presenting to emergency departments or outpatient clinics with abdominal pain, appendicitis is the most frequent surgical etiology.[2,3] Seventy-seven thousand pediatric hospital discharges each year are for appendicitis and other appendiceal conditions, at a cost of $680 million.[4] In one-third of children with appendicitis, the appendix ruptures prior to operative treatment.[5,6] Particularly in young, preverbal toddlers, the risk of perforation at the time of appendicitis diagnosis is quite high due to both the rarity of the condition in this age group as well as the difficulty in distinguishing appendicitis from more common causes of abdominal pain. In children younger than 4 years, appendiceal perforation occurs in the vast majority of cases, with rates reported as high as 80% to 100%.[7-9] In contrast, appendicitis in children aged 10 to 17 years is more common, yet the perforation rate is much lower (10%-20%).[6,7,10,11] Appendicitis is most common in the second decade of life and is slightly more common in males than in females.[7]

The high incidence of appendicitis in children as well as its significant morbidity in the setting of perforation make prompt diagnostic accuracy important. However, distinguishing appendicitis from the many nonsurgical causes of abdominal pain is difficult in children, both because of the complexities of examining and communicating with children and because the presentation of appendicitis in childhood may deviate from a classic presentation. These difficulties likely contribute to the 28% to 57% rates of initially misdiagnosed appendicitis in children younger than 12 years.[12-14] Indeed, missed appendicitis is the second most common diagnosis (after meningitis) involved in pediatric emergency medicine malpractice claims.[15] A previous Rational Clinical Examination article focused on adult appendicitis[16]; however, the complexities of evaluating children with potential appendicitis suggest that an evidence-based review of pediatric appendicitis is warranted.

Anatomical and Physiological Origins of Appendicitis Signs and Symptoms

The pathophysiology of appendicitis in children differs from that of adults because of the changing anatomical location and susceptibility of the appendix throughout childhood. Neonates develop appendicitis infrequently because they have a less-susceptible, funnel-shaped appendix.[17] In addition, the soft diet, recumbent posture, and infrequent gastrointestinal and upper respiratory tract infections of infants help lower their appendicitis incidence.[18] When neonatal appendicitis occurs, the mortality rate historically has been quite high (64% in 1901-2000), although 1 recent report cites a lower mortality rate for neonatal appendicitis of 28%.[17]

Around age 1 to 2 years, the appendix assumes the typical adult shape and becomes more susceptible to appendicitis. Lymphoid follicle hyperplasia and follicular size gradually increase throughout childhood and peak in the adolescent years, corresponding to the period of highest incidence of appendicitis.[7,12] Adolescents tend to have a lower perforation rate than younger children, probably because they present earlier in the course of disease with more typical appendicitis symptoms.

In female adolescents, it can be difficult to distinguish appendicitis from pelvic inflammatory disease and other gynecologic disorders. As a result, girls and women aged 15 to 24 years are 2.5 times more likely than same-age boys and men to undergo a negative appendectomy (false-positive workup).[7] Although initial misdiagnosis (false-negative) rates among women of childbearing age with appendicitis are high (33% in 1 study of women aged 15-45 years),[19] girls do not have higher perforation rates than boys.[20]

How to Elicit the Relevant Symptoms

Obtaining a history from children frequently challenges nurses and physicians. The evaluation of abdominal pain is dependent on the age of the child because young infants require an entirely different approach to elicit a relevant history than older adolescents. Parents, siblings, and other caregivers may be present in the examining room; each may have a different perspective on the child's illness. Although most older children can give a history of their illness, toddlers and young school-aged children need a caregiver to communicate their history. In preverbal

children, who may not be able to express how they feel or localize their pain, clinicians need to detect potential pathologic findings based on how children have been eating, playing, sleeping, and stooling. Although parents might be good judges of how their child feels, clinicians must draw appropriate conclusions from parents' assumptions. Many children, especially younger ones, can be highly suggestible. Despite their contradictory meanings, questions such as "Does it hurt here?" and "This feels fine, right?" may yield the same "yes" response from many children.

Abdominal pain is a nearly universal symptom of appendicitis in older children, although the history of pain can be difficult to elicit in young children. The pain classically begins as poorly defined midabdominal or periumbilical pain that often migrates to the RLQ over a period of hours to days, and most school-aged children can reliably describe and localize their pain migration. However, younger children may not be able to recount an accurate pain history, and an examiner may be able to localize the current pain only by asking the child to point with a finger to where it hurts. In preverbal toddlers and preschoolers, a pain history is often impossible to elicit, and the examiner may have to rely on the physical examination to determine what currently hurts.

Fever is a common and nonspecific presenting symptom among children seeking medical care for many conditions, including appendicitis. A rectal temperature should be obtained in young children who are unable to keep an oral thermometer under their tongue. Tympanic thermometers are often unreliable, particularly in the hands of untrained operators.[21,22] Axillary temperature can be misleading, as it is almost universally lower than core body temperature.[23,24] Questions regarding the height of fever and how it was measured should be asked regarding any child presenting with abdominal pain, even if the child presents without fever. A history of tactile fever should not be dismissed, as parents are fairly reliable judges of fever in their children.[25,26] Caregivers should also be asked about analgesic and antipyretic use (eg, acetaminophen) because these medications may mask a fever.

Anorexia, nausea, vomiting, and diarrhea are associated with many abdominal and nonabdominal conditions of childhood. A history of anorexia can be elicited by asking school-aged children if they are hungry; in toddlers and preschoolers, anorexia may have to be inferred from a caregiver's history of food refusal or decreased appetite. Bilious vomiting and small-bowel obstruction can be presenting findings in appendicitis, but bilious vomiting also suggests the possibility of other emergent conditions, such as malrotation with midgut volvulus or intussusception. The character of diarrhea, if present, is an important historical detail. Bloody stools suggest a diagnosis other than appendicitis (eg, intussusception or infectious colitis).

Finally, the duration and progression of abdominal symptoms can be difficult to elicit in children but are critical to distinguish appendicitis from other, potentially resolving causes of abdominal pain. It may be helpful to ask school-aged children to identify the first meal that they did not want to eat and to distinguish this from the first time that they vomited. Often, children may recall some evidence of abnormal appetite 1 to 2 days prior to acute pain. Identifying the earliest onset of symptoms is important for promptly evaluating appendicitis and minimizing the risk of perforation, since perforation rates increase as duration of symptoms increases.[27] Treatment delayed for more than 36 hours increases the perforation rate to as high as 65%.[28]

How to Elicit the Relevant Signs

Physical examination techniques and findings are age-dependent. Most older children can cooperate with an abdominal examination and state whether specific maneuvers are painful. Younger children may have trouble cooperating with the examination, often because of fear or discomfort, and may not be able to answer questions clearly. Particularly in younger children, it can be helpful to spend several minutes talking and gaining trust prior to beginning the examination. Younger children may be more cooperative if kept on their caregiver's lap. If the parent and the examiner sit facing one another, the child can then lie between the 2 adults with his/her head on the parent's lap. Painless components of the examination should be done first. While examining the child, the clinician should be careful not to stare at the abdomen. Instead, the examiner should focus on the child's face both to reassure the child and to evaluate changes in his facial expression with various abdominal maneuvers.

