February 2023

# TEXAS CHILDREN'S HOSPITAL EVIDENCE-BASED OUTCOMES CENTER Acute Appendicitis/Appendectomy Evidence-Based Guideline

Texas Children's

Hospital

**Definition:** Acute appendicitis is the inflammation of the veriform appendix; a blind ended tube connected to the cecum of the bowel. Although the cause is unknown, most theories relate to an obstruction of the appendiceal lumen which prevents the escape of secretions and eventually leads to a rise in intra-luminal pressure with the appendix. The increased pressure can lead to mucosal ischemia with stasis, providing an environment for bacterial overgrowth. The obstruction may be caused by: fecolith, parasites, calculi, foreign body, neoplasm, stricture of worms, lymphoid hyperplasia secondary to Crohn's disease, carcinoid syndrome or viral illnesses including upper respiratory infection, mononucleosis, and gastroenteritis. <sup>(1,2)</sup>

**Incidence:** Acute appendicitis is the most common abdominal condition requiring surgery in children, accounting for more than 320,000 operations in the United States annually. Appendicitis accounts for 1/3 of all childhood admissions for abdominal pain. The incidence of perforated appendix is highest in infants. 70-95% of children <1 year, 70-90% of children 1-4 years, and 10-20% of adolescents with acute appendicitis have a perforated appendix. The reported median perforation rate in children is 38.7%. <sup>(1-5)</sup>

<u>Diagnosis</u>: The diagnosis of acute appendicitis must be considered in children who present with abdominal pain. It is most common in 4- to 15-year-olds. (4,5)

## Inclusion Criteria (1-6)

 Children ≥2 years presenting with abdominal pain and signs/symptoms highly suspicious of acute appendicitis

# Exclusion Criteria

- Children <2 years</li>
- Previous appendectomy
- History of bloody stools
- Crohn's disease
- History of cystic fibrosis, transplant or malignancy

# Diagnostic Evaluation (3,5-7)

Children with appendicitis have a risk of progressing to septic shock. Clinicians should immediately refer to the Septic Shock guideline and intervene rapidly if patient has toxic-appearance, ill-appearance, altered mental status, and/or compromised perfusion with abnormal vital signs.

| Vital Sign Changes | of | Sepsis | (8) |
|--------------------|----|--------|-----|
|--------------------|----|--------|-----|

| Age        | Heart Rate | Resp Rate | Systolic BP           | Temp (°C)    |
|------------|------------|-----------|-----------------------|--------------|
| 0d - 1m    | >205       | >60       | <60                   | <36 or >38   |
| >1m - 3m   | >205       | >60       | <70                   | <36 or >38   |
| >3m - 1y   | >190       | >60       | <70                   | <36 or >38.5 |
| >1y - 2y   | >190       | >40       | <70 + (age in yr x 2) | <36 or >38.5 |
| >2y - 4y   | >140       | >40       | <70 + (age in yr x 2) | <36 or >38.5 |
| >4y - 6y   | >140       | >34       | <70 + (age in yr x 2) | <36 or >38.5 |
| >6y - 10y  | >140       | >30       | <70 + (age in yr x 2) | <36 or >38.5 |
| >10y - 13y | >100       | >30       | <90                   | <36 or >38.5 |
| >13y       | >100       | >20       | <90                   | <36 or >38.5 |

# Signs and Symptoms of Shock <sup>(8)</sup>

| Exam Abnormalities                                 |                      |  |   |
|--|----------------------|--|---|
|  | Cold Shock           | Warm Shock   | Non-Specific  |
| Peripheral<br>Pulses                               | Decreased<br>or weak | Bounding   |   |
| Capillary<br>Refill (central<br>vs.<br>peripheral) | ≥3 sec               | Flash (<1 sec)                                       |   |
| Skin   | Mottled, cool        | Flushed, ruddy,<br>erythroderma<br>(other than face) | Petechiae below the nipple, any purpura   |
| Mental<br>Status                                   |                      |  | Decreased, irritability,<br>confusion, <u>inappropriate</u><br>crying or drowsiness,<br>poor interaction with<br>parents, lethargy,<br>diminished arousability,<br>obtunded |

Clinical history and physical (H&P) alone is sufficient for diagnosis when the index of suspicion for appendicitis is high or low. <sup>(5,9)</sup>

### History: Assess for

- Pain in the abdomen that is continuous even when lying down, first around the umbilicus, then moving to the lower right abdomen (McBurney's Point)
- Pain may also be in the right upper quadrant (RUQ) under the gallbladder, in the pelvis, across the top of the bladder, and behind the large intestine, depending on the position of the appendix
- Pain intensifies with activity, deep breathing, coughing, and sneezing
- Nausea, loss of appetite, lack of interest in favorite food, vomiting
- Frequent, small volume stool or mucous (tenesmus)
- · Fever, essentially always following onset of other symptoms
- Abdominal swelling
- Menstrual and sexual history

## Physical Examination: Assess for (6,7)

- A quiet child reluctant to move, sometimes with hips flexed
- Child reluctant to stand erect, walk, or make sudden movements
- Tenderness in the right lower quadrant (RLQ) of the abdomen (examine last)
- Peritoneal signs

