EVIDENCE-BASED
CLINICAL PRACTICE GUIDELINES
ON THE DIAGNOSIS AND TREATMENT OF
ACUTE APPENDICITIS

Authors:
Domingo S. Bongala, Jr., MD, FPCS
Rey Melchor F. Santos, MD, FPCS
Mario M. Panaligan, MD, FPSMID
Ferdinand E. Cercenia. MD, FPCS
Alberto A. Paulino, MD, FPCS
Isaac David E. Ampil II, MD, FPCS
Jose D. Quebral, MD, FPCS
Antonio L. Anastacio, MD, FPCS

For the

MESSAGE

It is finally out!

The Evidence-Based Clinical Practice Guidelines on Acute Appendicitis was prepared to serve as helpful tips for surgeons in the diagnosis and treatment of the most common emergency surgical condition.

The members of the Committee on Surgical Infections worked for half a year to ensure that these guidelines will measure up to international standards. The sheer volume of materials they reviewed and the many consultations they made are proof of their dedication and commitment.

The Philippine College of Surgeons shall forever be indebted to these fellows who unselfishly gave their precious time and talent to accomplish these guidelines that we can all be proud of.

Likewise, the College thanks all those who participated and contributed in one way or another in making this endeavor a reality.

FERNANDO L. LOPEZ, MD, FPCS
President

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INTRODUCTION

Acute appendicitis is the most common surgical emergency of the abdomen while appendectomy is one of the most frequently performed surgical procedures. Quite fortunately, the mortality rate particularly from perforated appendicitis has improved from near certain death a century ago to 10-20 per cent 50 years ago, 5 per cent during the 1960s and 1 per cent or less from the 1970s to the present. The morbidity rate, however, remains significant especially with appendiceal rupture where the incidence ranges from 17 per cent to 40 per cent with a median of 20 per cent. To reduce the incidence of perforation, the surgical community traditionally accepts that approximately 15 per cent of appendectomies over-all and 20 per cent in women will yield a non-inflamed appendix. In certain populations of patients, the rate of misdiagnosis may even reach 40 per cent.

Despite gaining a century of clinical experience with acute appendicitis however, the rates of unnecessary appendectomies and perforation have remained relatively high. The dramatic expansion of diagnostic testing options and the introduction of innovative surgical approaches during the last decade has actually caused even more debate and disagreement than resolution of issues.

In an attempt to better define the appropriate roles of the available diagnostic modalities and to formulate an efficient and cost-effective management scheme, the Philippine College of Surgeons through the Committee on Surgical Infections decided to formulate these "Evidence-Based Clinical Practice Guidelines on the Diagnosis and Treatment of Acute Appendicitis." It is hoped that the application of this set of standards will be rewarded with a marked decrease in morbidity rates. With the proper use of the recommended ancillary diagnostic tests and management strategies, surgeons should be able to realize a steady improvement in the balance between the two primary adverse outcomes in the management of appendicitis, that is, a low rate of misdiagnosis or negative laparotomies coupled with a reduced incidence of perforation.

The clinical practice guidelines to be presented herein are statements that bring together the best clinical evidence and other knowledge necessary for decision-making in the diagnosis and treatment of acute appendicitis. They were formulated to identify the most efficacious interventions in order to maximize the benefits for individual patients.

These guidelines, however, must be integrated with the surgeon's clinical expertise in deciding whether and how they match their patient's clinical state, predicament and preferences. The guidelines build on and reinforce the surgeon's clinical skills, judgment and experience. Guidelines are intended to inform, but can never replace, individual clinical expertise and it is this expertise that decides whether the guidelines apply to a particular patient and how the guidelines should be integrated into the clinical decision-making process.

To further ensure the validity of the recommendations and to prevent any bias that would appear to favor a pharmaceutical company, the Philippine College of Surgeons invited surgeons, internists and pediatricians who were not employed by any drug firm to comprise the technical working group and the panel of experts. The extent of participation of our friends from the pharmaceutical industry was likewise limited to their assistance with respect to technical matters.

The following clinical questions were addressed by the guidelines:
1. When should one suspect acute appendicitis?
2. What clinical findings are most helpful in diagnosing acute appendicitis?
3. What diagnostic tests are helpful in the diagnosis of acute appendicitis?
4. What is the appropriate treatment for acute appendicitis?
5. What is the recommended approach to the surgical management of acute appendicitis?
6. What is the role of laparoscopic appendectomy in the management of acute appendicitis in children?
7. What is the role of antibiotics in the management of acute appendicitis?
    a. Is antibiotic prophylaxis indicated for uncomplicated appendicitis?
    b. What antibiotic/s is/are recommended for prophylaxis in uncomplicated appendicitis an what is the appropriate dose and route of administration?
    c. What antibiotic/s is/are recommended for the treatment of complicated appendicitis and what is the appropriate dose, route and duration of administration?
8. Should gram stain and culture and sensitivity be routinely done in acute appendicitis?
9. How should localized peritonitis be managed?
10. What is the appropriate method of wound closure in patients with complicated appendicitis?
11. What is the optimal timing of surgery for patients with periappendiceal abscess?

METHODS

The Technical Working Group was composed of:
1. Domingo S. Bongala Jr., MD, FPCS – Chairman
2. Isaac David E. Ampil II, MD, FPCS
3. Antonio L. Anastacio, MD, FPCS
4. Ferdinand E. Cercenia, MD, FPCS
5. Mario M. Panaligan, MD, FPCP, FPSMID
6. Alberto A. Paulino, MD, FPCS
7. Jose D. Quebral, MD, FPCS
8. Rey Melchor F. Santos, MD, FPCS – Regent-in-Charge

A search of publications was carried out using a sensitive search strategy combining MESH and free text searches. This strategy included an extensive search of the following databases:
1. Medline (1966 to present)
2. Cochrane Library (2002 issue 2)
3. Health Research and Development Network (Herdin)
4. Phil. Journal of Surgical Specialties CD-ROM (1975 to 1999) and hand searches from 2000 to the present

From the search results, the Technical Working Group (TWG) selected relevant articles for full-text retrieval using the Nominal Group Technique. Retrieved studies were then assessed for eligibility according to the criteria set by the guideline developers. The methodologic quality of the studies was appraised by two independent reviewers using a quality assessment instrument developed by the Philippine Cardiovascular Research Group.

The pertinent results of the selected articles as based on the clinical questions were summarized and compared. When appropriate and where relevant data were available, the sensitivities, specificities, accuracies, predictive values and likelihood ratios, including the 95 per cent confidence intervals were calculated for diagnostic articles; the relative risks, risk differences, and the number needed to treat (NNT) were computed and compared for articles on therapy.

The clinical evidence was then rated according to the assessment system of the Infectious Disease Society of America:

Level I – Evidence from at least one properly designed randomized controlled trial or meta-analysis

Level II - Evidence from at least one well-designed clinical trial without proper randomization, from cohort or case-controlled analytic studies (preferably from one center), from multiple time-series, or from dramatic results in uncontrolled experiments

Level III- Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees

The members of the Technical Working Group prepared the evidence-based report based on the articles retrieved and appraised. A total of 832 article titles with abstracts were retrieved by the electronic literature search. After evaluation and validity appraisal, 68 articles were chosen and used to answer the clinical questions. The TWG then held several meetings to discuss each clinical question and the corresponding evidence, formulate the initial recommendations and thereafter reach a consensus utilizing the Nominal Group Technique. A consensus was reached after having attained 70 per cent agreement among the members of the TWG.

The TWG together with the panel of experts reviewed the interim report during the Surgical Infection Forum held at the Fontana Leisure Park, Clark Special Economic Zone, Pampanga on November 24, 2002. Each clinical question, the evidence and the recommendations were analyzed and the participants given the opportunity to express their opinions and views. The modified Delphi Technique was then used to determine the degree of consensus regarding the recommendations.

The panel of experts included Drs. Dexter S. Aison, Isaac David E. Ampil II, Ma. Luisa D. Aquino, Antonio L. Anastacio, Romarico M. Azores Jr., Gyneth Bibera, Domingo S. Bongala Jr., Ferdinand E. Cercenia, Edgardo R. Cortez, Leonardo A. Cua, Daniel A. de la Paz, Arturo S. de la Pena, Raymund Joaquin F. Erese, Henry G. Falcotelo, Amado M. Lavalle Jr., Gabriel L. Martinez, Arturo E. Mendoza Jr., Narciso S. Navarro, Jr., Mario Panaligan, Enrico P. Ragaza, Francisco DJ. Sales III, Rey Melchor F. Santos, Stephen S. Siguan and Kim Shi C. Tan.

The strength of the recommendations for the guidelines was categorized according to the level of agreement of the panel of experts after a votation of the participants:

Category A – Recommendations that were approved by consensus (at least 75 per cent of the multi-sectoral expert panel)

Category B - Recommendations that were somewhat controversial and did not meet consensus

Category C – Recommendations that caused real disagreements among the members of the panel

The draft guidelines were then presented to the stakeholders during the Philippine College of Surgeons Annual Convention held at the EDSA Shangri-la Hotel, Mandaluyong City on December 4, 2002. The invited participants included practicing surgeons and representatives from the pharmaceutical companies and concerned government agencies.

The Evidence-Based Clinical Practice Guidelines on the Diagnosis and Treatment of Acute Appendicitis was then submitted to the 2003 PCS Board of Regents for final approval in February 2003.

OPERATIONAL DEFINITIONS

Uncomplicated Appendicitis - includes the acutely inflamed, phlegmonous, suppurative, or mildly inflamed appendix with or without peritonitis

Complicated Appendicitis - includes gangrenous appendicitis, perforated appendicitis, localized purulent collection at operation, generalized peritonitis and periappendiceal abscess

Equivocal Appendicitis – a patient with right lower quadrant abdominal pain who presents with an atypical history and physical examination and the surgeon cannot decide whether to discharge or to operate on the patient

EXECUTIVE SUMMARY

When should one suspect acute appendicitis?

Consider the diagnosis of acute appendicitis when a patient presents with right lower quadrant abdominal pain.

LEVEL III EVIDENCE
CATEGORY A RECOMMENDATION

What clinical findings are most helpful in diagnosing acute appendicitis?

Acute appendicitis should be suspected in any patient (especially male) who presents with a high intensity of perceived abdominal pain of at least 7-12 hours duration, with migration to the right lower quadrant, and followed by vomiting.

Although symptoms alone have a low discriminating power, the diagnosis of acute appendicitis becomes more certain when the physical examination findings include right lower quadrant tenderness, guarding, rebound tenderness and other signs of peritoneal irritation.

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

What diagnostic tests are helpful in the diagnosis of acute appendicitis?

Although the diagnosis of acute appendicitis is primarily based on the clinical findings, the following examinations may be helpful:
>   A. All Cases
>   1.White blood cell with differential count
>   **LEVEL I EVIDENCE**
>   **CATEGORY A RECOMMENDATION**
>   B. Equivocal Appendicitis in Adults
>   1. CT scan
>   2. Ultrasound

Whenever feasible, CT scan should be preferred over ultrasonography in clinically equivocal appendicitis in adults because of its superior accuracy.

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

C. Equivocal Appendicitis in the Pediatric Age Group
      1. Ultrasound (graded compression)
      2. CT scan

Although CT scan and ultrasound have comparable accuracy in the diagnosis of appendicitis in the pediatric age group, ultrasound is preferred because of its lack of radiation, cost-effectiveness and availability compared to CT scan.

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LEVEL II EVIDENCE
CATEGORY A RECOMMENDATION

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D. Selected Cases
      1.Diagnostic Laparoscopy

Despite its statistically significant favorable effects, diagnostic laparoscopy should be viewed as an invasive procedure requiring anesthesia and having risks similar to appendectomy. It should be utilized at this time only in selected cases.