For children who do not want their abdomens examined, there are several useful distraction techniques. Engaging verbal children in conversation before and during the examination often helps. Most children will keep talking as long as the maneuvers are not painful. Children who are fearful of the abdominal examination may guard or tell you that it hurts when it does not. Telling a child that you are going to listen to his/her abdomen and then palpating all 4 quadrants with a stethoscope, first lightly and then more deeply, can provide a sense of where tenderness lies and whether involuntary guarding and rebound are present. In children who remain uncooperative despite all efforts at relaxation and distraction, an examination during spontaneous sleep can be helpful.

The abdominal examination should focus on eliciting the location of the pain and the presence of involuntary guarding or rebound tenderness. Guarding is a state of contraction of the abdominal muscles and can be either voluntary or involuntary. Voluntary guarding is often due to fear of pain rather than actual pain but can usually be partially or fully overcome by using relaxation and distraction techniques. Involuntary guarding, also referred to as rigidity, is a reflexive spasm of the abdominal musculature in the

setting of peritoneal irritation, such as with appendicitis, and cannot be overcome by distraction.

In addition to involuntary guarding, focal peritonitis can also be detected by rebound tenderness. Rebound is elicited by the quick removal of the examiner's hand from the abdominal wall and is elicited by pressing the area in question with either a hand or stethoscope deeply enough to depress the peritoneum; keeping pressure constant for 15 to 30 seconds; then removing the hand suddenly. Rebound tenderness is an increase in pain with release rather than with compression. However, particularly in young children, this maneuver may be stressful. In these situations, peritoneal irritation can also be detected by maneuvers such as asking the child to jump or cough, tapping the feet, or jiggling the bed while watching for facial signs of discomfort. In addition, it is helpful to determine whether peritoneal irritation is localized over the RLQ, as is common in early appendicitis, or is present throughout the abdomen, as with appendiceal perforation and subsequent diffuse peritonitis. Some experts suggest that abdominal pain on deep knee squats is associated with retrocecal appendicitis.

In addition to the age of the child, the abdominal examination findings may also depend on other factors, such as the anatomical location of the appendix and the time course of the inflammatory process. For example, children with a retrocecal or pelvic appendix may present with different signs and symptoms, such as back or pelvic pain, than those with a more anterior appendix. Similarly, children seen early in their illness with minimal appendiceal inflammation may have few abdominal findings; however, these signs can progress and become more apparent as the appendix becomes more inflamed.

In addition to a thorough abdominal examination, a complete physical examination is mandatory when assessing any child with abdominal pain, including a pelvic examination in sexually active girls. Several medical (eg, lower-lobe pneumonia) and surgical (eg, testicular torsion) conditions can cause symptoms and signs similar to appendicitis in children and may be overlooked if the examiner focuses exclusively on the abdomen.

METHODS

Search Strategy and Quality Review

We searched MEDLINE via PubMed for articles published between January 1966 and March 2007. We crossed the parent search strategy for the Rational Clinical Examination with the terms *appendicitis* AND *diagnosis*, limited to articles in English involving children aged 0 to 18 years. The titles and abstracts (when available) of the final set of 2521 articles were independently reviewed by 3 authors (D.G.B., J.S.B., and E.A.L.). Articles selected by at least 2 authors were retrieved for full-text review; those selected by only 1 author were reexamined by all 3 reviewers and selected by consensus. For our secondary search, we hand-searched the bibliographies of retrieved articles and reviews. We also consulted widely used medical history taking and physical examination textbooks for relevant signs, symptoms, and citations.[29-32] Sign- and symptom-focused MEDLINE searches and Cochrane Database searches further supplemented our secondary search. Our combined searches yielded 256 articles for full-text review.

From the 256 full-text articles examined, we identified 42 that (1) provided primary data on children in whom the diagnosis of appendicitis was considered; (2) presented medical history data, physical examination findings, or basic laboratory data; and (3) confirmed or excluded appendicitis by surgical pathologic findings, clinical observation, or follow-up. Studies that assessed combinations of signs and symptoms were included, but only if they reported data from a population different than the one used to derive the system. Each of these articles underwent independent quality review by 3 authors (D.G.B., J.S.B., and E.A.L.) using the methodological filter previously described in this series.[33] We assigned level 1 to articles with an independent, blind comparison of symptoms, signs, or laboratory results with surgical pathologic findings, clinical observation, or follow-up among 200 or more children with abdominal pain. We assigned level 2 to similar articles that evaluated fewer than 200 children. Level 1 and level 2 articles addressed series of children presenting with undifferentiated abdominal pain. Level 3 was reserved for articles that reported an independent, blind comparison among nonconsecutive patients. Studies in this group were most often series of patients admitted, referred, or operated on for suspected appendicitis. These articles were not assigned to level 1 or 2 because they were not consecutive patients evaluated with abdominal pain but represented more limited groups of children deemed worrisome enough to warrant additional action. This difference results in the higher prevalence of confirmed appendicitis observed in level 3 studies compared with level 1 or level 2 studies. Level 4 studies (nonindependent comparison of signs and symptoms with a gold standard among "grab" samples of patients who obviously have the target condition and healthy individuals) and level 5 studies (same as level 4 except comparison with a standard of uncertain validity) were excluded from analysis. Disagreements in evidence quality level were resolved by discussion.

Statistical Analyses

Two authors independently extracted data from all selected articles. These original data were used to calculate sensitivity, specificity, and positive and negative likelihood ratios (LRs) for each sign, symptom, or laboratory test. Likelihood ratios and associated 95% confidence intervals (CIs) for items that had null outcomes in any cell of the 2×2 table were calculated by adding 0.5 to all cells. Because level 1 and level 3 studies comprise different patient populations, we did not combine their results. Find-

ings reported in only 2 level 3 studies are listed as ranges. For symptoms and signs evaluated in 3 or more level 3 studies, we report summary measures using a random-effects measure (Fast*pro software, version 1.8; Academic Press, Boston, Massachusetts).[34] Random-effects measures provide conservative (ie, broader) CIs than fixed-effects measures and better display the uncertainty in the point estimates. Only 2 of 11 findings (rectal tenderness and white blood cell count >14 900-15 000/μL) displayed statistical heterogeneity in both the positive and negative LRs. When there was heterogeneity, the range of the point estimates was virtually identical to the 95% CIs. Thus, reporting the LR point estimate with its 95% CI provides clinicians with a better anchor for clinical reasoning than the range alone.