# Classic Signs and Symptoms for High Index of Suspicion Cases: <sup>(5)</sup>

- Nausea, anorexia (less reliable in young children)
- Point of maximal tenderness in RLQ
- Vomiting after onset of pain
- Progressive increase in pain
- Migration of pain to RLQ after onset in mid abdomen (usually periumbilical)

# Classic Signs and Symptoms for Low Index of Suspicion Cases: <sup>(5)</sup>

- Absence of nausea, emesis or anorexia
- Minimal or absent abdominal tenderness without localization in RLQ
- Normal WBC and differential
- · Pain that is intermittent or cramping in nature

## Pediatric Appendicitis Score (PAS) [point value] (10-13)

- Migration of pain [1]
- Anorexia [1]
- Nausea/Vomiting [1]
- RLQ tenderness [2]
- Cough/Hopping/Percussion tenderness in RLQ [2]
- Elevation of temperature [1]
- Leukocytosis (≥10,000) [1]
- Differential WBC with left shift [1]

\*The PAS is the cumulative point total from all clinical findings

#### PAS ≤4: Low suspicion for appendicitis PAS 5-7: Equivocal for appendicitis

PAS  $\geq$ 8: High suspicion for appendicitis

### **Critical Points of Evidence\***

### **Evidence Supports**

- Use the PAS to predict the presence of appendicitis in children ≥4 years. <sup>(10-13)</sup> Strong recommendation, moderate quality evidence
- Utilize ultrasound (US) as the initial imaging modality in children with appendicitis. CT should be obtained only when US is equivocal or further investigation is needed in diagnosing appendicitis in children. <sup>(15, 17-21)</sup> Strong recommendation, moderate quality evidence. Remarks: CT is more accurate than US in diagnosing appendicitis in children. However, the risk of radiation exposure needs to be considered. Texas Children's Hospital data supports US as equivalent to CT in diagnosing appendicitis in the majority of children, excluding some obese patients. <sup>(22)</sup>
- A timely diagnosis of appendicitis should be made by physicians in the ED. <sup>(23)</sup> Strong recommendation, low quality evidence
- Laparoscopic appendectomy is the preferred surgical approach (vs. open surgery) for children with appendicitis. <sup>(24-28)</sup> Strong recommendation, moderate quality evidence
- Postoperative pain medications should be scheduled. <sup>(29,30)</sup> Strong recommendation, low quality evidence
- In complicated/advanced appendicitis, monotherapy should be administered for a minimum of 3 days to reduce postoperative
  infectious complications in children undergoing an appendectomy. <sup>(31-34)</sup> Strong recommendation, moderate quality evidence
- An ultrasound should be used postoperatively to determine whether or not an abscess is present in patients with complicated appendicitis. <sup>(35)</sup> – Strong recommendation, very low quality evidence
- A localized fluid collection should be drained if the collection has an estimated size of >4cm. <sup>(36-38)</sup> Strong recommendation, very low quality evidence
- Discontinue antibiotic therapy at discharge once clinical discharge criteria are met (afebrile, tolerating regular diet, pain controlled with oral pain medications, ambulating, and benign abdominal physical exam with no tenderness or mass). <sup>(39-44)</sup> – Strong recommendation, low quality evidence

### **Evidence Against**

- Do not withhold analgesia. Withholding analgesia does not aid in the diagnosis of appendicitis. (45-50) Strong recommendation, high quality evidence
- Do not routinely obtain perioperative cultures. <sup>(51-56)</sup> Strong recommendation, low quality evidence Remarks: All children with drained abscesses should have anaerobic and aerobic cultures obtained from abscess fluid.
- Do not routinely administer postoperative antibiotics to children with simple appendicitis. <sup>(57,58)</sup> Strong recommendation, moderate guality evidence
- Do not use biomarker testing to predict further antibiotic therapy in pediatric patients with complicated appendicitis with ongoing signs and symptoms post-appendectomy. <sup>(40,44,59-63)</sup> – Strong recommendation, low quality evidence

### Evidence Lacking/Inconclusive

- Children with complicated appendicitis and a penicillin allergy should be treated with IV ciprofloxacin and metronidazole; if they meet clinical but not laboratory discharge criteria, transition to PO ciprofloxacin and metronidazole for discharge to home. – Consensus recommendation
- Patients with complicated appendicitis who do not achieve discharge criteria should be imaged at 6-7 days only if clinical suspicion for abscess. Consensus recommendation
- In patients with complicated appendicitis who require percutaneous drainage, keep the drain in place until output is <10 20 mL/day
  and the patient is clinically improving. Routinely flush the drain with 10mL of saline per day. Consider TPA in complex collections
  with minimal output from a correctly placed drainage catheter after discussion between clinical teams, including surgery and IR. The
  amount of TPA should be determined based on size and location of collection. Consensus recommendation</li>
- There is insufficient evidence for the following topics: non-operative management of appendicitis, <sup>(16,64-68)</sup> interval appendectomies for abscesses or phlegmons. <sup>(69-71)</sup>

\*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

# Laboratory Assessment (5,14)

# Diagnostic:

 Utilize only in cases where H&P is not definitive for acute appendicitis (exception: urine pregnancy test in postpubescent females).