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LEVEL III EVIDENCE
CATEGORY A RECOMMENDATION

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The following examinations are generally not useful in the diagnosis of acute appendicitis:
      1. Plain Abdominal X-ray
      2. Barium Enema
      3. Scintigraphy

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LEVEL II EVIDENCE
CATEGORY A RECOMMENDATION

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What is the appropriate treatment for acute appendicitis?

Appendectomy is the appropriate treatment for acute appendicitis.

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LEVEL II EVIDENCE
CATEGORY A RECOMMENDATION

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What is the recommended approach to the surgical management of acute appendicitis?

Open appendectomy is the recommended primary approach to the treatment of acute appendicitis in our setting. Therapeutic laparoscopic appendectomy is an alternative for selected cases.

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LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

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What is the role of laparoscopic appendectomy in the management of acute appendicitis in children?

Laparoscopic appendectomy may be recommended as an alternative to open appendectomy in the pediatric age group.

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

What is the role of antibiotics in the management of acute appendicitis?

A.   Is antibiotic prophylaxis indicated for uncomplicated appendicitis?

Yes. Antibiotic prophylaxis is effective in the prevention of surgical site infection for patients who undergo appendectomy and should be considered for routine use.

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

B. What antibiotic/s is/are recommended for prophylaxis in uncomplicated appendicitis and what is the appropriate dose and route of administration ?

The following antibiotics are recommended for prophylaxis in uncomplicated appendicitis :

Cefoxitin 2 grams IV single dose (Adults)
40 mg/kg IV single dose (Children)

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

Alternative agents:
Ampicillin-sulbactam 1.5-3 grams IV single dose (Adults)
75 mg/kg IV single dose (Children)

Amoxicillin-clavulanate 1.2 –2.4 grams IV single dose (Adults)
45 mg/kg IV single dose (Children)

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

For patients with allergy to beta-lactam antibiotics:

Gentamicin 80-120 mg IV single dose plus
Clindamycin 600 mg IV single dose (Adults)

Gentamicin 2.5 mg/kg IV single dose plus
Clindamycin 7.5 – 10 mg/kg IV single dose (Children)

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

C. What antibiotic/s is/are recommended for the treatment of complicated appendicitis and what is the appropriate dose, route and duration of administration?

The recommended antibiotics for therapy of complicated appendicitis in adults are
Ertapenem 1 gram IV every 24 hours
Tazobactam-piperacillin 3.375 grams IV every 6 hours or
4.5 grams IV every 8 hours

For adults with beta-lactam allergy:
Ciprofloxacin 400 mg IV every 12 hours plus
Metronidazole 500 mg IV every 6 hours

The recommended antibiotic for therapy of complicated appendicitis in pediatric patients is
Ticarcillin-clavulanic acid 75 mg/kg IV every 6 hours

Alternative agents for pediatric patients include:
Imipenem-Cilastatin 15-25 mg/kg IV every 6 hours

For children with beta-lactam allergy
Gentamicin 5 mg/kg IV every 24 hours plus
Clindamycin 7.5 –10 mg/kg IV every 6 hours

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

For gangrenous appendicitis, the recommended form of management is to treat in the same manner as uncomplicated appendicitis. **(LEVEL II EVIDENCE, CATEGORY A RECOMMENDATION)**

The duration of therapy may vary depending on the clinician's assessment after the operation. The therapy may be maintained for 5-7 days. Sequential therapy to oral antibiotics may be considered when gastrointestinal function has returned. **(LEVEL I EVIDENCE, CATEGORY A RECOMMENDATION)**

The absence of fever for 24 hours (temperature < 38 C), the ability to tolerate oral intake, and a normal WBC count with 3 per cent or less band forms are useful parameters for the discontinuation of antibiotic therapy. **(LEVEL II EVIDENCE, CATEGORY A RECOMMENDATION)**

Should gram stain and culture and sensitivity be routinely done?

Gram stain and culture with sensitivity testing of intra-operative specimens (purulent peritoneal fluid or tissue) should not be routinely performed except in high-risk and immuno-compromised patients.

LEVEL II EVIDENCE
CATEGORY A RECOMMENDATION

How should localized peritonitis be managed?

No necrotic tissue or purulent material should be left behind as much as possible. General peritoneal lavage is not recommended for localized peritonitis. Intra-peritoneal drains, while most useful in patients with a well-established and localized abscess cavity, should be selectively utilized.

LEVEL II EVIDENCE
CATEGORY A RECOMMENDATION

What is the appropriate method of wound closure in patients with complicated appendicitis ?

The incision may be closed primarily in patients with complicated appendicitis.

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

What is the optimal timing of surgery for patients with periappendiceal abscess?

A patient with a peri-appendiceal abscess should undergo surgery as soon as the diagnosis is made.

LEVEL III EVIDENCE
CATEGORY A RECOMMENDATION

<h1 style="text-align:center">PRACTICE GUIDELINES</h1>

When should one suspect acute appendicitis?

Consider the diagnosis of acute appendicitis when a patient presents with right lower quadrant abdominal pain.

LEVEL III EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

The panel of experts feel that delays in diagnosis can be avoided by considering acute appendicitis in the differential diagnosis when examining patients with right lower quadrant abdominal pain. (LEVEL III EVIDENCE)

What clinical findings are most helpful in diagnosing acute appendicitis?

Acute appendicitis should be suspected in any patient (especially male) who presents with a high intensity of perceived abdominal pain of at least 7-12 hours duration, with migration to the right lower quadrant, and followed by vomiting.

Although symptoms alone have a low discriminating power, the diagnosis of acute appendicitis becomes more certain when the physical examination findings include right lower quadrant tenderness, guarding, rebound tenderness and other signs of peritoneal irritation.

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

A prospective study (Andersson 1999) involving 496 patients aged 10-86 years with suspected appendicitis was done to compare the diagnostic value of 21 elements of the history, clinical findings, body temperature and laboratory examinations. The authors found that no single variable had sufficiently high discriminating or predicting power to be used as a true diagnostic test.

Based on disease history, acute appendicitis was more likely in patients over 40 years of age, male, with a history of vomiting, a 7-12 hours duration of symptoms, with a high intensity of the perceived pain, and with a history of migration of pain (Likelihood Ratio of 1.47 to 2.25). Appendicitis was less likely when the intensity of the perceived pain was low, when movements or cough did not provoke pain, or when the duration of symptoms was greater than 48 hours (LR 0.46 to 0.58). However, all elements of the disease history had low power in discriminating for uncomplicated and complicated appendicitis.

Except for the site of tenderness that had an ROC value of 0.66, all elements of the clinical findings had better discriminating power than the history with the ROC values ranging from 0.76 to 0.80. Appendicitis was likely when there was a strong intensity of guarding and rebound tenderness and a moderate intensity of peritoneal irritation (LR 7.45 to 8.06). Appendicitis was likely if the tenderness was distinctly localized over McBurney's point (LR of 2.01; 95% CI 1.58 to 2.56) and less likely if tenderness was found outside the right iliac fossa (LR of 0.35; 95% CI 0.23 to 0.53). Appendicitis was unlikely when abdominal tenderness was absent (LR of 0.10; 95% CI 0.04 to 0.26), if the general condition was normal or if guarding, rebound tenderness or signs of peritoneal irritation were absent (LR of 0.23 to 0.31).

Rectal tenderness is of low or no diagnostic value in acute appendicitis. Right-sided rectal tenderness was found to be slightly more common in patients without appendicitis (35 per cent) than in those with appendicitis (26 per cent).

After analyzing the discriminating power of a combination of variables using multiple logistic regression, the authors found that the clinical findings had, as a group, the highest discriminating power in appendicitis (ROC of 0.87) followed by the inflammatory parameters (ROC of 0.85) and the disease history (ROC of 0.78). They also found that the patient's gender (male with Odds Ratio of 2.81; 95% CI 1.52 to 5.19) and rebound tenderness and abdominal tenderness (Odds Ratio of 26.00; 95% CI 11.83 to 57.12) were 3 of the 6 independent predictors of appendicitis. (LEVEL I EVIDENCE)

A meta-analysis (Wagner 1996) which reported the clinical usefulness of the various signs and symptoms in adults with appendicitis underscored the importance of right lower quadrant pain (positive LR of 8.0), rigidity (positive LR of 3.76), and pain migration from the peri-umbilical area to the right lower quadrant (positive LR of 3.2). Appendicitis was noted to be less likely with a history of previous similar pain (negative LR of 0.3), absence of right lower quadrant pain (negative LR of 0 to 0.28), and absence of classic pain migration (negative LR of 0.5). The presence of vomiting before pain made the diagnosis of appendicitis unlikely. Notably, the absence of anorexia, nausea, and vomiting had little impact on the likelihood of appendicitis. Rebound tenderness varied too widely among studies to accurately assess the effect of a positive test. (LEVEL I EVIDENCE)

A prospective study (Ohmann 1995) involving 1,254 patients was done to evaluate the performance of 10 different diagnostic scoring systems for acute appendicitis on one database using standardized criteria and to compare the results with published data. The authors believed that an adequate scoring system should fulfill the following criteria: a negative appendectomy rate of 15 per cent or less, a potential perforation rate of 35 per cent or less, a missed perforation rate of 15 per cent or less, and a missed appendicitis rate of 5 per cent or less. A re-evaluation of the published data showed that the Alvarado score was the only scoring system that fulfilled all four of these criteria and the Lindberg, the Fenyo

and the Christian scores fulfilled two criteria each. When applied to the database of the study (acute abdominal pain, suspected appendicitis), none of the scores fulfilled any of the given criteria. The authors concluded that the evaluation of the scores using the study's database resulted in poor performances for all of them. (LEVEL II EVIDENCE)

A prospective study (Kalan 1994) was done to assess the accuracy of the Alvarado score in the preoperative diagnosis of appendicitis. While a high score was found to be an easy and satisfactory aid to the early diagnosis of acute appendicitis in children and men, it had a high false-positive rate in women. (LEVEL II EVIDENCE). It is advised however that the clinician exercise caution when using clinical scoring systems as diagnostic aids in appendicitis. Although these diagnostic scores focus attention on pertinent clinical features, there are certain limitations.

What diagnostic tests are helpful in the diagnosis of acute appendicitis?

Although the diagnosis of acute appendicitis is primarily based on the clinical findings, the following examinations may be helpful:

A.   **All Cases**
      1. White blood cell with differential count
                LEVEL I EVIDENCE
                CATEGORY A RECOMMENDATION

B.   **Equivocal Appendicitis in Adults**
      1. CT scan
      2. Ultrasound

Whenever feasible, CT scan should be preferred over ultrasonography in clinically equivocal appendicitis in adults because of its superior accuracy.
                LEVEL I EVIDENCE
                CATEGORY A RECOMMENDATION

C.   **Equivocal Appendicitis in the Pediatric Age Group**
      1. Ultrasound (graded-compression)
      2. CT scan

Although CT scan and ultrasound have comparable accuracy in the diagnosis of acute appendicitis in the pediatric age group, ultrasound is preferred because of its lack of radiation, cost-effectiveness and availability compared to CT scan.