Table 1. Characteristics of Included Studies

Source	Quality Level	Setting	Prevalence, No. (%)	Age Range	Inclusion Criteria
O'Shea et al,[35] 1988	1	Emergency department	246 (10)	3-18 y	Presented to ED with abdominal pain <1 wk; no history of trauma or recurrent abdominal pain
Pearl et al,[20] 1995	3	Hospital	1366 (89)	6 mo–18 y	Underwent nonincidental appendectomy
Schneider et al,[36] 2007[a]	3	Emergency department	588 (34)	3-21 y	Presented to ED with abdominal pain; received surgical consultation for possible appendicitis
Kharbanda et al,[37] 2005[a]	3	Emergency department	425 (37)/176 (31)[b]	3-18 y	Presented to ED with abdominal pain; received surgical consultation for possible appendicitis
Wu et al,[38] 2003	3	Hospital	260 (82)	0-18 y	Underwent appendectomy for suspected appendicitis
Dickson and MacKinlay,[39] 1985	3	Hospital	201 (51)	<14 y	Admitted for possible acute appendicitis
Dado et al,[40] 2000	3	Hospital	197 (76)	2-17 y	Admitted from ED with clinical diagnosis of acute appendicitis; underwent emergency appendectomy
Dixon et al,[41] 1991	3	Hospital	195 (52)	0-15 y	Admitted with chief symptom of right lower quadrant pain
Bond et al,[42] 1990	3	Emergency department	189 (61)	2-17 y	Presented to ED with abdominal pain <1 wk in duration, referred to the study, and had white blood cell count done
Harland,[43] 1991	3	Hospital	187 (77)	2-15 y	Underwent appendectomy for suspected appendicitis
Graham et al,[44] 1980	3	Hospital	183 (85)	10 mo–5 y	Underwent appendectomy with preoperative diagnosis of acute appendicitis
Peltola et al,[45] 1986	3	Hospital	162 (58)	1-15 y	Admitted with "symptoms of appendicitis"
Mikaelsson and Arnbjornsson,[46] 1984	3	Hospital	156 (72)	≤15 y	Underwent acute appendectomy for suspected appendicitis
Dolgin et al,[47] 1992	3	Hospital	143 (65)	"Children" (age not specified)	Consulted by pediatric surgery division for possible appendicitis
Lintula et al,[48] 2005	3	Emergency department	127 (34)/106 (25)[b]	4-15 y	Presented to ED with suspected appendicitis; seen by attending surgeon
Rodríguez-Sanjuán et al,[49] 1999	3	Hospital	124 (84)	2-14 y	Underwent appendectomy for suspected appendicitis
Macklin et al,[50] 1997	3	Hospital	118 (32)	4-14 y	Admitted to pediatric surgical service with acute abdominal pain
Türkyilmaz et al,[51] 2006	3	Hospital	105 (58)	3-16 y	Admitted with acute right lower abdominal pain
Paajanen et al,[52] 1997	3	Hospital	100 (48)	0-5 y	Underwent emergency appendectomy for suspected appendicitis
Van den Broek et al,[53] 2004	3	Hospital	99 (66)	<11 y	Referred to the hospital by general practitioners for suspected appendicitis
Bonello and Abrams,[54] 1979	3	Hospital	95 (92)	<12 y	Underwent appendectomy for suspected appendicitis
Paajanen and Somppi,[55] 1996	3	Hospital	90 (46)	0-5 y	Underwent emergency appendectomy for suspected appendicitis
Miskowiak and Burcharth,[56] 1982	3	Hospital	74 (28)	<15 y	Admitted with suspected appendicitis
Owen et al,[57] 1992	3	Hospital	70 (61)	"Children" (age not specified)	Admitted with diagnosis of possible appendicitis
Mollitt et al,[58] 1988	3	Hospital	54 (44)	3-17 y	Referred from ED or clinic to the pediatric surgical service for evaluation of possible appendicitis

Abbreviation: ED, emergency department.
[a] Studies by Schneider et al[36] and Kharbanda et al[37] were derived from overlapping data sets.
[b] Derivation set/validation set.

RESULTS

Search Results and Quality of Evidence

Forty-two studies met our inclusion criteria and were assigned a level of evidence. Of these, 25 studies were level 3 or better (level 1: n=1; level 3: n=24) and are included in this analysis (TABLE 1). One additional study provided precision data only.

Prior Probability

The prior probability (prevalence) of appendicitis in the only level 1 study was 10%.[35] This study evaluated all children aged 3 to 18 years presenting to an emergency department with abdominal pain of less than 1 week in duration, excluding children with a history of trauma or recurrent abdominal pain. Appendicitis prevalence peaked in the 10- to 12-year age group, though numbers in each subgroup were small: for ages 3 to 6 years, 10%; 7 to 9 years, 9%; 10 to 12 years, 17%; 13 to 15 years, 12%; and 16 to 18 years, 6%. All of the level 3 studies had higher prior probabilities of disease (25%-89%), reflecting the more selected nature of the patients studied.

Precision of Symptoms and Signs

We found 1 study of interexaminer precision in the physical examination of children with abdominal pain. Yen et al[59] evaluated interexaminer precision among pediatric emergency medicine physicians (attending or fellow), residents rotating in the emergency department (pediatric, emergency medicine, and family medicine), and pediatric surgeons in training (senior surgical resident or fellow). For 7 clinical findings (abdominal distention, tenderness to percussion, tenderness to palpation, abdominal guarding, rebound tenderness, absent bowel sounds, and clinical diagnosis of peritonitis), interexaminer precision was poor. Rebound tenderness was the only finding with a κ statistic of greater than 0.5 (κ=0.54).

Accuracy of Symptoms

Pain Symptoms. Abdominal pain is a nearly universal finding in pediatric appendicitis. Since the presence of abdominal pain was an inclusion criterion in the majority of the articles we included, we could not evaluate the independent significance of abdominal pain as a presenting symptom. Whether the duration of pain was more or less than 24 hours did not affect the likelihood of appendicitis in either unselected children with abdominal pain (level 1 study) or select groups of children undergoing further evaluation for appendicitis (level 3 studies) (TABLE 2). In the level 3 studies, presence of RLQ pain had minimal impact on the likelihood of appendicitis (summary LR, 1.2; 95% CI, 1.0-1.5); absence of RLQ pain, however, did decrease the likelihood (summary LR, 0.56; 95% CI, 0.43-0.73). Presence of pain that began midabdominally and migrated to the RLQ was more useful (LR range, 1.9-3.1), while absence of this pain evolution had a similar LR compared with that for the absence of RLQ altogether (LR range for absence of RLQ migratory pattern, 0.41-0.72).

Other Symptoms. Five studies evaluated the sensitivity and specificity of fever. The definition of fever within the articles ranged from greater than 37°C to greater than 38.1°C and was not reported in all studies; we defined fever as present or absent based on the individual article definitions. Results for fever as a discriminating variable were mixed. The only level 1 study found that a fever increases the likelihood of appendicitis by about 3-fold (LR, 3.4; 95% CI, 2.4-4.8) while the absence of a fever lowers the likelihood of appendicitis by about two-thirds (LR, 0.32; 95% CI, 0.16-0.64).[35] Fever was not as useful a symptom in the 4 level 3 studies that evaluated fever (summary positive LR, 1.2 [95% CI, 1.1-1.4]; summary negative LR, 0.53 [95% CI, 0.29-0.97]). Similar to the diagnostic usefulness of fever, the presence of vomiting or diarrhea appeared more useful in the level 1 study (LRs for the presence of vomiting, 2.2 [95% CI, 1.7-2.9] and diarrhea, 2.6 [95% CI, 1.3-4.9]) than in the level 3 studies. The absence of vomiting was similarly useful across all studies with a summary LR, 0.57 (95% CI, 0.47-0.69). In contradistinction, the absence of diarrhea did not confer much information and was similar in poor performance across all studies (summary LR, 1.0; 95% CI, 0.97-1.1).