## Radiologic Evaluation (5,10-13,15,16)

- US is the initial imaging modality for children with appendicitis.
- CT should be obtained only when US is equivocal or further investigation is needed

# **Condition-Specific Elements of Clinical Management**

# **Classification of Appendicitis**

- Appendicitis is classified based upon intraoperative findings
- Complicated appendicitis includes the presence of an ileus, diffuse peritonitis, fibrino-purulent fluid in location other than RLQ, and/or a visible hole in appendix.
- Gangrenous appendicitis is treated as simple appendicitis.

# Surgical Approach (24,25)

 Laparoscopic approach is preferred; perform open appendectomies only for: (1) very small children in whom insufflation is not technically feasible, (2) cases of neglected perforated appendicitis with large abscesses, or (3) as a conversion from laparoscopy due to inappropriate visualization, extreme inflammation.

# Perioperative Cultures (45-48)

- Intraoperative cultures should not be routinely be obtained.
- All children with drained abscesses should have anaerobic and aerobic cultures obtained from abscess fluid.

# Pain Management (29,30,39-44,73-75)

- Administer analgesia to promote comfort.
- Withholding analgesia does not improve diagnostic accuracy.
- Schedule postoperative pain medication.

# Antibiotics (31-34,40,44,59-63,76,77)

- Administer piperacillin/tazobactam (Zosyn<sup>®</sup>) monotherapy as soon as possible once the diagnosis is confirmed.
- Administer a second dose of monotherapy prior to making the surgical incision if it has been ≥2 hours since the last dose.
- Continue monotherapy for a minimum of 3 days in children with complicated appendicitis.
- If the patient has a penicillin allergy or the intraoperative culture shows *Pseudomonas*, use/change to PO ciprofloxacin and metronidazole.
- Discontinue antibiotic therapy at discharge once clinical discharge criteria are met (afebrile, tolerating regular diet, pain controlled with oral pain medications, ambulating, and benign abdominal physical exam with no tenderness and mass).
- Postoperative antibiotics are unnecessary in children with simple appendicitis.

# Postoperative Imaging and Procedures – Complicated Appendicitis <sup>(35)</sup>

- Perform US at 6-7-days postoperatively to rule out abscess in patients with complicated appendicitis, if clinical suspicion for abscess.
- Drain localized fluid collection if estimated size ≥4 cm.

# Discharge Criteria

- Afebrile
- Tolerating regular diet
- Pain controlled with oral pain medications
- Benign abdominal physical exam (no tenderness/mass)
- Ambulating

# Consults/Referrals

- Consult Surgery for a PAS ≥8 or proven appendicitis.
- Consult IR for abscess confirmation.
- Consult Infectious Disease if complicated intra-abdominal abscess(es), recurrent abscess or multiple drains, prolonged length of stay.
- Request to see Child Life for coping techniques, procedural teaching, and psychosocial support.
- Request to see Nutritional Support for dietary modifications related to surgery and healing.

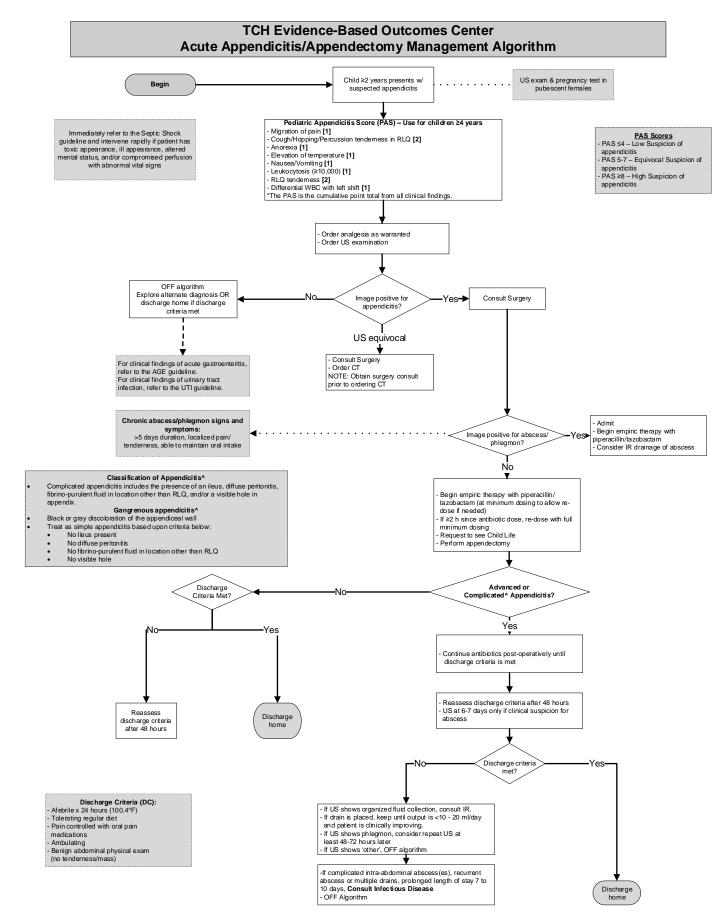
# <u>Measures</u>

### Process

- Perforation rates noting ED admit time, time at which diagnosis was made, and time of surgery
- Appropriateness of antibiotic therapy
- Diagnostic accuracy (sensitivity, specificity) of US and CT
- BMI of children who received CT
- Indication for ordering CT
- Frequency of lab orders for diagnostic purposes where the PAS is 5-7
- Frequency of radiologic studies in patients where the PAS is 1-4 or ≥8
- Percentage of CT scans to rule out abscess in patients with complicated appendicitis
- Percentage of undrainable collections found when imaging to rule out abscess at 6 days or 7 days