                LEVEL II EVIDENCE
                CATEGORY A RECOMMENDATION

D.   **Selected Cases**
                1.Diagnostic Laparoscopy

        Despite its statistically significant favorable effects, diagnostic laparoscopy should be viewed as an invasive procedure requiring anesthesia and having risks similar to appendectomy. It should be utilized at this time only in selected cases.
                        LEVEL III EVIDENCE
                        CATEGORY A RECOMMENDATION

   The following examinations are generally not useful in the diagnosis of acute
        appendicitis:
                1.Plain Abdominal X-ray
                2.Barium Enema
                3. Scintigraphy
                        LEVEL II EVIDENCE
                        CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

A. ALL CASES

1.   WBC COUNT, POLYMORPHONUCLEAR CELL COUNT AND RATE

        A prospective study (Andersson 1999) involving 496 patients was done to assess the diagnostic value of elements of the laboratory examination for patients with suspected appendicitis. They found that appendicitis was likely at the highest WBC count and polymorphonuclear cell count (PMNC) and rate (WBC count greater than 15 x 10 -9 cells/L, PMNC count greater than 13 x 10 -9 cells/L or PMNC rate greater than 85 per cent with positive LR values of 5.96 to 8.27). On the other hand, appendicitis was unlikely at the lowest levels of WBC count and the PMNC count and rate (WBC count less than 8.0 x 10-9 cells/L, PMNC count less than 7.0 x 10 -9 cells/L or PMNC rate less than 70 per cent with positive LR values of 0.16 to 0.28).

        The authors found that the inflammatory variables had power for discriminating for appendicitis similar to that of the clinical findings and were especially important discriminators for complicated appendicitis. Using multiple logistic regression, three of the six independent predictors of appendicitis were laboratory examinations, namely the WBC count, the PMNC rate and the CRP concentration. After combining these three laboratory examinations with the other three independent predictors of appendicitis (patients' gender, rebound tenderness and abdominal rigidity), the ROC for this model was 0.93 for all appendicitis and 0.95 for complicated appendicitis.

        Although CRP concentration was found to be one of the independent predictors of appendicitis, it is deemed unnecessary because it only had a high power in discriminating for complicated appendicitis (ROC area 0.81) but not for all cases of appendicitis (ROC area 0.70). This is probably because CRP is a late

marker of inflammation so that significant increases in CRP concentration are noted only in complicated appendicitis. (LEVEL I EVIDENCE)

A prospective study (Lau 1989) involving 1,032 patients was done to determine the value of the total leukocyte count and neutrophil percentage in the diagnosis of acute appendicitis. The upper limit of normal for the total leukocyte count was 10 x 109/L. The upper limit of normal for the neutrophil percentage was 75 per cent for all patients above 15 years of age while for children below 15 years of age, the total lymphocyte and neutrophil percentage varied with age and the upper limits used were those reported by Mann. A raised total lymphocyte count had a sensitivity of 81.4 per cent and specificity of 77.3 per cent. With a raised total lymphocyte count and neutrophil percentage, the sensitivity decreased to 65.7 per cent but the specificity increased to 81.4 per cent. The authors concluded that a raised total lymphocyte count, preferably combined with a raised neutrophil percentage, are useful as diagnostic aids in acute appendicitis especially in patients 15-65 years of age. It must however be emphasized that the total lymphocyte count and neutrophil percentage should only be interpreted in the light of the physical findings in patients with suspected appendicitis. (LEVEL II EVIDENCE)

A retrospective study (Gronroos 1999) involving 300 patients was done to determine the value of the leukocyte count and the C-reactive protein (CRP) in the diagnosis of appendicitis. The authors found that all 200 patients with acute appendicitis had either a leukocyte count or CRP value, or both, above the normal limits. The authors concluded that the leukocyte count was a better laboratory test than CRP in diagnosing uncomplicated appendicitis because it is a very early marker of inflammation. On the other hand, the CRP value was superior to the leukocyte count in reflecting appendiceal perforation or abscess formation. (LEVEL II EVIDENCE)

A retrospective study (Sanjuan 1998) involving 124 pediatric patients was done to determine the diagnostic accuracy of C-reactive protein and its possible advantage, if any, over the leukocyte count in children with acute appendicitis. Correlating the CRP and the leukocyte count with the pathologic diagnosis of acute appendicitis, the mean CRP values were found to increase as the pathologic inflammation type progressed. The CRP receiver operating characteristic curve showed that the CRP value with the highest accuracy was 1.7 mg/dl. CRP had a sensitivity of 58 per cent, specificity of 80 per cent, accuracy of 83.8 per cent, PPV of 94 per cent and NPV of 26 per cent. A comparison of the respective receiver operating characteristic curves demonstrates that CRP, leukocyte count, and the combination of both tests all have a good diagnostic value but without any significant difference. The authors concluded that although the serum CRP has adequate diagnostic accuracy, it is neither individually nor in combination with the WBC count better than the WBC count alone. (LEVEL II EVIDENCE)

B. EQUIVOCAL APPENDICITIS IN ADULTS

Various adjunctive diagnostic procedures have been studied in an attempt to improve the diagnostic accuracy and consequently the management of clinically equivocal cases of acute appendicitis. Among these procedures, CT scan and ultrasound have been extensively studied and have been shown to reduce the negative appendectomy rate, move patients from observation to earlier operation or discharge from the hospital, and prevent the inappropriate discharge of patients with appendicitis.

Several studies directly comparing the usefulness of CT scan in contrast to ultrasound in the diagnosis of appendicitis in equivocal cases have proven that CT scan is more accurate than ultrasound.

A prospective study (Wilson 2001) involving 99 patients who were all subjected to both right lower quadrant ultrasound and limited pelvic CT scan with rectal contrast was done to compare the accuracy of the two procedures and to determine which subset of patients will benefit from their use. CT scan had a sensitivity of 94 per cent, specificity of 92 per cent, PPV of 92 per cent, NPV of 94 per cent and positive LR of 10.78 (3.54 to 32.85). Ultrasound had a sensitivity of 94 per cent, specificity of 12.5 per cent, PPV of 71 per cent, NPV which was not calculable because of the lack of negative test results, and a positive LR of 2.38 (1.08 to 5.23). Although the authors found that CT scan was more reliable than ultrasound, they do not advocate its routine use. CT scan should only be used as an adjunctive modality in clinically equivocal appendicitis. (LEVEL I EVIDENCE)

In the same prospective study (Wilson 2001), the cost-effectiveness of CT scan was compared with the cost incurred with standard in-hospital observation of patients and the total cost of surgery for each patient. The net savings for those patients who underwent CT scan proved greater when the total hospitalization costs saved from those patients who were either sent home or operated on early and those who were spared unnecessary surgery because of a more accurate diagnosis using CT scan were considered. (LEVEL I EVIDENCE)

A prospective study (Horton 2000) involving 89 patients with equivocal appendicitis was done to compare limited non-contrast CT scan with ultrasound. CT scan had a sensitivity of 97 per cent, specificity of 100 per cent, accuracy of 94 per cent, PPV of 100 per cent and NPV of 91.7 per cent. Ultrasound had a sensitivity of 76 per cent, specificity of 90 per cent, accuracy of 83 per cent, PPV of 95.8 per cent, and NPV of 56.3 per cent. The authors concluded that patients with equivocal appendicitis derive the most benefit from diagnostic imaging and for this group, CT scanning offers the highest accuracy and specificity. (LEVEL II EVIDENCE)

A prospective study (Stroman 1999) involving 107 patients with equivocal appendicitis was done to determine the accuracy of oral and intravenous contrast-enhanced spiral abdominal and pelvic CT and to compare CT with full abdominal and pelvic ultrasound. CT scan had a sensitivity of 92 per cent, specificity of 85 per cent, accuracy of 88 per cent, PPV of 75 per cent, NPV of 95 per cent and positive LR of 5.92 (95% CI 3.41 to 10.28). In 40 per cent (43 of 107 patients) of those who were also imaged with ultrasound before CT imaging, ultrasound was found to have a sensitivity of 30 per cent, specificity of 75 per cent, accuracy of 69 per cent, PPV of 27 per cent, NPV of 77 per cent and positive LR of 1.2. The authors concluded that CT scan was superior to ultrasound for patients suspected to have appendicitis but with equivocal clinical findings. CT scan should be considered as an imaging alternative to facilitate improved patient selection for operative intervention. (LEVEL II EVIDENCE)

A prospective randomized study (Walker 2000) involving 128 patients was done to assess the value of CT scan with rectal contrast compared with the standard management of serial abdominal examination or ultrasound. The study showed that CT scan had a sensitivity of 94 per cent, specificity of 100 per cent, accuracy of 96 per cent, PPV of 100 per cent, NPV of 93 per cent, and positive LR of 26.57 (95% CI 3.38 to 183.6). In contrast, standard management had a sensitivity of 100 per cent, specificity of 79 per cent and accuracy of 89 per cent. The authors concluded that CT scan was an effective modality for diagnosing acute appendicitis. (LEVEL II EVIDENCE)

A prospective study (Wise 2000) involving 100 patients with clinically suspected appendicitis was done to evaluate the following five appendiceal imaging techniques: graded compression sonography, unenhanced focused appendiceal CT, standard abdominopelvic CT using IV contrast material, focused appendiceal CT using colonic contrast material, and sonography using colonic contrast material. The mean sensitivity, specificity, positive and negative predictive values, inter- and intra-observer variability, and diagnostic confidence scores of all observers were used for comparative performance assessments. Both sonographic techniques had high specificities of 86-89 per cent and comparable accuracies of 74-76 per cent but low sensitivities (32-34 per cent) and inter- and intra-observer variability (0.15 – 0.20 and 0.39 – 0.43, respectively). Unenhanced focused appendiceal CT, abdomino-pelvic CT, and focused appendiceal CT with colonic contrast material all significantly outperformed sonography (p<0.0001), with sensitivities of 83 per cent, 71 per cent, and 74 per cent; specificities of 85 per cent, 91 per cent, and 87 per cent; accuracies of 85 per cent, 87 per cent, and 84 per cent; PPV of 58 per cent, 71 per cent, and 70 per cent; and NPV of 95 per cent, 91 per cent, and 90 per cent, respectively. Abdomino-pelvic CT gave the greatest confidence in cases with negative findings (p=0.001) and focused appendiceal CT with colonic contrast material gave the greatest confidence for patients with positive findings (p=0.02). In terms of inter- and intra-observer variability, focused appendiceal CT with colonic contrast material yielded the highest agreement (inter-observer 0.45 and intra-observer 0.85) while unenhanced focused appendiceal CT yielded the lowest agreement (inter-observer 0.36 and

intra-observer 0.76). The authors recommend that standard abdomino-pelvic CT be the initial examination for appendicitis in adult patients. Focused appendiceal CT with colonic contrast material however should be used as a problem-solving technique in difficult cases. (LEVEL II EVIDENCE)

A prospective study (Rao 1997) involving 200 patients was done to determine the sensitivity, specificity, and diagnostic value of the individual signs at helical appendiceal CT with oral and/or colon contrast material. Each individual CT sign of appendicitis present was documented, including an abnormal appendix, right lower quadrant inflammatory changes, and cecal apical changes. The CT signs and their sensitivity and specificity, respectively, included an enlarged (>6 mm) unopacified appendix (93%, 100%); appendicolith (44%, 100%); fat stranding (100%, 80%); adenopathy (62%, 66%); paracolic gutter fluid (18%, 86%); abscess (11%, 100%); extraluminal air (8%, 97%); phlegmon (7%, 99%); ileal (3%, 86%) or sigmoid (3%, 95%) wall thickening; diffuse cecal wall thickening (0%, 91%); focal cecal apical thickening (69%, 100%); arrowhead sign (23%, 100%); and cecal bar (10%, 100%). The authors found that an enlarged appendix with periappendiceal fat stranding occurs in 93 percent of the CT scans of patients with appendicitis. Less common but specific signs (cecal apical changes, appendicolith) are usually present in the remaining appendicitis cases. Some signs seen with appendicitis (adenopathy, fat stranding, adjacent bowel thickening, fluid) can also be noted with alternative conditions, and in these cases identification of the normal appendix is the key to excluding appendicitis. (LEVEL II EVIDENCE)