Presence or absence of anorexia or nausea was less useful in the level 1 study, so these findings are of uncertain value. Constipation, lethargy, and dysuria were each evaluated in 1 study, but the 95% CIs for all of these findings included 1.

Accuracy of Signs

Level 1 data were available for only 1 sign, localized abdominal tenderness; this sign was not helpful in predicting appendicitis (TABLE 3). In the more limited groups of children evaluated in level 3 studies, the presence of RLQ tenderness on palpation was of minimal value, but the absence of RLQ tenderness had about the same LR as the absence of the symptom of RLQ pain (summary LR for the absence of RLQ tenderness, 0.45; 95% CI, 0.35-0.59). Rebound tenderness was the most useful sign evaluated in at least 3 studies. In these level 3 studies, the presence of rebound tenderness tripled the odds of appendicitis (summary LR, 3.0; 95% CI, 2.3-3.9) while its absence decreased the odds by more than two-thirds (summary LR, 0.28; 95% CI, 0.14-0.55). Involuntary guarding, evaluated in only 2 studies, appeared to be about as useful as rebound tenderness (positive LR range, 1.6-2.6; negative LR range, 0.21-0.61). The presence of rectal tenderness also increased the likelihood of appendicitis (summary LR, 2.3; 95% CI, 1.3-4.1) but its absence was not as useful (summary LR, 0.7; 95% CI, 0.56-0.87). Likewise, a psoas sign may be useful when present (LR range, 2.0-2.5) but not when absent (LR range, 0.75-0.86). All other reported findings were reported in only 1 study, making their usefulness uncertain.

Symptoms and Signs With Insufficient Data to Evaluate

We identified a number of symptoms and signs in our review that have been

Table 2. Accuracy of Symptoms

Symptoms by Source	Sensitivity	Specificity	Positive Likelihood Ratio (95% Confidence Interval)	Negative Likelihood Ratio (95% Confidence Interval)
Pain Symptoms				
Symptom duration <24 h				
O'Shea et al,[35] 1988	0.50	0.40	0.83 (0.55-1.2)	1.3 (0.82-1.9)
Lintula et al,[48] 2005	0.44	0.46	0.82 (0.56-1.2)	1.2 (0.85-1.7)
Right lower quadrant pain				
Summary, level 3 studies			1.2 (1.0-1.5)	0.56 (0.43-0.73)
Pearl et al,[20] 1995	0.96	0.05	1.0 (0.98-1.0)	0.73 (0.35-1.5)
Kharbanda et al,[37] 2005	0.77	0.44	1.4 (1.2-1.6)	0.52 (0.38-0.72)
Mollitt et al,[58] 1988	0.62	0.63	1.7 (0.97-3.0)	0.59 (0.33-1.1)
Abdominal pain migrating to right lower quadrant				
Kharbanda et al,[37] 2005	0.45	0.76	1.9 (1.4-2.5)	0.72 (0.62-0.85)
Dolgin et al,[47] 1992	0.68	0.78	3.1 (1.8-5.3)	0.41 (0.30-0.57)
Abrupt (vs gradual) onset of pain				
Kharbanda et al,[37] 2005	0.44	0.57	1.0 (0.82-1.3)	0.98 (0.82-1.2)
Intermittent (vs persistent) pain				
Kharbanda et al,[37] 2005	0.20	0.58	0.48 (0.33-0.70)	1.4 (1.2-1.6)
Lintula et al,[48] 2005	0.40	0.48	0.75 (0.49-1.2)	1.3 (0.91-1.8)
Unable to walk normally				
Kharbanda et al,[37] 2005	0.80	0.53	1.7 (1.4-2.0)	0.38 (0.27-0.54)
Other Symptoms				
Fever				
O'Shea et al,[35] 1988	0.75	0.78	3.4 (2.4-4.8)	0.32 (0.16-0.64)
Summary of level 3 studies			1.2 (1.1-1.4)	0.53 (0.29-0.97)
Pearl et al,[20] 1995	0.26	0.75	1.1 (0.80-1.4)	1.0 (0.89-1.1)
Graham et al,[44] 1980	0.93	0.39	1.5 (1.1-2.1)	0.18 (0.09-0.38)
Van den Broek,[53] 2004	0.72	0.50	1.4 (1.0-2.1)	0.55 (0.33-0.93)
Paajanen and Somppi,[55] 1996	0.83	0.29	1.2 (0.93-1.4)	0.60 (0.27-1.3)
Anorexia				
O'Shea et al,[35] 1988	0.21	0.73	0.77 (0.34-1.7)	1.1 (0.87-1.35)
Summary of level 3 studies			1.4 (1.2-1.6)	0.57 (0.44-0.73)
Kharbanda et al,[37] 2005	0.75	0.44	1.4 (1.2-1.6)	0.56 (0.41-0.76)
Graham et al,[44] 1980	0.68	0.50	1.4 (0.92-2.0)	0.65 (0.42-1.0)
Mollitt et al,[58] 1988	0.88	0.40	1.5 (1.0-2.0)	0.31 (0.10-0.98)
Nausea				
O'Shea et al,[35] 1988	0.29	0.79	1.4 (0.70-2.7)	0.90 (0.69-1.2)
Summary of level 3 studies			1.0 (0.50-2.0)	0.50 (0.38-0.66)
Kharbanda et al,[37] 2005	0.82	0.41	1.4 (1.2-1.6)	0.44 (0.31-0.64)
Graham et al,[44] 1980	0.75	0.61	1.9 (1.2-3.0)	0.41 (0.28-0.62)
Lintula et al,[48] 2005	0.60	0.52	1.3 (0.91-1.8)	0.75 (0.49-1.2)
Vomiting				
O'Shea et al,[35] 1988	0.79	0.64	2.2 (1.7-2.9)	0.33 (0.15-0.71)
Summary of level 3 studies			1.4 (1.3-1.6)	0.57 (0.47-0.69)
Kharbanda et al,[37] 2005	0.64	0.58	1.5 (1.3-1.8)	0.61 (0.48-0.78)
Graham et al,[44] 1980	0.86	0.39	1.4 (1.0-1.9)	0.36 (0.20-0.66)
Dolgin et al,[47] 1992	0.77	0.34	1.2 (0.93-1.5)	0.66 (0.39-1.1)
Paajanen and Somppi,[55] 1996	0.63	0.69	2.1 (1.3-3.4)	0.53 (0.34-0.82)
Diarrhea				
O'Shea et al,[35] 1988	0.33	0.87	2.6 (1.3-4.9)	0.77 (0.58-1.0)
Summary of level 3 studies			0.83 (0.59-1.1)	1.0 (0.97-1.1)
Kharbanda et al,[37] 2005	0.15	0.78	0.72 (0.46-1.1)	1.1 (0.98-1.2)
Graham et al,[44] 1980	0.16	0.86	1.1 (0.41-2.9)	1.0 (0.84-1.2)
Dolgin et al,[47] 1992	0.20	0.78	0.91 (0.47-1.8)	1.0 (0.85-1.2)
Paajanen and Somppi,[55] 1996	0.10	0.90	1.0 (0.27-3.3)	1.0 (0.88-1.2)
Constipation				
Dolgin et al,[47] 1992	0.19	0.84	1.2 (0.53-2.7)	1.0 (0.81-1.1)
Lethargy				
O'Shea et al,[35] 1988	0.04	0.95	0.84 (0.11-6.2)	1.0 (0.92-1.1)
Dysuria				
O'Shea et al,[35] 1988	0	0.97	0.59 (0.03-10.1)	1.0 (0.95-1.1)