# Outcome

- Return visit within 24 hours of previous ED visit
- Length of stay (ED, Inpatient and Special Care)
  Readmission rate for postoperative complications within 30
- Readmission rate for postoperative complications within 30 days
- Complications (negative appendectomy, abscess, and wound infection)
- Percentage of patients experiencing any moderate or severe pain in the first 3 postoperative days
- Percentage of patients experiencing >1 episode of moderate or severe pain on any of the first 3 postoperative days



#### **References**

- 1. Humes, D. J., & Simpson, J. (2007). Acute appendicitis. BMJ, 333(7567), 530-534.
- 2. DynaMed Editorial Team. Appendicitis. Last Updated: October 22, 2007: 1-25.
- 3. Newman, K., Ponsky, T., Kittle, K., Dyk, L., Throop, C., Gieseker, K., et al. (2003). Appendicitis 2000: Variability in practice, outcomes, and resource utilization at thirty pediatric hospitals. *Journal of Pediatric Surgery*, *38*(3), 372-379.
- 4. Morrow, S. E., & Newman, K. D. (2007). Current management of appendicitis. Seminars in Pediatric Surgery, 16(1), 34-40.
- 5. Kwok, M. Y., Kim, M. K., & Gorelick, M. H. (2004). Evidence-based approach to the diagnosis of appendicitis in children. *Pediatric Emergency Care,* 20(10), 690-698.
- 6. National Institute of Diabetes and Digestive and Kidney Diseases, National Digestive Diseases Clearinghouse, NIH. (2004). Appendicitis.
- American Pediatric Surgical Association. Resources: Appendicitis. Adapted from: O'Neill, J., Grosfeld, J., & Fonkalsrud, E. (2003). Principles of Pediatric Surgery, Mosby.
- 8. American Heart Association & American Academy of Pediatrics. (2016). Pediatric Advanced Life Support: Provider Manual. Dallas, TX: American Heart Association.
- Bundy, D. G., Byerley, J. S., Liles, E. A., Perrin, E. M., Katznelson, J., & Rice, H. E. (2007). Does this child have appendicitis? JAMA, 298(4), 438-451.
- Goldman, R. D., Carter, S., Stephens, D., Antoon, R., Mounstephen, W., & Langer, J. C. (2008). Prospective validation of the Pediatric Appendicitis Score. Journal of Pediatrics, 153(2), 278-282
- 11. Bhatt, M., Joseph, L., Ducharme, F. M., Dougherty, G., & McGillivray, D. (2009). Prospective validation of the Pediatric Appendicitis Score in a Canadian pediatric emergency department. *Academic Emergency Medicine, 16*(7), 591-596.
- 12. Samuel, M. (2002). Pediatric appendicitis score. Journal of Pediatric Surgery, 37(6), 877-881
- 13. Lintula, H., Kokki, H., Kettunen, R., & Eskelinen, M. (2009). Appendicitis score for children with suspected appendicitis. A randomized clinical trial. Langenbeck's Archives of Surgery, 394(6), 999-1004.
- 14. Kwan, K. Y., & Nager, A. L. (2010). Diagnosing pediatric appendicitis: Usefulness of laboratory markers. The American Journal of Emergency Medicine, 28(9), 1009-1015.
- Krishnamoorthi, R., Ramarajan, N., Wang, N. E., Newman, B., Rubesova, E., Mueller, C. M., et al. (2011). Effectiveness of a staged US and CT protocol for the diagnosis of pediatric appendicitis: Reducing radiation exposure in the age of ALARA. *Radiology*, 259(1), 231-239.
- Andersson, R. E., & Petzold, M. G. (2007). Nonsurgical treatment of appendiceal abscess or phlegmon: A systematic review and meta-analysis. Annals of Surgery, 246(5), 741-748
- 17. Tsao, K., St. Peter, S. D., Valusek, P. A., Spilde, T. L., Keckler, S. J., Nair, A., et al. (2008). Management of pediatric acute appendicitis in the computed tomographic era. *Journal of Surgical Research*, 147(2), 221-224.
- 18. van Randen, A., Bipat, S., Zwinderman, A. H., Ubbink, D. T., Stoker, J., & Boermeester, M. A. (2008). Acute appendicitis: Meta-analysis of diagnostic performance of CT and graded compression US related to prevalence of disease. *Radiology*, 249(1), 97-106.
- Ramarajan, N., Krishnamoorthi, R., Barth, R., Ghanouni, P., Mueller, C., Dannenburg, B., et al. (2009). An interdisciplinary initiative to reduce radiation exposure: Evaluation of appendicitis in a pediatric emergency department with clinical assessment supported by a staged ultrasound and computed tomography pathway. Academic Emergency Medicine, 16(11), 1258-1265.
- Schuh, S., Man, C., Cheng, A., Murphy, A., Mohanta, A., Moineddin, R., et al. (2011). Predictors of non-diagnostic ultrasound scanning in children with suspected appendicitis. *Journal of Pediatrics*, 158(1), 112-118.