A retrospective study (Styrud 2000) involving 251 patients was done to determine the sensitivity and specificity of graded-compression ultrasound and plain CT scan in patients with suspected appendicitis. CT scan had a sensitivity of 88 per cent, specificity of 95 per cent and positive LR of 17.6 while ultrasound had a sensitivity of 82 per cent, specificity of 97 per cent and positive LR of 27.33. The authors concluded that CT scan has a higher sensitivity and the same specificity as ultrasound. (LEVEL II EVIDENCE)

A retrospective study (Balthazar 1998) involving 146 patients with equivocal appendicitis was done to determine the impact of abdominal CT scan with oral and intravenous contrast on the negative appendectomy rate and perforation rate. CT scan was found to have a sensitivity of 96.5 per cent, specificity of 96.8 per cent, accuracy of 96.5 per cent, PPV of 99 per cent, NPV of 88.2 per cent and positive LR of 30.16. The use of CT led to an over-all negative appendectomy rate of 4 per cent, with 8.3 per cent seen in female patients of childbearing age, and a perforation rate of 22.1 per cent. The authors concluded that the judicious use of high-resolution CT imaging significantly improves the diagnostic accuracy particularly in patients presenting with equivocal clinical findings and in women of menstruating age. The use of CT scan also resulted in a substantial decrease in the negative appendectomy rate compared to previously published reports without incurring an increase in the perforation rate. (LEVEL II EVIDENCE)

A retrospective study (Schuler 1998) involving 97 patients with equivocal appendicitis showed CT scan with IV and oral contrast to have a sensitivity of 98 per cent, specificity of 91 per cent, accuracy of 96 per cent, PPV of 92 per cent, NPV of 98 per cent and positive LR of 45.16 (6.49 to 314.18). (LEVEL II EVIDENCE)

A retrospective study (Peck 2000) involving 401 patients was done to determine the accuracy and clinical utility of non-contrast helical CT scan for appendicitis. CT scan had a sensitivity of 92.8 per cent, specificity of 99.6 per cent, accuracy of 97.5 per cent, PPV of 99 per cent, NPV of 96.9 per cent and positive LR of 234.77 (33.17 to 1,661.37). The best radiological indicators for a positive CT for appendicitis were pericecal inflammation (88%), appendicolith (57%), and an enlarged (>6 mm) appendix (47%). Alternative diagnoses were identified in 22 per cent of patients and the negative appendectomy rate was 5.4 per cent. The authors concluded that the use of noncontrast helical CT results in a low negative appendectomy rate and a high degree of confidence that a negative CT will allow patients to be sent home safely. (LEVEL II EVIDENCE)

Studies have also been done which showed the relative accuracy of ultrasound in the diagnosis of appendicitis in equivocal cases. In a meta-analysis (Orr 1995) done to review the usefulness of ultrasound, the authors reported an overall sensitivity of 84.7 per cent and specificity of 92.1 per cent. More importantly, the study demonstrated the impact of pretest probability of disease upon the accuracy and usefulness of a test. In a group with high prevalence of appendicitis (about 80%), a negative test result had a negative PV of only 59.5 per cent; conversely, in a group of low prevalence appendicitis, a positive test had a positive predictive value of only 19.5 per cent. A balanced "test performance accuracy" was demonstrated only in those patients with an intermediate prevalence of appendicitis. The authors concluded that ultrasonography is most useful in those with an intermediate probability of disease and should be avoided in patients with high or low likelihood of disease because they are associated with high false-positive and false-negative rates. (LEVEL I EVIDENCE)

A randomized controlled trial (Douglas 2000) involving 302 patients comparing the clinical diagnosis (control group) with a diagnostic protocol incorporating ultrasonography and the Alvarado score (intervention group) was done to determine whether diagnosis with graded-compression ultrasonography improves clinical outcomes for patients with suspected appendicitis. Ultrasound had a sensitivity of 94.7 per cent, specificity of 88.9 per cent, accuracy of 93 per cent and positive LR of 8.5. The intervention group had a significantly shorter mean time to operation (7.0 vs. 10.2 hours, p=0.016) but there were no statistically significant differences between the two groups with respect to the mean duration of hospital stay, the proportion of patients undergoing a non-therapeutic operation or delayed treatment in association with perforation. The authors concluded that although graded compression ultrasonography is an accurate test when performed by experienced sonographers, ultrasonography has

not been shown to produce better outcomes than clinical diagnosis alone. (LEVEL II EVIDENCE)

C. EQUIVOCAL APPENDICITIS IN THE PEDIATRIC AGE GROUP

A prospective study (Lessin 1999) involving 215 children was done to compare the accuracy of the clinician's impression with ultrasonography in patients with equivocal signs of acute appendicitis and to examine the value of selective ultrasound use. Ultrasound findings suggestive of acute appendicitis included identification of a non-compressible tubular structure in the right lower abdomen exceeding 6 mm. in diameter, identification of an appendicolith, or identification of fluid suggestive of appendiceal perforation and/or abscess formation. In equivocal cases, the initial clinical impression had a sensitivity of 50 per cent, specificity of 85 per cent, PPV of 63 per cent, and a NPV of 78 per cent. Ultrasound alone had a sensitivity of 88 per cent, specificity of 96 per cent, PPV of 90 per cent, NPV of 94 per cent, and positive LR of 19.54 (7.009 – 57.38). Ultrasonography decreased the false-positive rate from 10 per cent after the first clinical impression to 3 per cent, while decreasing the false-negative rate from 16 per cent to 4 per cent. Combining both a positive ultrasound reading with a positive clinical impression, the PPV was 87.5 per cent. A combination of a negative ultrasound reading and a negative clinical impression resulted in a NPV of 96.5 per cent. The authors concluded that the early and selective use of ultrasonography in equivocal cases could rapidly allow an accurate diagnosis. (LEVEL II EVIDENCE)

A retrospective study (Davidson 1999) involving 253 children was done to examine the roles of graded compression ultrasound (GCUS) and the Alvarado score in patients in whom the diagnosis of appendicitis was uncertain. The GCUS result was categorized as "suggestive of appendicitis" when there was a tender, blind-ending, non-compressible, non-peristaltic tube in the right iliac fossa, target-like in cross-section, with a diameter of over 6 mm., and demonstrating increased mucosal wall thickness. GCUS alone had a sensitivity of 89 per cent, specificity of 95 per cent, accuracy of 93 per cent, PPV of 87 per cent, NPV of 96 per cent and positive LR of 16.21 (9.008 – 29.73). Clinical data alone had a sensitivity of 60 per cent, specificity of 82 per cent, accuracy of 76 per cent, PPV of 54 per cent, and NPV of 85 per cent. In a discriminant analysis with cross-validation study combining the clinical data with the GCUS findings, the over-all result showed a sensitivity of 91 per cent, specificity of 94 per cent, accuracy of 93 per cent, PPV of 84 per cent, and NPV of 97 per cent. The data showed that there was no improvement in the accuracy of diagnosis when the authors combined the clinical data with GCUS over the results for GCUS alone. (LEVEL II EVIDENCE)

A retrospective study (Ramachandrah 1996) involving 453 patients between one to 20 years of age was done to determine the sensitivity and specificity of graded-compression RLQ ultrasonography as a diagnostic modality in children with possible appendicitis. Of the 180 patients in group I who underwent ultrasound even if the diagnosis of appendicitis was obvious clinically, ultrasound had a sensitivity of 88 per cent and specificity of 96 per cent. Of the 272 patients in group II in whom the clinical diagnosis of appendicitis was equivocal, ultrasound had a sensitivity of 92 per cent, specificity of 97 per cent, PPV of 90 per cent, NPV of 98 per cent, and positive LR of 32.39 (15.12 – 70.55). In the over-all group of 452 children, ultrasound had a sensitivity of 90 per cent, specificity of 96 per cent, and accuracy of 95 per cent. (LEVEL II EVIDENCE)

A retrospective cohort study (Ang 2001) involving 317 children was done to determine the accuracy of graded-compression ultrasonography of the right lower quadrant in the diagnosis of clinically equivocal appendicitis in the setting of a pediatric hospital emergency department. Ultrasound had a sensitivity of 91 per cent, specificity of 89 per cent, PPV of 92 per cent, NPV of 88 per cent, a positive LR of 8.6 (5.1-14.5), a negative LR of 0.11 (0.06 – 0.018) and an equivocal LR of 0.67 (0.38 – 1.17). (LEVEL II EVIDENCE)

A retrospective study (Mullins 2001) involving 199 children between one to 18 years of age was done to determine the accuracy and feasibility of limited helical CT with colonic contrast material in the evaluation of suspected appendicitis in children compared with adults. Focused CT had a sensitivity of 97 per cent, specificity of 99 per cent, PPV of 98 per cent, NPV of 98 per cent, and positive LR of 126.09 (17.88 - 889.13) and also provided the alternative diagnosis in 48 per cent of patients in whom the CT findings were negative for appendicitis. The authors concluded that focused helical CT was as accurate in pediatric patients as it was in adults. (LEVEL II EVIDENCE)

A retrospective study (Sivit 2000) involving 154 patients between one to 20 years of age was done to evaluate the accuracy of whole abdominal helical CT with oral and rectal contrast for the diagnosis of clinically equivocal appendicitis and to determine its utility in establishing alternative diagnoses. CT scan had a sensitivity of 95 per cent, specificity of 94 per cent, PPV of 91 per cent, NPV of 97 per cent and positive LR of 14.77 (7.09 – 31.85). In addition, helical CT gave an alternative diagnosis in 34 per cent (32 of 93 patients) who did not have appendicitis. (LEVEL II EVIDENCE)

A prospective study (Pena 1999) involving 139 patients between 3 to 21 years of age was done to determine the diagnostic value of a protocol involving both ultrasonography and limited CT with rectal contrast in the diagnosis of appendicitis in equivocal cases. Ultrasonography had a sensitivity of 44 per cent, specificity of 93 per cent, accuracy of 76 per cent, PPV of 79 per cent, and NPV of 75 per cent. CT with rectal contrast done after ultrasonography with negative or equivocal results had a sensitivity of 97 per cent, specificity of 94 per cent,

accuracy of 94 per cent, PPV of 85 per cent, and NPV of 99 per cent. The protocol had a sensitivity of 97 per cent, specificity of 97 per cent, PPV of 93 per cent , NPV of 93 per cent, positive LR of 38.14(9.69-150.09), negative LR 0.13 (0.01-1.74) and equivocal LR 0.88 (0.095-8.11). The authors concluded that CT with rectal contrast should be reserved for those children in whom the diagnosis remains uncertain even after a full clinical evaluation. In a population with a low pretest probability of acute appendicitis, ultrasonography is a useful primary diagnostic modality because it is able to diagnose appendicitis in almost 40 per cent of patients with the disease. (LEVEL II EVIDENCE)

A prospective study (Sivit 2000) involving 386 pediatric and young adult patients was done to compare the diagnostic accuracy of graded compression sonography with helical CT for the diagnosis of equivocal appendicitis. Two hundred thirty-three patients underwent sonography only, 71 patients underwent CT only, and 82 patients underwent both sonography and CT. Use of graded-compression sonography alone had a sensitivity of 78 per cent, specificity of 93 per cent, accuracy of 89 per cent and positive LR of 10.69 (6.74 – 17.14). Use of CT alone had a sensitivity of 95 per cent, specificity of 93 per cent, accuracy of 94 per cent and positive LR of 14.58 (7.02 – 31.51). In a comparison of the two procedures in the 82 patients who underwent both examinations, CT had a sensitivity of 93 per cent, specificity of 93 per cent, and accuracy of 93 per cent compared with sonography which had a sensitivity of 48 per cent, specificity of 91 per cent, and accuracy of 76 per cent. The authors noted that CT was particularly useful for patients with normal findings on sonographic examination. (LEVEL II EVIDENCE)