postulated to help predict appendicitis in children but for which there are inadequate or no data to determine whether they may be helpful (BOX). Data regarding these symptoms and signs are absent, available for adults only, or not of sufficient methodological quality to be included in this review.

Accuracy of Laboratory Studies

Data on laboratory findings were available only from level 3 studies of children in whom the diagnosis of appendicitis was suspected. A WBC count was frequently obtained in such children (TABLE 4). Four studies used a threshold value of greater than 10 000/μL or greater than 10 100/μL; while there was variability in the significance of WBC count above this threshold (summary LR, 2.0; 95% CI, 1.3-2.9), the LR for a WBC count below this threshold was virtually identical in 3 of the 4 studies ($P = .06$ for homogeneity for the negative LR). A WBC count of less than 10 000/μL lowered the likelihood of appendicitis, with a summary LR of 0.22 (95% CI, 0.17-0.30). Increasing the cut point to 14 900/μL or 15 000/μL does not improve the LRs: the 95% CIs around both the positive and negative LRs for this threshold value include 1. A WBC count of less than 8850/μL, however, made appendicitis much less likely (LR, 0.06; 95% CI, 0.02-0.17). One study used age-specific upper limits of normal for WBC count, with children older than 10 years using a lower

Table 3. Accuracy of Signs

Signs by Source	Sensitivity	Specificity	Positive Likelihood Ratio (95% Confidence Interval)	Negative Likelihood Ratio (95% Confidence Interval)
RLQ tenderness				
Summary of level 3 studies			1.3 (1.1-1.4)	0.45 (0.35-0.59)
Pearl et al,[20] 1995	0.97	0.05	1.0 (0.99-1.1)	0.54 (0.25-1.1)
Kharbanda et al,[37] 2005	0.80	0.41	1.4 (1.2-1.5)	0.49 (0.35-0.70)
Dolgin et al,[47] 1992	0.81	0.52	1.7 (1.2-2.3)	0.37 (0.23-0.61)
Paajanen and Somppi,[55] 1996	0.93	0.18	1.1 (0.97-1.3)	0.40 (0.12-1.4)
Rebound tenderness				
Summary of level 3 studies			3.0 (2.3-3.9)	0.28 (0.14-0.55)
Kharbanda et al,[37] 2005	0.53	0.80	2.6 (2.0-3.5)	0.59 (0.50-0.71)
Graham et al,[44] 1980	0.84	0.86	5.9 (2.4-14.6)	0.19 (0.13-0.28)
Van den Broek,[53] 2004	0.88	0.76	3.7 (2.0-6.9)	0.16 (0.08-0.32)
Rectal tenderness				
Summary of level 3 studies			2.3 (1.3-4.1)	0.70 (0.56-0.87)
Dickson and MacKinlay,[39] 1985	0.53	0.88	4.4 (2.5-7.6)	0.53 (0.43-0.66)
Dixon et al,[41] 1991	0.48	0.60	1.2 (0.87-1.7)	0.87 (0.68-1.1)
Kharbanda et al,[37] 2005	0.27	0.90	2.8 (1.3-6.2)	0.81 (0.67-0.98)
Bonello and Abrams,[54] 1979	0.55	0.75	2.2 (0.65-7.4)	0.60 (0.38-0.95)
Psoas sign				
Kharbanda et al,[37] 2005	0.36	0.86	2.5 (1.7-3.7)	0.75 (0.66-0.86)
Lintula et al,[48] 2005	0.26	0.87	2.0 (0.92-4.1)	0.86 (0.71-1.0)
Localized abdominal tenderness				
O'Shea et al,[35] 1988	0.21	0.81	1.1 (0.47-2.4)	1.0 (0.79-1.2)
Pain with percussion, hopping, cough				
Kharbanda et al,[37] 2005	0.78	0.62	2.0 (1.7-2.4)	0.36 (0.26-0.50)
Abdominal distention				
Graham et al,[44] 1980	0.23	0.96	6.5 (0.93-45.5)	0.80 (0.71-0.89)
Lintula et al,[48] 2005	0.16	0.93	2.3 (0.82-6.4)	0.90 (0.78-1.0)
Diffuse peritonitis				
Paajanen and Somppi,[55] 1996	0.24	1.00	25.0 (1.5-414.1)	0.76 (0.63-0.90)
Abdominal mass				
Graham et al,[44] 1980	0.12	1.00	6.9 (0.43-111.0)	0.90 (0.83-0.97)
Guarding				
Kharbanda et al,[37] 2005	0.62	0.63	1.6 (1.4-2.0)	0.61 (0.49-0.76)
Dolgin et al,[47] 1992	0.86	0.67	2.6 (1.7-3.9)	0.21 (0.12-0.36)
Bowel sounds decreased (vs increased/normal)				
Kharbanda et al,[37] 2005	0.33	0.87	2.5 (1.6-3.7)	0.77 (0.68-0.88)
CVA tenderness				
Kharbanda et al,[37] 2005	0.09	0.90	0.87 (0.45-1.7)	1.0 (0.95-1.1)
Obturator sign				
Kharbanda et al,[37] 2005	0.28	0.87	2.2 (1.4-3.4)	0.82 (0.73-0.93)
Rovsing sign				
Kharbanda et al,[37] 2005	0.30	0.84	1.9 (1.3-2.8)	0.83 (0.74-0.93)

Box. Unsupported Symptoms and Signs of Appendicitis (Due to Inadequate Evidence in Pediatrics)

Symptoms
- Cat's eye symptom (pain going over a bump in the road)
- Cutaneous hyperesthesia
- Family history of appendicitis
- Tenesmus

Signs
- Abdominal wall tenderness
- Characteristic facial expression[a]
- Ill appearance
- Elevated skin temperature over right (as opposed to left) lower abdominal quadrant
- Tenderness at the Lanwei acupoint[b]

[a]Described as an "aura of malaise" with "an upward curling of the upper lip"; see photograph in Odom.[60]

[b]Located approximately 1 to 2 in (2.54-5.08 cm) anterolateral to the tibial crest, 4 finger breadths inferior to the lateral inferior border of the patella, down to approximately the same area at midshaft of the tibia.

cutoff (13 000/μL) than children aged 10 years or younger (15 000/μL).[51] White blood cell counts above these age-specific limits increased the likelihood of appendicitis (LR, 3.4; 95% CI, 1.9-6.3). An absolute neutrophil count of 6750/μL or lower substantially decreased the likelihood of appendicitis (LR, 0.06; 95% CI, 0.03-0.16).