- Brenner, D., Elliston, C., Hall, E., & Berdon, W. (2001). Estimated risks of radiation-induced fatal cancer from pediatric CT. American Journal of Roentgenology, 176(2), 289-296.
- 22. Dilley, A., Wesson, D., Munden, M., Hicks, J., Brandt, M., Minifee, P., et al. (2001). The impact of ultrasound examinations on the management of children with suspected appendicitis: A 3-year analysis. *Journal of Pediatric Surgery*, 36(2), 303-308.
- 23. Kharbanda, A. B., Fishman, S. J., & Bachur, R. G. (2008). Comparison of pediatric emergency physicians' and surgeons' evaluation and diagnosis of appendicitis. Academic Emergency Medicine, 15(2), 119-125.
- 24. Simon, P., Burkhardt, U., Sack, U., Kaisers, U. X., & Muensterer, O. J. (2009). Inflammatory response is no different in children randomized to laparoscopic or open appendectomy. Journal of Laparoendoscopic & Advanced Surgical Techniques, 19, s71-s76.
- Schmelzer, T. M., Rana, A. R., Walters, K. C., Norton, H. J., Bambini, D. A., & Heniford, B. T. (2007). Improved outcomes for laparoscopic appendectomy compared with open appendectomy in the pediatric population. *Journal of Laparoendoscopic & Advanced Surgical Techniques*, 17(5), 693-697.
- 26. Kaselas, C., Molinaro, F., Lacreuse, I., & Becmeur, F. (2009). Postoperative bowel obstruction after laparoscopic and open appendectomy in children: a 15-year experience. *Journal of Pediatric Surgery, 44*(8), 1581-1585.
- Kouhia, S. T., Heiskanen, J. T., Huttunen, R., Ahtola, H. I., Kiviniemi, V. V., & Hakala, T. (2010). Long-term follow-up of a randomized clinical trial of open versus laparoscopic appendicectomy. *British Journal of Surgery*, 97(9), 1395-1400.
- 28. Markides, G., Subar, D., & Riyad, K. (2010). Laparoscopic versus open appendectomy in adults with complicated appendicitis: Systematic review and meta-analysis. *World Journal of Surgery, 34*(9), 2026-2040.
- 29. Sutters, K. A., Miaskowski, C., Holdridge-Zeuner, D., Waite, S., Paul, S. M., Savedra, M. C., et al. (2005). Time-contingent dosing of an opioid analgesic after tonsillectomy does not increase moderate-to-severe side effects in children. *Pain Management Nursing*, 6(2), 49-57.
- Sutters, K. A., Miaskowski, C., Holdridge-Zeuner, D., Waite, S., Paul, S. M., Savedra, M. C., et al. (2010). A randomized clinical trial of the efficacy of scheduled dosing of acetaminophen and hydrocodone for the management of postoperative pain in children after tonsillectomy. *Clinical Journal of Pain*, 26(2), 95-103.
- 31. Andersen BR, Kallehave FL, Andersen HK. Antibiotics versus placebo for prevention of postoperative infection after appendicectomy. *Cochrane Database of Systematic Reviews*, 2005(3), CD001439.
- Goldin, A. B., Sawin, R. S., Garrison, M. M., Zerr, D. M., & Christakis, D. A. (2007). Aminoglycoside-based triple-antibiotic therapy versus monotherapy for children with ruptured appendicitis. *Pediatrics*, 119(5), 905-911.
- 33. St. Peter, S. D., Little, D. C., Calkins, C. M., Murphy, J. P., Andrews, W. S., Holcomb Iii, G. W., et al. (2006). A simple and more cost-effective antibiotic regimen for perforated appendicitis. *Journal of Pediatric Surgery*, *41*(5), 1020-1024.
- Taylor, E., Berjis, A., Bosch, T., Hoehne, F., & Ozaeta, M. (2004). The efficacy of postoperative oral antibiotics in appendicitis: A randomized prospective double-blinded study. American Surgeon, 70(10), 858-862.
- 35. Ein, S. H., Wales, P., Langer, J. C., & Daneman, A. (2008). Is there a role for routine abdominal imaging in predicting postoperative intraabdominal abscess formation after appendectomy for pediatric ruptured appendix? *Pediatric Surgery International*, 24(3), 307-309.
- Kumar, R. R., Kim, J. T., Haukoos, J. S., Macias, L. H., Dixon, M. R., Stamos, M. J., et al. (2006). Factors affecting the successful management of intra-abdominal abscesses with antibiotics and the need for percutaneous drainage. *Diseases of the Colon & Rectum*, 49(2), 183-189.
- Piper, H. G., Derinkuyu, B., Koral, K., Perez, E. A., & Murphy, J. T. (2011). Is it necessary to drain all postoperative fluid collections after appendectomy for perforated appendicitis? *Journal of Pediatric Surgery*, 46(6), 1126-1130.
- Serour, F., Herman, A., Witzling, M., Gorenstein, A., & Dalal, L. (2009). Sonographic findings following appendectomy for uncomplicated appendicitis in children. *Pediatric Radiology*, 39(9), 926-932.