In the same study by Sivit et. al. where the comparison between the two procedures was further stratified according to age group, helical CT had a significantly higher sensitivity (97% vs. 71%) and higher accuracy (97% vs. 91%) compared to sonography in patients more than 10 years old. In patients 10 years old or younger, the sensitivity (94% vs. 84%), specificity (87% vs. 86%), and accuracy (90% vs. 86%) of CT and sonography were not significantly different. The authors concluded that helical CT with rectal contrast was superior to graded-compression sonography in patients more than 10 years old. In patients 10 years old and younger however, the findings of the two imaging modalities were not significantly different. (LEVEL II EVIDENCE)

A prospective study (Teo 2000) involving 129 children between 2 to 15 years of age was done to evaluate the respective roles and effectiveness of graded compression ultrasound with helical CT scanning of the upper abdomen and lower pelvis in a clinical algorithm. Ultrasound was performed after patients were clinically graded as having high, intermediate or equivocal, or low probability of having acute appendicitis. Thereafter, CT was only performed in the 12 cases where the clinical picture was incompatible with the ultrasound findings or where the ultrasound was sub-optimal due to technical difficulties. Ultrasound had a sensitivity of 92.9 per cent, specificity of 96.9 per cent, accuracy of 96 per cent, PPV of 89.7 per cent, and NPV of 97.9 per cent. Utilizing CT scan with oral and

rectal contrast improved the sensitivity, specificity, accuracy, PPV, and NPV to 100 per cent. The authors concluded that ultrasound was most beneficial in the subgroup with equivocal clinical findings while CT should be reserved for selected situations. (LEVEL II EVIDENCE)

A retrospective study (Lowe 2001) involving 162 children was done to compare the accuracy of unenhanced limited CT of the abdomen with graded compression sonography with clinically equivocal appendicitis. CT had a sensitivity of 97 per cent, specificity of 100 per cent, accuracy of 99 per cent, PPV of 100 per cent, NPV of 97 per cent and positive LR of 70 (8.04 –669.94). Sonography, on the other hand, had a sensitivity of 100 per cent, specificity of 88 per cent, PPV of 74 per cent, NPV of 100 per cent, and a positive LR of 8.29 (4.23 –16.38). The authors concluded that unenhanced limited CT can achieve equal accuracy to full enhanced CT with IV and enteric contrast and compares favorably with sonography. (LEVEL II EVIDENCE)

D. SELECTED CASES

1. DIAGNOSTIC LAPAROSCOPY

A systematic review (Sauerland 2001) of 12 randomized controlled trials was done to assess the diagnostic effects of laparoscopy. In trials of unselected patients, diagnostic laparoscopy led to variable reductions in the rate of negative appendectomies. Although the over-all result is significant (RR of 0.21; 95% CI 0.13 to 0.33), it is influenced strongly by a recently published large trial (Pedersen 2001). In parallel to the reduction in negative appendectomy rate, the rate of unestablished diagnosis was significantly decreased after laparoscopy (RR of 0.34; 95% CI 0.22 to 0.53). In fertile women, in whom appendectomy was deemed necessary, diagnostic laparoscopy reduced the number of unnecessary appendectomies largely (RR of 0.19; 95% CI 0.11 to 0.34). Consequently, the number of patients without an established final diagnosis was smaller after laparoscopy (RR of 0.24; 95% CI 0.15 to 0.38). Both results are based on five similar trials without any signs of heterogeneity. (LEVEL I EVIDENCE)

Despite its statistically significant favorable effects however, the panel of experts feel that diagnostic laparoscopy should be viewed as an invasive procedure requiring anesthesia and having risks similar to appendectomy. It should be selectively utilized like in situations where the patient with clinically equivocal appendicitis is in the childbearing age group but in whom CT scan or ultrasound remain inconclusive. (LEVEL III EVIDENCE)

E. NON-HELPFUL TESTS

1. PLAIN ABDOMINAL RADIOGRAPHY

A retrospective study (Rao 1999) involving 642 patients was done to determine the diagnostic utility and hospital resource impact of plain abdominal radiography in patients with suspected appendicitis. It was found that there was no individual radiographic finding which was sensitive or specific for appendicitis. Plain abdominal radiographs showed findings in 51 per cent (sensitivity of 44.2 per cent to 54.3 per cent) of patients with appendicitis and in 47 per cent (46.6 per cent to 59.9 per cent) of patients without appendicitis. Radiological impressions were normal in 50 per cent (45.2 per cent to 55.2 per cent) of patients with appendicitis and in 60 per cent (specificity of 54 per cent to 66.6 per cent) without appendicitis. Plain abdominal radiographic interpretations suggested a specific diagnosis or alternative condition in 10 per cent of cases but these diagnoses failed to correlate with the final clinical diagnoses in 57 per cent of cases. Despite the lower cost for each plain radiographic series relative to appendiceal CT, the cost per specific and correct diagnosis of an abnormality was 5.9 times higher with plain abdominal radiography than with appendiceal CT. The authors concluded that plain abdominal radiographs in patients with suspected appendicitis are neither sensitive nor specific, are frequently misleading, are costly per specific and correct diagnosis, and should not be routinely obtained in patients with suspected appendicitis. (LEVEL II EVIDENCE)

2. BARIUM ENEMA

A prospective study (Ferzli 1990) involving 101 patients was done to assess the value of barium enema in patients who had equivocal clinical findings suggestive of appendicitis. The authors found that barium enema had a sensitivity of 83 per cent, specificity of 96 per cent, PPV of 88 per cent, NPV of 95 per cent and overall accuracy of 91.5 per cent. (LEVEL II EVIDENCE)

A retrospective study (Hatch 1981) involving 66 children was done to assess the usefulness of barium enema in the diagnosis of equivocal cases of appendicitis. It was found that barium enema has a sensitivity of 91.2 per cent, specificity of 83.3 per cent, PPV of 96.9 per cent, NPV of 62.5 per cent, positive LR of 10.75 (1.59 to 72.88), negative LR of 0.21(0.06 to 0.78) and equivocal LR of 0.47 (0.27 to 0.82). These results suggest that the use of barium enema as an adjunct in the diagnosis of acute appendicitis was helpful if it was positive but a negative barium enema could not be relied upon. (LEVEL II EVIDENCE)

A retrospective study (Garcia 1987) involving 18 children showed that barium enema had a sensitivity of 100 per cent, specificity of 50 per cent, PPV of 92.31 per cent, NPV of 100 per cent, positive LR of 3.2 (0.58 to 17.80), negative LR of 0.27 (0.05 to 1.35), and equivocal LR of 0.27 (0.02 to 3.39). This study

likewise showed that a positive barium enema is very reliable but a negative barium enema cannot rule out appendicitis. This study passed the validity criteria but is limited by the small sample size. (LEVEL II EVIDENCE)

Barium enema is not generally recommended as a diagnostic tool in equivocal cases because although it can likely predict the possibility of acute appendicitis, it cannot reliably rule it out.

3. SCINTIGRAPHY

A prospective study (Rypins 2000), involving 98 patients was done to evaluate the safety and efficacy of Tc-99m labeled anti CD 15 immunoglobulin M monoclonal antibody (LeuTech) in the scintigraphic detection of acute appendicitis in patients with equivocal clinical presentation. The authors found LeuTech to have a sensitivity of 98 per cent, specificity of 84 per cent, PPV of 81 per cent, NPV of 98 per cent, and positive LR of 6.28 (3.61 to 11.64). Although scintigraphy is highly sensitive, the specificity and the positive predictive value are low (LEVEL II EVIDENCE)

Scintigraphy will be unable to distinguish appendicitis from other inflammatory conditions in the right lower quadrant. In addition, the procedure is relatively expensive and exposes the reticuloendothelial system to significant doses of radiation.

What is the appropriate treatment for acute appendicitis?

Appendectomy is the appropriate treatment for acute appendicitis.
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LEVEL II EVIDENCE
CATEGORY A RECOMMENDATION
</div>

SUMMARY OF EVIDENCE

A prospective randomized controlled trial (Eriksson 1995) involving 40 patients was done to compare the results of conservative treatment with antibiotics and surgery in patients with acute appendicitis whose duration of abdominal pain was less than 72 hours. Nineteen patients treated with antibiotics alone were discharged within 2 days while one patient required surgery after 12 hours because of a perforated appendicitis. Seven of the remaining 19 patients (36 %) in the antibiotic group were subsequently readmitted within one year for recurrent appendicitis and underwent surgery. Based on this study, the total failure rate for using antibiotics as the only treatment in acute appendicitis is 40 per cent. (LEVEL II EVIDENCE)

What is the recommended approach to the surgical management of acute appendicitis?

Open appendectomy is the recommended primary approach to the treatment of acute appendicitis in our setting. Therapeutic laparoscopic appendectomy is an alternative in selected cases.
LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

A meta-analysis (Chung 1998) of 17 prospective randomized controlled trials involving 1,962 patients was done to determine the merits of laparoscopic appendectomy (LA) versus conventional open appendectomy (OA). The effect sizes for operating time, hospitalization, postoperative pain, return to normal activity, incisional surgical site infection, and intra-abdominal abscess were calculated using the random effect model for heterogeneity. An estimate of the robustness of all positive findings was also calculated. The authors found statistically significant effect sizes for four of the six outcome measures. Laparoscopic appendectomy takes 31.4 per cent longer to perform (effect size 0.92; 95% CI 0.26 to 1.58) but results in less post-operative pain (effect size of -0.41; 95% CI -0.62 to -0.19), 35 per cent faster recovery (effect size of -1.23; 95% CI -2.4 to -0.05) and 60 per cent lower incisional surgical site infection rates (effect size of -0.31; 95% CI -0.51 to -0.12) There was no statistically significant difference between the two procedures in terms of length of hospitalization (effect size of -0.35; 95% CI -0.75 to 0.04) and the development of intra-abdominal abscess (effect size of 0.21; 95% CI 0.46 to 0.05). Calculating for the robustness of the findings, the results suggest that the findings in both operative time (Rosenthal's fail safe N of 136) and post-operative pain (Rosenthal's fail-safe N of 105) are quite robust, but less so in incisional surgical site infection (Rosenthal's fail safe N of 78) and even less for recovery time (Rosenthal's fail safe N of 30). (LEVEL I EVIDENCE)

A systematic review (Sauerland 2001) of 45 randomized controlled trials was done to compare the diagnostic and therapeutic effects of laparoscopic and conventional "open" surgery in the treatment of appendicitis. Thirty-nine studies compared the therapeutic effects of LA and OA in adults. Of the various complications that were described, only two specific complications (incisional surgical site infections and intra-abdominal abscesses) were examined since it was impossible to extract data on overall complication rates from the included studies because the definition and reporting of complications were inconsistent.

Incisional surgical site infections were about half as likely to occur after LA than after OA (Peto OR 0.47; 95% CI 0.36 to 0.62), a highly significant result based on more than 4,000 patients. On the other hand, intra-abdominal abscesses were increased nearly threefold after LA (Peto OR 2.77; 95% CI 1.61 to 4.77) in the 15 studies that contributed data to this over-all result.

The duration of surgery was 14 minutes (95% CI 10 to19 minutes) longer for LA but there was strong heterogeneity present in these analyses. Pain measurements on day 1 after surgery showed a reduction of pain by 8 mm (95% CI 3 to13 mm) on a 100 mm visual analog scale but this finding was hampered by the fact that there was strong heterogeneity and the absolute pain levels varied between 6.5 and 2.9 cm.