C-reactive protein (CRP), which is increasingly available on an urgent basis, performed inconsistently as a predictor of appendicitis (Table 4). One level 3 study using ordinal cut points found that children with CRP levels of 25 mg/L or higher were more likely to have appendicitis (LR, 5.2; 95% CI, 1.7-16) than children with lower levels.[46] This result was confirmed in a recent study that used a threshold of greater than 17 mg/L (LR, 2.9; 95% CI, 1.2-7.0).[49] However, the 95% CIs are broad for the positive LR at each CRP threshold that has been studied. Levels of CRP below chosen thresholds show a decreased likelihood of appendicitis; with a CRP level of less than 8 to 10 mg/L, the LR range is narrow at 0.44 to 0.47, suggesting that a normal CRP level approximately halves the likelihood of appendicitis in children with suspected appendicitis. Erythrocyte sedimentation rate performed similarly to CRP: an erythrocyte sedimentation rate higher than 20 mm/h increased the likelihood of appendicitis (LR, 3.8; 95% CI, 1.8-8.1) and a normal erythrocyte sedimentation rate slightly lowered the likelihood (LR, 0.68; 95% CI, 0.56-0.81). The presence of white blood cells, red blood cells, or bacteria in the urine was not helpful for diagnosing appendicitis.

Accuracy of Symptom-Sign Combinations

We included 7 studies that evaluated combinations of symptoms and signs (TABLE 5); all were level 3 studies that focused on children with suspected appendicitis. Four studies prospectively evaluated the Alvarado, or MANTRELS, score (TABLE 6). Schneider et al[63] examined children referred for surgical consultation from a pediatric emergency department. Owen et al[57] studied children referred for admission to the pediatric surgical service for suspected appendicitis. Bond et al[42] evaluated children presenting to an emergency department with abdominal pain and reported the data at varying thresholds of the Alvarado score. Among children with a score of 4 or lower, none had appendicitis. The score performed best in the oldest age group. Taken together, these 3 studies show that an Alvarado score of 7 or higher increases the likelihood of appendicitis 4-fold (summary LR, 4.0; 95% CI, 3.2-4.9) while a score of less than 7 reduces the likelihood by four-fifths (summary LR, 0.20; 95% CI, 0.09-0.41). Macklin et al[50] evaluated a modified Alvarado score, eliminating the left-shift criterion. In this study of children admitted to the pediatric surgical service for evaluation of abdominal pain, the modified Alvarado score performed similarly to the full Alvarado score (positive LR, 3.6 [95% CI, 2.3-5.7]; negative LR, 0.30 [95% CI, 0.17-0.54]).

Using the same data set described above, Schneider et al[63] also examined the Pediatric Appendicitis Score,[62] a variant of the Alvarado score that had not previously been validated (Table 6). A score of 6 or higher on the Pediatric Appendicitis Score was somewhat less helpful than an Alvarado score of 7 or higher in the same patient cohort (positive LR, 2.4 vs 3.8, respectively); Pediatric Appendicitis Score values below the cutoff were somewhat more helpful than Alvarado scores below the cutoff (negative LR, 0.27 vs 0.40, respectively).

Two studies analyzed sets of patients to create novel scoring systems and second sets with which to test the scoring systems. Kharbanda et al[37] created 2 scoring systems using a data set overlapping with Schneider.[63] The first gave 2 points each for nausea, history of focal RLQ pain, and rebound tenderness/pain with percussion, 1 point each for migration of pain and difficulty walking, and 6 points for an absolute neutrophil count greater than 6750/μL. Of 14 possible points, children with a score of 5 or lower were unlikely to have appendicitis (LR, 0.10). The decision rule from the same study identified children as low risk if their absolute neutrophil count was 6750/μL or less and either they lacked nausea or had nausea but did not have maximal tenderness in the RLQ. Children identified as low risk by this rule were also very unlikely to have appendicitis (LR, 0.06). Lintula et al[48] developed a scoring system involving gender plus 8 signs and symptoms. A score of 15 or lower (of 32) significantly decreased the likelihood of appendicitis (LR, 0.20); a score of 21 or higher had the opposite effect (LR, 12). One study evaluated the accuracy of the modified Lindberg score, which includes 10 clinical and laboratory variables.[40] In this study of children admitted to the pediatric service from the emergency department

with a clinical diagnosis of appendicitis, the modified Lindberg score had a positive LR of 7.6 and a negative LR of 0.39.

Accuracy of the Clinical Gestalt Imputed From Abdominal Imaging

The existing literature does not completely address the role of the clinical evaluation in identifying which children with abdominal pain should undergo abdominal imaging. However, we can make some inferences about the overall clinical gestalt in identifying patients most likely to have appendicitis. This gestalt should help identify which children should have immediate surgical consultation for possible appendectomy and which children with more equivocal presentations of possible appendicitis should undergo further diagnostic evaluation, such as imaging. This clinical gestalt includes all data available to the clinician before ordering imaging (history, physical examination, and routine laboratory tests). This approach was used in a prior Rational Clinical Examination article to impute the LR of the clinical gestalt for adult cholecystitis.[64]

A recent meta-analysis of prospective studies evaluating computed tomography and ultrasonography among adults and adolescents (aged ≥14 years) found a prevalence of appendicitis of 45% in computed tomography studies and 50% in ultrasound studies.[65] The patients in these studies had either suspected appendicitis or abdominal discomfort with atypical features for appendicitis. The prevalences in the included studies in this meta-analysis are similar to the prevalence of appendicitis in the level 3 studies of children (Table 1). A second meta-analysis of both computed tomography and ultrasound found a 31% prevalence of appendicitis among children (in studies in which the maximum age was <20 years) referred for imaging.[66]

Because the prior probability of appendicitis in emergency department children evaluated for undifferentiated abdominal pain is 10%,[35] we can work backward to impute the LR for the clinical gestalt among patients referred for imaging. If the prevalence of childhood appendicitis is as much as 50% in children referred for imaging, then the clinical gestalt has a positive LR of 9.0 for appendicitis; if the prevalence is only as high as 25%, then the clinical gestalt has a positive LR of 3.0,