- Acker, S. N., Hurst, A. L., Bensard, D. D., Schubert, A., Dewberry, L., et al. (2016). Pediatric appendicitis and need for antibiotics at time of discharge: Does route of administration matter? *Journal of Pediatric Surgery*, 51(7), 1170-1173.
- 40. Desai, A. A., Alemayehu, H., Holcomb, G. W., 3rd, & St Peter, S. D. (2015). Safety of a new protocol decreasing antibiotic utilization after
- laparoscopic appendectomy for perforated appendicitis in children: A prospective observational study. *Journal of Pediatric Surgery*, *50*(6), 912-914. 41. Loux, T. J., Falk, G. A., Burnweit, C. A., Ramos, C., Knight, C., & Malvezzi, L. (2016). Early transition to oral antibiotics for treatment of perforated
- appendicitis in pediatric patients: Confirmation of the safety and efficacy of a growing national trend. *Journal of Pediatric Surgery*, *51*(6), 903-907.
  42. Robinson, J. R., Avritscher, E. B. C., Gay, J. C., Willis, Z. I., Putnam, L. R., et al. 2017). Measuring the value of a clinical practice guideline for children with perforated appendicitis. *Annals of Surgery*, *266*(1), 195-200.
- Shbat, L., Emil, S., Elkady, S., Baird, R., Laberge, J. M., et al. (2014). Benefits of an abridged antibiotic protocol for treatment of gangrenous appendicitis. *Journal of Pediatric Surgery*, 49(12), 1723-1725.
- 44. Willis, Z. I., Duggan, E. M., Bucher, B. T., Pietsch, J. B., Milovancev, M., et al. (2016). Effect of a clinical practice guideline for pediatric complicated appendicitis. *JAMA Surgery*, 151(5), e160194.
- 45. Bailey, B., Bergeron, S., Gravel, J., Bussières, J.-F., & Bensoussan, A. (2007). Efficacy and impact of intravenous morphine before surgical consultation in children with right lower quadrant pain suggestive of appendicitis: A randomized controlled trial. *Annals of Emergency Medicine*, 50(4), 371-378.
- 46. Green, R., Bulloch, B., Kabani, A., Hancock, B. J., & Tenenbein, M. (2005). Early analgesia for children with acute abdominal pain. *Pediatrics*, 116(4), 978-983.
- 47. Kim, M. K., Strait, R. T., Sato, T. T., & Hennes, H. M. (2002). A randomized clinical trial of analgesia in children with acute abdominal pain. Academic Emergency Medicine, 9(4), 281-287.
- Kokki, H., Lintula, H., Vanamo, K., Heiskanen, M., & Eskelinen, M. (2005). Oxycodone vs placebo in children with undifferentiated abdominal pain: A randomized, double-blind clinical trial of the effect of analgesia on diagnostic accuracy. Archives of Pediatrics & Adolescent Medicine, 159(4), 320-325.
- 49. Amoli, H. A., Golozar, A., Keshavarzi, S., Tavakoli, H., & Yaghoobi, A. (2008). Morphine analgesia in patients with acute appendicitis: A randomised double-blind clinical trial. *Emergency Medicine Journal*, 25(9), 586-589.
- 50. Yong, Y., Jia-yong, C., Hao, G., Yi, Z., Dao-ming, L., Dong, Z., et al. (2010). Relief of abdominal pain by morphine without altering physical signs in acute appendicitis. Chinese Medicine Journal, 123(2), 142-145.
- Akingboye, A., Davies, B., & Tien, T. (2019). Pus samples in complicated appendicitis: An important investigation or a waste of resources: A prospective cohort study. Scandinavian Journal of Surgery, 108(1), 55-60.
- 52. Dahlberg, M., Almstrom, M., Wester, T., & Svensson, J. (2019). Intraoperative cultures during appendectomy in children are poor predictors of pathogens and resistance patters in cultures from postoperative abscesses. Pediatric Surgery International, 35, 341-346.
- 53. Kenig, J., & Richter, P. (2013). The need for culture swabs in laparoscopically treated appendicitis. Videosurgery Miniinv 8(4), 310-314.
- 54. Montuori, M., Santurro, L., Gianotti, L., & Fattori, L. (2020). Uselessness of microbiological samples in acute appendicitis with frank pus: To collect or not to collect? European Journal of Trauma and Emergency Surgery, 46, 835-839.
- 55. Pena, M., Sadava, E., Laxague, F., & Schlottmann, F. (2020). Usefulness of intraoperative culture swabs in laparoscopic appendectomy for complicated appendicitis. Langenbecks Arch Surg, 405(5), 691-695.
- 56. Tack Son, J., Chun Lee, G., Ook Kim, H., Kim, T., Lee, D., Ryol Lee, S., Uk Jung, K., Kim, H., & Chun, H. (2020). Routine intraoperative bacterial culture may be needed in complicated appendicitis. Ann Coloproctol, 36(3), 155-162.