Not a single study reported a significant increase in hospital stay. In the summary statistics, therefore, a significant reduction of 0.7 days was calculated (95% CI 0.4 to 1.0). Return to normal activity, to work and to sporting activities were 6 days (95% CI 4 to 8 days), three days (9% CI 1 to 5 days) and 7 days (95% CI 3 to12 days) earlier after LA than after OA. While heterogeneity was visible for return to normal activity, it was not detectable in the other two comparisons. However, the raw data varied largely among the studies. Furthermore, while in some studies the return to normal activity was earlier than the return to work, in other studies the opposite was found.

Bowel function returned more quickly after LA than after OA but this finding is based on a smaller number of studies and also is of borderline significance only.

Only two studies assessed the cosmetic result by the use of the visual analog scale (VAS). Both noted a significant benefit of 10 mm VAS for LA versus OA.

The operation costs of LA were significantly higher than that of OA, but this finding is strongly influenced by one small trial with extreme results (Williams 1996). When comparing total costs within hospital stay and the costs outside the hospital, it seems cost increase and decrease cancel out each other. Although LA causes more in-hospital costs, it saves costs outside the hospital on the society level.

(LEVEL I EVIDENCE)

Several prospective studies have been done in the US and Europe to compare the cost-effectiveness of laparoscopic appendectomy to open appendectomy. These studies considered the operative and post-operative results, convalescence, complications and the operative, hospital, and total costs of the two procedures in their particular setting. The potential problem of these foreign studies however is that the economic parameters that were used cannot be shifted directly to other hospitals and to different health care systems. Especially when

estimating the loss of productivity and computing for the cost savings at the society level, these cost-effectiveness studies should consider and have a perspective of the whole health care system it is evaluating. Thus, the panel of experts feel that these foreign studies on the cost-effectiveness of the different surgical approaches in the treatment of acute appendicitis cannot be applied to the Philippine setting. (LEVEL III EVIDENCE)

The panel of experts feels that laparoscopic appendectomy will be most beneficial in certain patient populations. This subset would include women of childbearing age in whom up to 40 per cent have a normal appendix at the time of operation, obese individuals who would require larger skin incisions during open appendectomy, and athletic individuals who desire an earlier return to sporting activities. (LEVEL III EVIDENCE)

What is the role of laparoscopic appendectomy in the management of acute appendicitis in children?

Laparoscopic appendectomy may be recommended as an alternative to open appendectomy in the pediatric age group.
LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

A systematic review (Sauerland 2001) of three randomized controlled trials was done to compare open appendectomy with laparoscopic appendectomy in children. Although much less data was available, the results in children do not seem to be much different when compared to adults. Incisional surgical site infections were significantly reduced with LA (Peto OR 0.12; 95% CI 0.04 to 0.39) but not a single intra-abdominal infection was seen. Two trials that measured pain failed to find a reduction in pain with LA. The difference in VAS was -1 mm VAS (95% CI -8 to 7 mm). In the study by Lintula (2001), blinding lasted for seven days and a significant reduction in hospital stay in favor of LA was noted (-0.7 days; 95% CI –0.3 to –1.1 days). (LEVEL I EVIDENCE)

What is the role of antibiotics in the management of acute appendicitis?

A. Is antibiotic prophylaxis indicated for uncomplicated appendicitis?

Yes. Antibiotic prophylaxis is recommended for the prevention of surgical site infection in patients who undergo appendectomy and should be considered for routine use.
LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

A systematic review (Andersen 2002) of 44 randomized trials and controlled clinical trials involving 9,298 patients was done comparing any antibiotic regimen with placebo in patients undergoing appendectomy to determine whether these patients will benefit from antimicrobial prophylaxis.

Considering all patients with a clinical diagnosis of appendicitis, the incidence of incisional surgical site infection in the placebo group was 15.3 per cent (612 of 4002 patients) compared with 6.9 per cent (280 of 4049 patients) in the treatment group for an ARR of 8.4 per cent and an NNT of 12. The incidence of intra-abdominal abscess in the placebo group was 1.73 per cent (33 of 1905 patients) compared with 0.76 per cent (14 of 1843 patients) in the treatment group for an ARR of 0.97 per cent and an NNT of 1. This shows that the use of systemic antibiotics significantly reduces the incidence of incisional surgical site infection (Peto OR 0.33; 95% CI 0.28 to 0.38) and intra-abdominal abscess (Peto OR 0.45; 95% CI 0.25 to 0.80) of patients who undergo appendectomy for clinically diagnosed appendicitis.

Considering patients with pathology-proven appendicitis, the incidence of incisional surgical site infection in the placebo group was 12.57 per cent (95 of 756 patients) compared with 4.29 per cent (32 of 746 patients) in the treatment group for an ARR of 8.28 per cent and an NNT of 12. The incidence of intra-abdominal abscess in the placebo group was 2.39 per cent (9 of 376 patients) compared with 0.55 per cent (2 of 365 patients) in the treatment group for an ARR of 1.84 per cent and an NNT of 54. This also shows that the use of systemic antibiotics significantly reduces the incidence of incisional surgical site infection (Peto OR 0.31; 95% CI 0.20 to 0.45) and intra-abdominal abscess (Peto OR 0.28; 95% CI 0.08 to 0.91) of patients who undergo appendectomy and have pathology-proven appendicitis. (LEVEL I EVIDENCE)

Seven trials exclusively on children (age 0-15 years) were identified. Both the nature of the disease and treatment is comparable to the ones for adults. Interestingly, subgroup analysis of this population showed a non-significant reduction in infection rate with antibiotics. This can be explained by a limited number of patients without heterogeneity between single study results. Another factor is the reported pathogenesis of appendicitis in children that shows a higher incidence of complicated appendicitis. However, although not divided into specific sub-populations, the majority of studies included children in their analysis. It is only reasonable to assume that the overall antibiotic efficacy also is representative for children. Several non-randomized studies have revealed differences in the pathology of the diagnosed appendicitis that could explain the non-significant reduction in the infection rate. (LEVEL I EVIDENCE)

B. What antibiotic/s is/are recommended for prophylaxis in uncomplicated appendicitis and what is the appropriate dose and route of administration?

The following antibiotics are recommended for prophylaxis in uncomplicated appendicitis :

Cefoxitin 2 grams IV single dose (Adults)
40 mg/kg IV single dose (Children)

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

Alternative agents:

Ampicillin-sulbactam 1.5-3 grams IV single dose (Adults)
75 mg/kg IV single dose (Children)
Amoxicillin-clavulanate 1.2 –2.4 grams IV single dose (Adults)
45 mg/kg IV single dose (Children)

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

For patients with allergy to beta-lactam antibiotics:

Gentamicin 80-120 mg IV single dose plus
Clindamycin 600 mg IV single dose   (Adults)

Gentamicin 2.5 mg/kg IV single dose plus
Clindamycin 7.5 – 10 mg/kg IV single dose   (Children)

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

Knowledge of the commonly isolated organisms in specific clinical conditions gives the clinician an insight as to what would be the appropriate antibiotic to administer for prophylaxis or for therapy in order to lower the incidence of surgical site infection. Based on the studies by Berne (1996), Bilik (1998), McNamara (1993), Mosdell (1991), Schropp (1991), and Stone (1975), the most commonly isolated organisms in cases of acute appendicitis are the aerobic gram-negative enteric bacteria, mainly E. coli. Obligate anaerobes particularly Bacteroides fragilis, are also frequently isolated either as a pure culture or as part of a mixed infection. Gram-positive organisms, which include Enterococcus sp. are only occasionally isolated. Since the susceptibility patterns of the commonly isolated organisms in acute appendicitis are quite predictable, the appropriate choice of antibiotics for prophylaxis or therapy can be based on the reported spectrum of activity and the pharmacokinetic properties of the particular antibiotic chosen.

Several randomized controlled trials included in the systematic review by Andersen (2002) have evaluated the use of systemic antibiotics for prophylaxis in simple or uncomplicated appendicitis. The largest placebo-controlled randomized trial (Bauer 1989) involving 1735 patients evaluated the efficacy of using cefoxitin 2 gm IV single dose intra-operatively for prophylaxis in uncomplicated appendicitis. Among the patients clinically-diagnosed to have uncomplicated appendicitis, 6.4 per cent (52 of 818 patients) in the placebo group and 1.6 per cent (12 of 730 patients) in the treatment group developed incisional surgical site infections. With an ARR of 4.8 per cent, NNT of 21 and Odds Ratio of 0.3 (95% CI 0.18 to 0.50), this study showed that there is a significant reduction in the risk of incisional surgical site infection after the administration of a single dose of cefoxitin. Among patients with pathology-confirmed uncomplicated appendicitis, 5.0 per cent in the placebo group and 1.2 per cent in the treatment group developed incisional surgical site infections. The ARR is 3.8 per cent, the NNT is 26 and the Odds Ratio is 0.28 (95% CI 0.11 to 0.71). Perhaps due to the low event rate however, there was no significant benefit afforded by cefoxitin in the prevention of organ-space infection among patients with clinically-diagnosed appendicitis (0.011 vs. 0.014; OR of 0.74; 95% CI 0.31 to 1.79) or with pathology-confirmed appendicitis (0.008 vs. 0.01; OR of 0.73; 95% CI 0.13 to 4.27). (LEVEL I EVIDENCE)

The use of gentamicin plus clindamycin is recommended for patients with allergy to beta-lactams because this combination offers appropriate coverage against aerobic gram-negative enteric pathogens and anaerobes. A randomized controlled trial (Rowlands 1982) involving 71 patients evaluated the efficacy of gentamicin 120 mg IV plus clindamycin 600 mg IV pre-operatively. There was a significant reduction in the risk of surgical site infection from 20 per cent in the placebo group compared to 5 per cent in the treatment group among patients with uncomplicated appendicitis. The OR was 19.2 (95% CI 0.04 to 0.89), the ARR was 15 per cent and NNT of 7. Perhaps due to the limited number of subjects however, there was no significant benefit provided by the gentamicin-clindamycin combination (0.25 vs. 0.62) over placebo in the prevention of surgical site infection among patients with complicated appendicitis. (LEVEL I EVIDENCE)

Options for monotherapy and single dose prophylaxis are encouraged to minimize the risk of toxicity. Based on the Evidence-Based Clinical Practice Guidelines for Antibiotic Prophylaxis of the Philippine College of Surgeons and if one were to consider coverage against the commonly isolated organisms, other acceptable alternatives for prophylaxis would include ampicillin-sulbactam and amoxicillin-clavulanic acid. These antibiotics have in fact been identified as two of the recommended choices for prophylaxis especially for elective colorectal operations. (LEVEL I EVIDENCE)

Based on the systematic review by Andersen, the administration of a single dose of antibiotic for prophylaxis is as effective as multiple doses. (LEVEL I EVIDENCE)

C. What antibiotic/s is/are recommended for the treatment of complicated appendicitis and what is the appropriate dose, route and duration of administration?