Table 4. Accuracy of Laboratory Studies

Laboratory Measurement (Cutoff or Range) by Source	Sensitivity	Specificity	Positive Likelihood Ratio (95% Confidence Interval)	Negative Likelihood Ratio (95% Confidence Interval)
White blood cell count, /μL				
Summary, >14 900 or >15 000			1.7 (0.83-3.4)	0.77 (0.52-1.1)
Peltola et al,[45] 1986 (>14 900)	0.60	0.84	3.7 (2.1-6.5)	0.48 (0.37-0.63)
Paajanen et al,[52] 1997 (>15 000)	0.56	0.44	1.0 (0.71-1.4)	1.0 (0.64-1.5)
Miskowiak and Burcharth,[56] 1982 (>15 000)	0.19	0.85	1.3 (0.42-3.8)	1.0 (0.75-1.2)
Summary, >10 000 or >10 100			2.0 (1.3-2.9)	0.22 (0.17-0.30)
Pearl et al,[20] 1995 (>10 000)	0.90	0.38	1.5 (1.3-1.6)	0.26 (0.20-0.34)
Wu et al,[38] 2003 (>10 000)	0.92	0.29	1.3 (1.1-1.6)	0.26 (0.14-0.49)
Harland,[43] 1991 (>10 000)	0.92	0.70	3.1 (1.9-4.8)	0.11 (0.06-0.20)
Van den Broek,[53] 2004 (>10 100)	0.80	0.76	3.4 (1.8-6.3)	0.26 (0.16-0.44)
Kharbanda et al,[37] 2005 (>8850)	0.98	0.40	1.6 (1.5-1.8)	0.06 (0.02-0.17)
Türkyilmaz et al,[51] 2006 (age-specific)[a]	0.70	0.79	3.4 (1.9-6.3)	0.37 (0.24-0.56)
Absolute neutrophil count, /μL				
Kharbanda et al,[37] 2005 (>6750)	0.97	0.51	2.0 (1.7-2.2)	0.06 (0.03-0.16)
C-reactive protein, mg/L				
Mikaelsson and Arnbjornsson,[46] 1984				
≥25			5.2 (1.7-16)[b]	
13-24			0.23 (0.12-0.43)[b]	
≤12			1.1 (0.79-1.6)[b]	
Rodriguez-Sanjuan et al,[49] 1999 (>17)	0.58	0.80	2.9 (1.2-7.0)	0.53 (0.39-0.72)
Peltola et al,[45] 1986 (>10)	0.64	0.82	3.6 (2.1-6.2)	0.44 (0.33-0.59)
Paajanen et al,[52] 1997 (>10)	0.85	0.33	1.3 (1.0-1.6)	0.45 (0.20-0.98)
Wu et al,[38] 2003 (>8)	0.79	0.44	1.4 (1.1-1.8)	0.47 (0.31-0.72)
Erythrocyte sedimentation rate, mm/h				
Peltola et al,[45] 1986 (>20)	0.39	0.90	3.8 (1.8-8.1)	0.68 (0.56-0.81)
Urinalysis				
Paajanen and Somppi,[55] 1996				
>3 White blood cells per high-power field	0.27	0.90	2.6 (0.99-7.0)	0.81 (0.66-1.00)
>3 Red blood cells per high-power field	0.05	0.90	0.48 (0.10-2.3)	1.1 (0.94-1.2)
Positive bacteria culture	0.02	1.00	3.6 (0.15-85.4)	1.0 (0.91-1.0)

[a] Upper limit of normal defined as 15 000/μL for ages 3 to 10 years and 13 000/μL for ages 11 to 16 years.
[b] Stratum-specific likelihood ratios.

Table 5. Accuracy of Clinical Scoring Systems

Scoring System (Score Cutoff) by Source	Sensitivity	Specificity	Positive Likelihood Ratio (95% Confidence Interval)	Negative Likelihood Ratio (95% Confidence Interval)
Alvarado/MANTRELS				
Summary of level 3 studies (≥7)			4.0 (3.2-4.9)	0.20 (0.09-0.41)
Schneider et al,[36] 2007 (≥7)	0.72	0.81	3.8 (3.0-4.7)	0.40 (0.27-0.43)
Owen et al,[57] 1992 (≥7)	0.93	0.82	5.0 (2.3-11)	0.09 (0.03-0.26)
Bond et al,[42] 1990				
≥7			3.1 (2.2-4.5)[a]	
6			0.29 (0.12-0.73)[a]	
5			0.31 (0.12-0.80)[a]	
≤4			0.05 (0-0.85)[a]	
Modified Alvarado				
Macklin et al,[50] 1997 (≥7)	0.76	0.79	3.6 (2.3-5.7)	0.30 (0.17-0.54)
Pediatric Appendicitis Score				
Schneider et al,[36] 2007 (≥6)	0.82	0.65	2.4 (2.0-2.8)	0.27 (0.20-0.37)
Kharbanda logistic score				
Kharbanda et al,[37] 2005 (>5)	0.96	0.36	1.5 (1.3-1.7)	0.10 (0.03-0.41)
Kharbanda recursive partitioning decision tree				
Kharbanda et al,[37] 2005 ("high risk")	0.98	0.32	1.4 (1.3-1.6)	0.06 (0.01-0.41)
Lintula appendicitis score				
Lintula et al,[48] 2005				
≥21			12 (4.3-32.0)[a]	
16-20			1.2 (0.56-2.6)[a]	
≤15			0.20 (0.08-0.50)[a]	
Modified Lindberg				
Dado et al,[40] 2000 (≥–2)	0.65	0.92	7.6 (3.0-19.6)	0.39 (0.31-0.49)

[a] Stratum-specific likelihood ratios.

Table 6. Alvarado/MANTRELS[61] and Pediatric Appendicitis[62] Scoring Systems

Variables	Score
Alvarado/MANTRELS	
Migration of pain to the right lower quadrant	1
Anorexia	1
Nausea/vomiting	1
Tenderness in the right lower quadrant	2
Rebound pain	1
Elevation of temperature (≥37.3°C)	1
Leukocytosis (WBC >10 000/μL)	2
Shift of WBC count to the left (>75% neutrophils)[a]	1
Maximum score	**10**
Pediatric Appendicitis Score	
Migration of pain to the right lower quadrant	1
Anorexia	1
Nausea/vomiting	1
Tenderness in the right lower quadrant	2
Cough/hopping/percussion tenderness in the right lower quadrant	2
Elevation in temperature[b]	1
Leukocytosis (WBC >10 000/μL)	1
Shift of WBC count to the left (not defined)	1
Maximum score	**10**

Abbreviation: WBC, white blood cell.
[a] The modified Alvarado score excludes this variable and has a score range of 0 to 9.
[b] Elevation in temperature not defined by Samuel.[62]

given the prior probability of 10%. These values are consistent with the positive LR for an Alvarado score of 7 or higher (Table 5) and would explain why experienced clinicians more often rely on clinical gestalt rather than on formal scoring systems.

Comparison With Adult Data

Comparing the current analysis in children with the previous Rational Clinical Examination article examining appendicitis in adults[16] yields noteworthy similarities and differences. Right lower quadrant abdominal pain, typically identified as a classic symptom of appendicitis, was a much stronger predictor in adults (LRs, 7.3-8.5) than in children (summary LR, 1.2). Fever, anorexia, nausea, and vomiting were all poor independent predictors of appendicitis in both adults and children. Rebound tenderness and the psoas sign performed similarly in children and adults.