- 57. Aslan, A., Karaveli, Ç., Ogunc, D., Elpek, O., Karaguzel, G., & Melikoglu, M. (2007). Does noncomplicated acute appendicitis cause bacterial translocation? *Pediatric Surgery International*, 23(6), 555-558.
- Helmer, K. S., Robinson, E. K., Lally, K. P., Vasquez, J. C., Kwong, K. L., Liu, T. H., et al. (2002). Standardized patient care guidelines reduce infectious morbidity in appendectomy patients. *American Journal of Surgery*, 183(6), 608-613.
- 59. Acharya, A., Markar, S. R., Ni, M., & Hanna, G. B. (2017). Biomarkers of acute appendicitis: systematic review and cost-benefit trade-off analysis. Surgical Endoscopy, 31(3), 1022-1031.
- 60. Yang, S. K., Xiao, L., Zhang, H., Xu, X. X., Song, P. A., et al. (2014). Significance of serum procalcitonin as biomarker for detection of bacterial peritonitis: a systematic review and meta-analysis. *BMC Infectious Diseases, 14*, 452.
- Slieker, J. C., Aellen, S., Eggimann, P., Guarnero, V., Schafer, M., & Demartines, N. (2017). Procalcitonin-guided antibiotics after surgery for peritonitis: A randomized controlled study. *Gastroenterology Research and Practice*, 2017, 3457614.
- Fallon, S. C., Brandt, M. L., Hassan, S. F., Wesson, D. E., Rodriguez, J. R., & Lopez, M. E. (2013). Evaluating the effectiveness of a discharge protocol for children with advanced appendicitis. *Journal of Surgical Research*, 184(1), 347-351.
- 63. Huang, T. S., Huang, S. S., Shyu, Y. C., Lee, C. H., Jwo, S. C., et al. (2014). A procalcitonin-based algorithm to guide antibiotic therapy in secondary peritonitis following emergency surgery: a prospective study with propensity score matching analysis. *PLoS One, 9*(3), e90539.
- 64. Aprahamian, C. J., Barnhart, D. C., Bledsoe, S. E., Vaid, Y., & Harmon, C. M. (2007). Failure in the nonoperative management of pediatric ruptured appendicitis: Predictors and consequences. *Journal of Pediatric Surgery, 42*(6), 934-938.
- 65. Ein, S. H., Langer, J. C., & Daneman, A. (2005). Nonoperative management of pediatric ruptured appendix with inflammatory mass or abscess: Presence of an appendicolith predicts recurrent appendicitis. *Journal of Pediatric Surgery*, 40(10), 1612-1615.
- 66. Puapong, D., Lee, S. L., Haigh, P. I., Kaminski, A., Liu, I.-L. A., & Applebaum, H. (2007). Routine interval appendectomy in children is not indicated. *Journal of Pediatric Surgery, 42*(9), 1500-1503.
- 67. Raval, M. V., Lautz, T., Reynolds, M., & Browne, M. (2010). Dollars and sense of interval appendectomy in children: A cost analysis. *Journal of Pediatric Surgery*, 45(9), 1817-1825.
- 68. Shindoh, J., Niwa, H., Kawai, K., Ohata, K., Ishihara, Y., Takabayashi, N., et al. (2010). Predictive factors for negative outcomes in initial nonoperative management of suspected appendicitis. *Journal of Gastrointestinal Surgery*, *14*(2), 309-314.
- 69. Samuel, M., Hosie, G., & Holmes, K. (2002). Prospective evaluation of nonsurgical versus surgical management of appendiceal mass. *Journal of Pediatric Surgery*, 37(6), 882-886.
- Simillis, C., Symeonides, P., Shorthouse, A. J., & Tekkis, P. P. (2010). A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). Surgery, 147(6), 818-829.
- St. Peter, S. D., Aguayo, P., Fraser, J. D., Keckler, S. J., Sharp, S. W., Leys, C. M., et al. (2010). Initial laparoscopic appendectomy versus initial nonoperative management and interval appendectomy for perforated appendicitis with abscess: A prospective, randomized trial. *Journal of Pediatric Surgery*, 45(1), 236-240.
- 72. York, D., Smith, A., Phillips, J. D., & von Allmen, D. (2005). The influence of advanced radiographic imaging on the treatment of pediatric appendicitis. *Journal of Pediatric Surgery, 40*(12), 1908-1911.
- 73. Williams, D. G., Patel, A., & Howard, R. F. (2002). Pharmacogenetics of codeine metabolism in an urban population of children and its implications for analgesic reliability. *British Journal of Anaesthesia, 89*(6), 839-845.
- 74. Voronov, P., Przybylo, H. J., & Jagannathan, N. (2007). Apnea in a child after oral codeine: A genetic variant an ultra-rapid metabolizer. *Pediatric Anesthesia*, *17*(7), 684-687.
- 75. Gasche, Y., Daali, Y., Fathi, M., Chiappe, A., Cottini, S., Dayer, P., et al. (2004). Codeine intoxication associated with ultrarapid CYP2D6 metabolism. *New England Journal of Medicine, 351*(27), 2827-2831.