The recommended antibiotics for therapy of complicated appendicitis in adults are

      1) Ertapenem 1 gram IV every 24 hours

      2) Tazobactam-piperacillin 3.375 grams IV every 6 hours or
                       4.5 grams IV every 8 hours

For adults with beta-lactam allergy:
      Ciprofloxacin 400 mg IV every 12 hours plus
      Metronidazole 500 mg IV every 6 hours

The recommended antibiotic for therapy of complicated appendicitis in pediatric patients is
      Ticarcillin-clavulanic acid 75 mg/kg IV every 6 hours

Alternative agents for pediatric patients include:
      Imipenem-Cilastatin 15-25 mg/kg IV every 6 hours

For children with allergy to beta-lactams:
      Gentamicin 5 mg/kg IV every 24 hours plus
      Clindamycin 7.5 –10 mg/kg IV every 6 hours

**LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION**

      For gangrenous appendicitis, the recommended form of management is to treat in the same manner as uncomplicated appendicitis. **(LEVEL II EVIDENCE, CATEGORY A RECOMMENDATION)**
      The duration of the therapy may vary depending on the clinician's assessment after the operation. The therapy may be maintained for 5-7 days. Sequential therapy to oral antibiotics may be considered when gastrointestinal function has returned. **(LEVEL I EVIDENCE, CATEGORY A RECOMMENDATION)**
      The absence of fever for 24 hours (temperature < 38 C), the ability to tolerate oral intake, and a normal WBC count with 3 percent or less band forms are useful parameters for the discontinuation of antibiotic therapy. **(LEVEL II EVIDENCE, CATEGORY A RECOMMENDATION)**

SUMMARY OF EVIDENCE

Antimicrobial therapy is a critical adjunctive treatment that combats bacteremia during the operation, limits the spread of peritonitis, and speeds the resolution of the intra-abdominal infectious process. Accordingly, the selection of efficacious antimicrobial therapy can result in reduced incisional and organ-space infection, early recovery of intestinal function and timely discharge from the hospital. On the other hand, the selection of antimicrobials which do not have an effective spectrum or to which the organisms are resistant can result in post-operative infectious complications and longer periods of hospitalization. Optimal empiric antibiotic therapy for the treatment of complicated appendicitis should include an agent or agents active against both gram-negative enteric bacilli such as E. coli and anaerobic bacteria such as B. fragilis.

A survey (Mosdell 1991) regarding the choice of empiric antibiotic therapy for acute bacterial peritonitis was conducted in 5 major hospitals in the US. Majority of the 480 patients who underwent surgery for secondary bacterial peritonitis received a single agent drug, with cefoxitin and ampicillin-sulbactam as the preferred choices. Interestingly, patients treated with a single-broad spectrum antibiotic had a better outcome than those receiving multiple-drug regimens. Furthermore, empiric coverage of community-acquired Enterococcus and Pseudomonas species with the initial antibiotic regimen did not appear to be essential for a successful outcome. (LEVEL III EVIDENCE)

There are several issues regarding the importance of certain microorganisms isolated in secondary peritonitis. Although enterococci are frequently isolated as part of a polymicrobial intra-abdominal infection, their role as pathogens and the need for antibiotic coverage specifically toward this organism remains unclear. In a review of several trials (Gorbach 1993), the rate of isolation of Enterococcus in initial cultures performed for patients with intra-abdominal infections ranged from 14 per cent to 33 per cent. The analysis failed to reveal any cases that could be considered as a treatment failure due to infection by Enterococcus. (LEVEL III EVIDENCE)

On the other hand, a randomized trial (Burnett 1995) done to determine the role of enterococci in intra-abdominal infections reported that enterococcal isolates are associated with treatment failure. Enterococcal isolates were obtained from 22 per cent of the patients and failures were twice as high in this subset of patients (28% vs. 14%). Using stepwise logistic regression, higher APACHE II scores and isolation of enterococci were independently associated with treatment failure. The study likewise identified several predictors for the presence of enterococcus and this included age, APACHE II score pre-infection length of hospital stay and post-operative infections. Interestingly, patients with enterococcus isolated at initial drainage were less likely to have an appendiceal source but more likely to have a colonic or small bowel source. (LEVEL II EVIDENCE)

Enterococci are unlikely pathogens in healthy patients with infections that are diagnosed rapidly and treated definitively but they may be selected as pathogens in patients who are elderly, debilitated, immunocompromised, severely ill, hospitalized for prolonged periods, or are undergoing a re-operation for surgical complications or intractable disease. In fact, most experts recommend that coverage against Enterococcus must be initiated only when a patient shows no clinical improvement or response despite having been previously treated with antibiotics or in situations where the organism is persistently isolated in repeat cultures. (LEVEL III EVIDENCE)

Data are conflicting regarding the role of Pseudomonas isolated in primary cultures. Pseudomonas aeruginosa is isolated in initial cultures of appendiceal specimens and specimens collected after penetrating trauma at rates that vary from 5-20 per cent in various US hospitals. A review of two studies (Gorbach 1993) in which relatively resistant strains of Pseudomonas and Enterobacter were isolated in initial cultures showed no advantage for a clindamycin/aminoglycoside regimen over a single agent such as cefoxitin or moxalactam. Another community-based study found no advantage in including an aminoglycoside in the initial regimen even when Pseudomonas was present in primary cultures. (LEVEL III EVIDENCE)

A randomized double-blind controlled trial (Solomkin 2002) involving 615 evaluable adult patients was done (60% of whom had complicated appendicitis) to determine the efficacy and safety of ertapenem compared to tazobactam-piperacillin in the treatment of complicated intra-abdominal infections. The clinical cure rate for ertapenem of 79.3 per cent was comparable to that following piperacillin-tazobactam of 76.2 per cent. The ARR was 3.1 per cent (95% CI 3.6 to 9.8). The efficacy rate for ertapenem of 88.6 per cent was likewise comparable to that of piperacillin-tazobactam of 90.3 per cent. (LEVEL I EVIDENCE)

A randomized controlled trial (Allo 1999) involving 250 patients was done to compare ticarcillin-clavulanic acid with imipenem-cilastatin in the treatment of complicated appendicitis. There was no statistically significant difference in the clinical success rates (96.9% vs. 95.9%) and bacteriologic success rates (100% vs. 98.5%) between the two antibiotics. (LEVEL I EVIDENCE)

A randomized controlled trial (Sirinek 1991) involving 99 children and young adult patients was done to compare the efficacy of ticarcillin-clavulanic acid with the combination of clindamycin and gentamicin for complicated appendicitis. There was no significant difference in the clinical cure rates (86% vs. 84%) and bacteriologic success rates (98% vs. 92%) between the two regimens. (LEVEL I EVIDENCE)

A randomized double-blind study (Christou 1996) involving 213 patients (26% of whom had perforated appendicitis) was done to compare cefoxitin with imipenem-cilastatin in the treatment of intra-abdominal infections. The resolution

rate for the cefoxitin group was 81.7 per cent compared to the imipenem-cilastatin group with 82.7 per cent. Neither treatment failure nor mortality rates differed between the two groups. (LEVEL I EVIDENCE)

A prospective randomized controlled trial (Canadian Metronidazole Clindamycin Study Group, 1983) involving 141 patients (30% of whom had acute appendicitis) was done to compare the efficacy of metronidazole with clindamycin, each with gentamicin, in the treatment of serious intra-abdominal infection. The failure rate was 5.5 per cent (4 of 72 patients) for the metronidazole-gentamicin group and 4.3 per cent (3 of 69 patients) for the clindamycin-gentamicin group. The authors concluded that clindamycin and metronidazole performed equally well as therapy for intra-abdominal infections. (LEVEL I EVIDENCE)

A prospective randomized double-blind study (Smith 1980) involving 57 patients was done to compare the efficacy of clindamycin plus tobramycin with metronidazole plus tobramycin in the treatment of intra-abdominal sepsis. The failure rate of 13 per cent for the clindamycin/tobramycin group was comparable to the 17.6 per cent failure rate for the metronidazole/tobramycin group. (LEVEL I EVIDENCE)

Combination treatment regimens in which either clindamycin or metronidazole with an aminoglycoside are used enjoy an unbroken record of efficacy in the treatment of serious intra-abdominal infections. Each of the anti-anaerobe drugs has its supporters; clindamycin is favored by some authorities because of its added spectrum of activity against staphylococci and streptococci, although it is recognized that resistant strains of anaerobes have developed and there is concern about gastrointestinal side effects. Metronidazole has excellent activity against a broad range of anaerobic bacteria but not against microaerophilic or facultative streptococci. At present, most clinicians accept that clindamycin and metronidazole are equivalent in efficacy for the treatment of intra-abdominal infections when added to aminoglycosides.

The panel of experts recommend that cases of gangrenous appendicitis be managed as uncomplicated appendicitis, i.e. administer a single dose of the antibiotic as prophylaxis. A randomized controlled trial (Bauer 1989) involving 1735 patients who underwent appendectomy either for uncomplicated or complicated appendicitis showed a 74 per cent reduction in the risk of incisional surgical site infection among clinically diagnosed patients who received cefoxitin 2 grams IV single dose intra-operatively (0.08 vs. 0.31; OR of 0.21; 95% CI 0.10 to 0.46). The ARR was 23 per cent and the NNT was 4. Among patients with gangrenous appendicitis, 30.6 per cent in the placebo group and 8.3 per cent in the cefoxitin group developed incisional surgical site infections. The ARR was 22.3 per cent and the NNT was 5. However, there was no significant reduction in the risk for the development of an intra-abdominal abscess (1/109 vs. 2/72; OR of 0.33; 95% CI 0.03 to 3.29). The authors concluded that a single dose of cefoxitin given before surgery is sufficient and not inferior to post-operative antibiotic

treatment in preventing incisional surgical site infection after appendectomy for gangrenous appendicitis. (LEVEL I EVIDENCE).

Successful treatment of intra-abdominal sepsis entails the removal of the source of infection, eradication of residual bacteria and metabolic and hemodynamic support to counteract the physiologic alterations that occur with sepsis. The panel of experts believe that in gangrenous appendicitis, emphasis should be placed on effective surgical intervention that includes removal of the source of infection since source control is perhaps the most important of these treatment modalities. (LEVEL III EVIDENCE)

Sequential therapy from intravenous to oral antibiotics may be considered among patients with perforated appendicitis who need prolonged antibiotic therapy but who can tolerate oral intake. In the pilot trial (Rice 2001) comparing prolonged intravenous antibiotic therapy using ampicillin, gentamicin plus clindamycin with sequential therapy utilizing intravenous ampicillin, gentamicin plus clindamycin followed by oral amoxycillin-clavulanic acid plus metronidazole for children with perforated appendicitis, the success rates of the two regimens were found to be equivalent. (LEVEL II EVIDENCE)

A randomized controlled trial (Cohn 2000) involving 459 adult patients with complicated intra-abdominal infections (34% of whom had appendicitis) showed that patients who have clinically improved after being treated with intravenous antibiotics for at least 24 hours can be safely switched to oral antibiotic therapy. In this study, the patients were initially given either tazobactam-piperacillin or a combination of ciprofloxacin plus metronidazole intravenously. The combination of oral ciprofloxacin and metronidazole was then used for sequential therapy. Of the 282 patients who were evaluated for efficacy (151 CIP + MET, 131 PIP/TAZO), 64 per cent CIP + MET and 57 per cent PIP/TAZO patients were considered candidates for oral therapy. Overall clinical resolution rates were significantly higher for CIP + MET (74%) compared with PIP/TAZO (63%). The corresponding rates in the subgroup suitable for oral therapy were 85 per cent for CIP + MET and 70 per cent for PIP/TAZO. Incisional surgical site infection rates were lower in CIP + MET (11%) than in PIP/TAZO patients (19%). The mean length of stay was 14 days for CIP + MET and 17 days for PIP/TAZO patients. In this study, sequential therapy after 48 hours among eligible patients was shown to generate cost savings. Initial therapy with intravenous ciprofloxacin and metronidazole also allows switching to the oral preparation using the same drugs with equivalent bioavailability in adult patients with complicated appendicitis. (LEVEL I EVIDENCE)

The above-mentioned trials have clearly documented the importance of antibiotics in the treatment of acute appendicitis. However, the true value of one anti-infective regimen over another has become difficult to substantiate in current practice because of the potency of the currently available choices. In addition, although a wide variety of antibiotics that might be useful in the treatment of acute appendicitis have been around for the past several years, only a few have

sufficient published clinical experience to recommend their use. Despite these limitations and in order to provide guidance to surgeons in regard to the selection of the appropriate anti-infective therapy, the panel of experts based their recommendations on the analysis of the in vitro activity against enteric bacteria, the results of experiments in animal models, a review of the available prospective randomized clinical trials and certain theoretical concerns regarding the pharmacokinetics, mechanisms of action, safety profile and cost of the different antimicrobial agents.