Limitations of the Literature

The published literature describing the utility of signs, symptoms, and basic laboratory tests for the diagnosis of appendicitis in children has several limitations. First, most studies that include data on pediatric and adult patients do not stratify the results by age, making evaluation of child-specific data impossible. The differential diagnosis of abdominal pain varies substantially depending on the age of the patient; research methods should reflect this variation. Even in studies involving exclusively children, age stratification would be helpful. Abdominal pain in a 2-year-old might suggest intussusception, whereas this diagnosis would be unusual in a 14-year-old. Likewise, pelvic inflammatory disease might enter the differential diagnosis for a 16-year-old girl but not for a 3-year-old girl.

Verification bias is a second limitation of the literature we reviewed. Verification bias occurs when the gold standard diagnostic test is only applied to a subset of the original population at risk of a disease and when the probability of applying the gold standard test depends on the original test result, other

clinical variables, or both.[67] In general, verification bias results in overestimation of sensitivity and underestimation of specificity of diagnostic tests. Studies examining selective series of children (level 3) have verification bias because large numbers of children in whom the diagnosis of appendicitis was initially considered are not included in the analysis. The verification bias creates a problem for clinicians who want to extrapolate data from patients at higher risk of having appendicitis to all children presenting with abdominal pain. By underestimating specificity, verification bias may cause findings to appear less useful for identifying children with appendicitis than they actually are. This may explain, for example, the aforementioned difference seen between adults and children in RLQ pain. Conversely, the overestimated sensitivity from verification bias may cause clinical findings to appear more useful at lowering the likelihood of appendicitis than they actually are.

In addition to involving different patient populations, level 3 studies were also conducted in different settings, by different personnel, and with different information available to clinicians than in the level 1 study. Nonetheless, the level 3 studies produced likelihood results that are clinically similar to each other, and the random-effects estimates with their 95% CIs provide insight into their potential usefulness or lack of utility. Most level 3 studies were conducted in inpatient settings, many among children undergoing appendectomy, and most involved surgeons evaluating patients once other front-line personnel had suspected appendicitis in these patients. Like verification bias, these differences in study characteristics make extrapolation of level 3 data to level 1 children (ie, children with undifferentiated abdominal pain) problematic.

A final limitation of the reviewed literature is that much of the data reported were collected retrospectively. Retrospective data may be less reliable than prospective data because the former may not be collected or documented in a standard fashion. In addition, history or physical examination data may have been collected or documented after other results (eg, radiological studies) were already available, potentially biasing the results. Studies in which a fixed list of variables is collected prospectively in a standardized fashion, prior to the availability of other clinical data, offer the strongest evidence.

SCENARIO RESOLUTION

Case 1

This boy's history, physical examination, and laboratory studies are strongly suggestive of acute appendicitis. His age-specific pretest probability for appendicitis is approximately 10%. In this setting of undifferentiated abdominal pain, his fever alone confers a 3.4-fold increased odds of appendicitis and a posttest probability of 27%. A surgical consultation is requested, and, with an Alvarado score of 9 of 10, the decision is made to perform an immediate appendectomy.

Case 2

This girl's symptoms and signs raise concerns for possible appendicitis, although several other diagnoses are possible. Her age-specific pretest probability is 9%. Her Alvarado score is 5 of 10, which, in this setting of possible appendicitis following a thorough evaluation, lowers her likelihood of appendicitis (negative LR, 0.09-0.31) and yields a posttest probability of 1% to 3%. The surgical consultant recommends close outpatient observation and follow-up with her primary care physician; presumptive treatment for a urinary tract infection is prescribed.

CLINICAL BOTTOM LINE

Despite methodological limitations of the literature, clinical evaluation of children with abdominal pain can help identify which children should undergo immediate surgical consultation for potential appendectomy and which children should undergo further diagnostic evaluation. Our review identified a single study that evaluated the utility of signs and symptoms to diagnose appendicitis in an unselected sample of children presenting to the emergency department with abdominal pain.[35] These data are helpful to the clinicians who initially evaluate children before laboratory, radiology, or consultant data are available. In this study,[35] O'Shea et al identified fever as the single most useful symptom (positive LR, 3.4; negative LR, 0.32). With a pretest probability of appendicitis of 10%, the absence of fever reduced the posttest probability to 3.4%; the presence of fever increased the posttest probability to 27%.

The many level 3 studies identified in this review provide important data for a more narrowly defined population of children with abdominal pain: those in whom the diagnosis of appendicitis is suspected. This group of children typically undergoes a more thorough evaluation for possible appendicitis, including either immediate surgical consultation or further evaluation such as diagnostic imaging. In this subgroup of patients, rebound tenderness is nearly as valuable as fever is in the unselected population (positive LR, 3.0; negative LR, 0.28). A normal WBC count (eg, $<$10 000/μL) substantially decreases the likelihood of appendicitis (negative LR, 0.22). These 2 variables may be helpful in making the decision to operate vs observe, particularly when imaging is performed and is equivocal.

Scoring systems can be helpful for identifying children who do not require further evaluation for appendicitis among those in whom the diagnosis is initially considered. Children with Alvarado scores of less than 5, for example, are unlikely to have appendicitis (negative LR, 0.05) and could be spared further evaluation for this diagnosis. The logistic score of Kharbanda et al[37] is nearly as helpful as the Alvarado score at reducing the likelihood of appendicitis when negative (negative LR, 0.10) and used 2 fewer variables. The decision tree of Kharbanda et al is even more effective at identifying a low-risk group (negative

LR, 0.06) and could exclude approximately 1 in 5 children with suspected appendicitis from further workup. The evaluation of combinations of findings is important because without such evaluations, it is impossible to know whether the individual findings are independent. Both the Alvarado score and the Kharbanda logistic score included rebound tenderness and a WBC variable (Alvarado: WBC count; Kharbanda: absolute neutrophil count), the 2 most useful independent variables identified across the level 3 studies. Additional variables shared by these 2 scoring systems include nausea, migration of pain to the RLQ, and focal RLQ pain/tenderness, none of which were particularly helpful when evaluated independently.

Barriers to the use of scoring systems in real-world (ie, nonresearch) settings are formidable and include time pressures and difficulties with implementation; these barriers favor simple systems over more complex ones. In our review, more complex scoring systems did not perform appreciably better than the simpler Alvarado or Kharbanda systems. Future research, therefore, could aim to unify these 2 systems and validate the resulting system in larger groups of unselected children with abdominal pain. Although experienced clinicians may not improve their diagnostic performance with scoring systems, less-experienced clinicians might use them to focus their examination on the scoring systems' independently useful findings.

In summary, the clinical examination plays a key part in determining which children with abdominal pain should undergo immediate surgical consultation for potential appendectomy and which children should undergo further diagnostic evaluation, including diagnostic imaging, clinical observation, and surgical consultation. Children with a low likelihood of appendicitis may be spared the expense and risk of a more invasive and costly workup for appendicitis and may be safely sent home with careful follow-up. However, particularly in young children, in whom the diagnosis of appendicitis is difficult to make, clinicians will continue to rely on radiological studies and surgical evaluation to evaluate potential appendicitis, since the clinical examination cannot definitively confirm this diagnosis. Future research generating prospective, age-specific data on large cohorts of children with undifferentiated, acute abdominal pain could further increase the usefulness of the clinical examination in identifying children with possible appendicitis.

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