- 76. Solomkin, J. S., Mazuski, J. E., Bradley, J. S., Rodvold, K. A., Goldstein, E. J. C., Baron, E. J., et al. (2010). Diagnosis and management of complicated intra-abdominal infection in adults and children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Surgical Infections, 11(1), 79-109.
  77. Snydman, D. R., Jacobus, N. V., McDermott, L. A., Golan, Y., Hecht, D. W., Goldstein, E. J., et al. (2010). Lessons learned from the anaerobe
- survey: Historical perspective and review of the most recent data (2005-2007). Clinical Infectious Diseases, 50(Suppl 1), S26-S33.

### **Clinical Standards Preparation**

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

#### Appendicitis Content Expert Team

Melissa Ard, Clinical Data Specialist, Surgery Sanjeev Ayyangar Vasudevan, MD, Surgery Charlene Barclay, Clinical Data Specialist, Surgery Valentina Briceno Marmol, Nursing, Surgery Eric Choy, MD, Pediatric Hospital Medicine Celia Flores, APP, West Campus Jose Hernandez, MD, Radiology Stephanie McGee, PA, Woodlands Campus Julie McManemy, MD, Emergency Medicine Debra Palazzi, MD, Infectious Disease Vipul Parikh, MD, Pediatric Hospital Medicine Krista Preisberga, MD, Pediatric Hospital Medicine Ruben Rodriguez, MD, Surgery Marla Sammer, MD, Radiology Yan Shi, MD, Surgery Ellen Thompson, APP, Main Campus Veronica Victorian, APP, Surgery

#### EBOC Team

Andrea Jackson, MBA, RN, Evidence-Based Practice Specialist Binita Patel, MD, Chief Medical Quality Officer

#### Additional EBOC Support

Betsy Lewis, MSN, RN, CNL, Evidence-Based Practice Specialist Sheesha Porter, MS, RN, Evidence-Based Practice Specialist Anne Dykes, MSN, RN, Manager

#### **Development Process**

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

- 1. Review Preparation
  - PICO questions established
  - Evidence search confirmed with content experts
- 2. Review of Existing External Guidelines
  - Cincinnati Children's Hospital Emergency Appendectomy, BMJ Clinical Evidence on Appendicitis, American College of Emergency Physicians Clinical Policy: Critical Issues in the Evaluation and Management of Emergency Department Patients with Suspected Appendicitis, Surgical Infection Society and Infectious Disease Society of America Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children, Therapeutic Agents Committee of the Surgical Infection Society Guidelines on Antimicrobial Therapy for Children with Appendicitis, International Pediatric Endosurgery Group Guidelines for Appendectomy
- 3. Literature Review of Relevant Evidence
  - Searched: Searched: Cochrane, PubMed, CINHAL, Google Scholar, ProQuest, and SumSearch
- 4. Critically Analyze the Evidence
  - 9 systematic reviews, 21 randomized controlled trials, and 39 nonrandomized studies
- 5. Summarize the Evidence
- Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in an appendicitis/appendectomy evidence-based review manual within EBOC.

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in* support of or against specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions. *"Evidence Supports"* provides evidence to support an intervention *"Evidence Against"* provides evidence against an intervention. *"Evidence Lacking/Inconclusive"* indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

| Recommendation |   |
|----------------|---|
| STRONG         | Desirable effects clearly outweigh undesirable effects or vice versa  |
| WEAK           | Desirable effects closely balanced with undesirable effects   |
| Quality        | Type of Evidence  |
| High           | Consistent evidence from well-performed RCTs or<br>exceptionally strong evidence from unbiased<br>observational studies   |
| Moderate       | Evidence from RCTs with important limitations (e.g.,<br>inconsistent results, methodological flaws, indirect<br>evidence, or imprecise results) or unusually strong<br>evidence from unbiased observational studies |
| Low            | Evidence for at least 1 critical outcome from<br>observational studies, RCTs with serious flaws or<br>indirect evidence   |
| Very Low       | Evidence for at least 1 critical outcome from<br>unsystematic clinical observations or very indirect<br>evidence  |

#### **Recommendations**

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies regarding appendicitis/appendectomies in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

### **Approval Process**

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

#### **Disclaimer**

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) <u>do not</u> set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

| Version History |  |  |
|-----------------|--|--|
| Date            | Comments   |  |
| Jan 2012        | Originally completed   |  |
| Apr 2015        | Addendum for postoperative management of<br>complicated appendicitis; remainder of guideline<br>reaffirmed |  |
| Mar 2018        | Removed TPN recommendation and clarified<br>algorithm wording for complicated appendicitis                 |  |
| July 2018       | Added two PICO questions, updated algorithm,<br>archived original question                                 |  |
| Jan 2019        | Revised the 'Vital Sign Changes of Sepsis' table   |  |
| Feb 2023        | Guideline Update   |  |