Clinical and laboratory tools may be used to decide when to discontinue antibiotic therapy. A prospective study (Hoelzer 1999) involving 33 patients was done to determine the value of the following parameters as guides in deciding when antibiotic therapy can be safely discontinued: afebrile for 24 hours, ability to tolerate food intake and a normal WBC count with 3 per cent or less band forms. Of the 32 children who were given antibiotics until they satisfied all the three criteria, 31 patients had unremarkable courses of recovery without any development of incisional surgical-site or organ-space infections (predictive value of criteria of 97 per cent). One patient who met the criteria required re-hospitalization for treatment of intra-abdominal abscess. Another patient was discharged prematurely as he was still having fever within 24 hours before discharge, although he was eating and his WBC count was normal. He was readmitted for surgical drainage of an intra-abdominal abscess, yielding a 100 per cent predictive value for the criterion mismatch. These findings, however, need to be validated among adult patients. (LEVEL II EVIDENCE)

Should gram stain and culture and sensitivity be routinely done in acute appendicitis?

Gram stain and culture with sensitivity testing of intra-operative specimens (purulent peritoneal fluid or tissue) should not be routinely performed except in high-risk and immuno-compromised patients.

LEVEL II EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

A retrospective study (Bilik 1998) involving 499 pediatric patients was done to determine the usefulness of intra-operative peritoneal cultures in patients with acute appendicitis. The subjects were divided into those with acute non-perforated appendicitis (Group A) and those with perforated appendicitis (Group B). Intra-peritoneal cultures were obtained in 30.1 per cent of the patients in group A and in 67.1 per cent of the patients in group B. Of the patients in group A, 57.9 per cent were treated preoperatively and 50.8 per cent were treated postoperatively by a single antibiotic agent whereas 58 per cent of the patients in Group B were started and kept on triple-agent antibiotics for significantly longer

periods. There was no significant difference between the two groups with respect to the postoperative complication rates (incisional surgical site infection, intra-abdominal abscess and small bowel obstruction) whether intra-abdominal cultures were obtained or not (5.9 per cent versus 4.7 per cent in group A and 21.2 per cent versus 21.9 per cent in group B, p value> 0.05). The authors concluded that the presence of colonic flora can be predicted in perforated appendicitis so antibiotic therapy should be given without any abdominal cavity culture. (LEVEL II EVIDENCE)

A retrospective study (McNamara 1993) involving 200 patients was done to evaluate the influence and use of intra-peritoneal cultures in the management of patients with acute appendicitis. Intra-operative cultures were obtained in 131 patients (65.5%), 80 of 136 patients (59%) in group A and 43 of 48 patients (90%) in group B. There were positive culture results in 16 per cent of the cultures in patients with uncomplicated appendicitis and in 88 per cent of the cultures in patients with complicated appendicitis. The complication rate in the nine patients with complicated appendicitis who had positive cultures and in whom antibiotic modifications were made based on the results was 25 per cent in contrast to the 29 per cent complication rate for the group as a whole. The authors concluded that intra-operative cultures in patients with uncomplicated appendicitis are rarely positive and do not influence antibiotic therapy or patient management. In patients with complicated appendicitis, antibiotic changes do not seem to alter patient outcome. Surgeons tend to rely on the proven efficacy of empiric antibiotic therapy and other basic surgical principles to afford the best outcome for their patients. (LEVEL II EVIDENCE)

The studies of Bilik and McNamara both recommend that the practice of obtaining routine intraperitoneal cultures in patients with appendicitis be abandoned because the etiologic agents causing peritonitis are highly predictable and effective broad-spectrum antibiotic therapy is currently available.

A review of 5 trials of antibiotic treatment for intra-abdominal infections (Hopkins 1993) involving 175 patients (83% of whom had appendicitis) was done to evaluate the relationship of the susceptibility patterns of intra-abdominal isolates to the incidence of therapeutic failures. Of 131 patients with resolution of the intra-abdominal infection, 57 patients (44%) had resistant isolates while 36 of 44 patients (82%) with post-operative infectious complications had resistant isolates. These results confirm the finding that if the original antibiotic therapy is inadequate, the number of post-operative infections increases. (LEVEL III EVIDENCE)

The panel of experts recommend that gram stain and culture and sensitivity not be routinely done except in high-risk and immuno-compromised patients in whom there is an increased risk of non-resolution of the intra-abdominal infection and increased mortality rates should there be inadequate empiric antibiotic coverage. (LEVEL III EVIDENCE)

How should localized peritonitis be managed?

No necrotic tissue or purulent material should be left behind as much as possible. General peritoneal lavage is not recommended for localized peritonitis. Intra-peritoneal drains, while most useful in patients with a well-established and localized abscess cavity, should be selectively utilized.

LEVEL II EVIDENCE
GRADE A RECOMMENDATION

SUMMARY OF EVIDENCE

The major goals of operative management in peritonitis are to reduce the bacterial inoculum and to prevent recurrent or persistent sepsis. At operation, gross or purulent exudates should be aspirated, and loculations in the pelvis and paracolic gutters should be gently opened and debrided. An attempt should be made to remove particulate debris which act as a nidus for intraperitoneal infection. Fibrin, the building block of adhesions, is believed to act as a nidus for infection. This was the historical rationale for radical peritoneal debridement which has long since fallen from favor. It is tedious, time-consuming, leads to significant blood loss and the only randomized controlled trial showed no benefit over the conservative approach.

Only one randomized controlled trial (Schein 1990) was done to compare no lavage to saline lavage with or without antibiotics in patients with proven intra-abdominal infections. Eighty seven patients operated on for diffuse or localized peritonitis were randomly assigned to one of three groups. There were no differences in mortality, morbidity or length of hospital stay between the three groups. (LEVEL II EVIDENCE)

Several antiseptics added to lavage fluid have been studied in the treatment of secondary peritonitis. These include povidone-iodine, noxythiolin, hydrogen peroxide, taurolin and chlorhexidine. No benefit has been demonstrated with any and many were found to be injurious.

The decision whether or not to place a drain in the post-operative abdomen following secondary peritonitis has long been a matter of controversy. The indications for drainage are: evacuation of an abscess, establishment of a controlled fistula and, if indicated, to provide post-operative lavage. The disadvantage of using drains is that they may erode into the bowels or vessels or provide external bacteria access into the peritoneum. Furthermore, by providing a site for bacterial adherence and fibrin formation, drains or other foreign bodies appear to act as adjuvants for infection.

A prospective study (MacKellar 1986) involving 158 children was done to assess the factors which contribute to the frequency of surgical site infection. The authors found that 4 of 19 patients (21%) who had drains compared to only 4 of

139 patients (3%) without drains developed post-operative infections. (LEVEL II EVIDENCE)

A retrospective study (Kokoska 1998) involving 279 patients was done to define the risk factors associated with the development of post-operative complications in children undergoing treatment for perforated appendicitis. The authors found that all children who had a post-operative abscess had more than 5 days of symptoms before operation. Within this subgroup, drain placement was associated with decreased postoperative abscess formation and shorter duration of fever and length of hospitalization. The incidence of mechanical obstruction or ileus was not increased and the rate of wound infection was actually lower after drainage. They concluded that drain placement appears to be helpful in children with late diagnosis but is of little benefit when the duration of symptoms is less than 5 days. (LEVEL II EVIDENCE)

The guidelines for usage of drains have been previously reported by Pissiotis et. al. (1993):
1. No drain is better than any drain.
2. Drain selection should consider anticipated risk of complication.
3. Active closed-system suction drains are better than simple passive drains.
4. Drain placement should be in a dependent area and exit near watertight anastomosis through a separate stab wound.
5. Drains require careful observation for malfunction, frequent irrigation and early removal when no longer required.

(LEVEL III EVIDENCE)

What is the appropriate method of wound closure in patients with complicated appendicitis?

The incision may be closed primarily in patients with complicated appendicitis.

LEVEL I EVIDENCE
CATEGORY A RECOMMENDATION

SUMMARY OF EVIDENCE

A meta-analysis (Rucinski 2000) of 27 prospective randomized trials and prospective trials compared with historical controls and involving 2,532 patients was done to determine the appropriate manner of wound closure for patients who undergo surgery for complicated appendicitis. Of the 1,724 patients in the 19 studies who had primary wound closure, 91 patients (4.7 %, 95% CI 3.7% to 5.7%) developed incisional surgical site infection while of the 808 patients in 8 studies who had delayed closure, 42 patients (4.6 %, 95% CI 3.2% to 5.9%) developed incisional surgical site infection. The RRR is 0.02 per cent, the ARR is 0.10 per cent and the NNT is 10. Primary wound closure therefore did not increase the incidence of incisional surgical site infection compared with delayed closure. (LEVEL I EVIDENCE)

What is the optimal timing of surgery for patients with peri-appendiceal abscess?

A patient with a peri-appendiceal abscess should undergo surgery as soon as the diagnosis is made.

<div align="center">

LEVEL III EVIDENCE
CATEGORY A RECOMMENDATION

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SUMMARY OF EVIDENCE

A prospective study (Kogut 2001) involving 101 patients was done to determine the efficacy of interval appendectomy for the treatment of perforated appendicitis with or without abscess and to identify factors associated with failures and complications. The 79 patients (78%) successfully treated with interval appendectomy had an over-all complication rate of 6.3 per cent and the total hospitalization averaged 5.2 days. Twenty-two patients (22%) who were initially treated non-operatively but who subsequently required early appendectomy had a complication rate of 50 per cent and were hospitalized an average of 12.8 days. Patients who required early appendectomy had a band count greater than 15 per cent on their initial differential blood cell count (22.6% vs. 7.6%, p < .0001) than those who were successfully treated with interval appendectomy. Other parameters such as patient age, duration of illness, temperature, finding of a fecalith on x-ray, identification of an abscess amenable to percutaneous drainage and the WBC count were not helpful in predicting the success or failure of interval appendectomy. The authors concluded that there is an 86.3 per cent chance of success for interval appendectomy in patients with a band count less than 15 per cent. In contrast, patients with a band count of 15 per cent or greater would require immediate operation to avoid the high rates of failure and complications associated with interval appendectomy. (LEVEL II EVIDENCE)

A retrospective study (Oliak 2001) involving 155 patients was done to compare initial operative with non-operative management for periappendiceal abscess. For the initial non-operative management group, the failure rate was 5.8 per cent and the appendicitis recurrence rate was 8 per cent after a mean follow-up of 36 weeks. There was no statistically significant difference between the initial non-operative and the initial operative group in terms of length of stay (9 vs. 9 days), days until WBC count normalized (3.8 vs. 3.1 days), days until temperature normalized (3.2 vs. 3.1 days), and days until regular diet was tolerated (4.7 vs. 4.6 days). The complication rate was significantly lower in the non-operative group (17% vs. 36%; p<0.008). The author's concluded that patients undergoing non-operative management have a lower risk of complications but are at risk for recurrent appendicitis. (LEVEL II EVIDENCE)

Although the optimal treatment of the appendiceal mass remains unclear because of the lack of randomized studies to provide conclusive evidence, the panel of experts recommend that a patient with a peri-appendiceal abscess should undergo appendectomy as soon as the diagnosis is made. Early appendectomy will eliminate the need for interval appendectomy with its associated risks, decrease the total hospital stay and complications associated with conservative treatment and avoid the high complication rate that results from a failure of the initial non-operative approach. (LEVEL III EVIDENCE)

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