Effect of Prophylactic Antibiotics in Acute Nonperforated Appendicitis

A Prospective, Randomized, Double-blind Clinical Study

RONALD W. BUSUTTIL, M.D., PH.D., F.A.C.S., ROBIN K. DAVIDSON, M.S., MARJORIE FINE, M.D., RONALD K. TOMPKINS, M.D., M.SC., F.A.C.S.

From the Department of Surgery, Division of General Surgery, UCLA Center for the Health Sciences, Los Angeles, California

A prospective, randomized, double-blind clinical study was performed to determine the efficacy of short-term (24 hr) perioperative antibiotics in preventing septic complications after emergency appendectomy for nonperforated appendicitis. The patients were stratified into three clinical arms: Group I (placebo, n = 45), Group II (cefamandole, n = 46) and Group III (cefamandole plus carbenicillin, n = 45). The three groups of patients were similar in regard to age, sex, duration of operation and pathologic classification of the appendix. The overall incidence of infection in the study was 5.1%. The infection rates in Groups II (2.2%) and III (0%) were significantly lower than Group I (placebo) (13.3%), ($p < 0.05$). No difference was observed between cefamandole alone and cefamandole plus carbenicillin. Average postoperative hospital days per patient for each group was: Group I—3.8 days; Group II—2.9 days; Group III—3.1 days. Cost analysis of hospitalization including cost of prophylactic antibiotics revealed a $247.99 per patient saving for Group II versus Group I and $95.53 for Group III versus Group I. Systemic prophylactic antibiotics can successfully reduce septic complications after appendectomy for nonperforated appendicitis, and a single drug (cefamandole) directed at the facultative pathogens is as effective as double drug therapy, which includes specific anaerobic coverage.

ACUTE APPENDICITIS IS THE MOST common cause of acute surgical abdomen, and appendectomy is the most frequently performed emergency operation. Despite the fact that the mortality rate has been dramatically reduced following appendectomy over the last three decades, septic complications continue to be a significant problem, occurring in a large percentage of patients. Although preoperative administration of prophylactic antibiotics has proven to be a safe and effective means to reduce wound and intra-abdominal septic complications after selected potentially contaminated operations, the role of such prophylactic therapy has not been adequately established to be beneficial in patients undergoing appendectomies for acute nonperforated appendicitis.

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Reprint requests: Ronald W. Busuttil, M.D., Ph.D., F.A.C.S., Department of Surgery, UCLA Center for the Health Sciences, Los Angeles, California 90024.

Materials and Methods

A prospective randomized double-blind clinical trial was conducted on the surgical service of the UCLA Medical Center, Los Angeles, California, between May 1977 and February 1980. During this time period, 189 consenting patients were enrolled in the study. Criteria for inclusion in the trial included adults and children admitted with a presumptive diagnosis of acute appendicitis and scheduled for appendectomy. Exceptions to inclusion in the study included: 1) age (under four years old), 2) allergy to cephalosporins or penicillins, 3) antibiotic therapy within 72 hours preceding operation, 4) pregnancy, 5) inability for a 30-day postoperative follow-up, and 6) serious underlying illness expected to require antibiotic therapy. In addition, those patients who, at operation, were found to have a ruptured appendix or bacterial peritonitis not originating from the appendix were excluded from the study. Patients who underwent appendectomy for a normal appendix and had no other intra-abdominal diseases were included.

Protocol

The patients were randomized into three groups of the trial. The details of randomization were un-

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known to all concerned with patient care or surveillance, and the master key was kept by the experimental protocol section of the hospital pharmacy, which dispensed the drugs.

Each patient was administered either cefamandole nafate (2 g) plus carbenicillin (3 g), cefamandole nafate (2 g) plus equivalent volume of diluent, or placebo (2 equal volumes of diluent) intravenously 30–45 minutes before operation, four hours after operation and every six hours thereafter for 24 hours. Appropriately scaled down doses (cefamandole 100–150 mg/kg/day and carbenicillin 400–500 mg/kg/day) were administered to children. The antibiotics and placebos were packaged identically in opaque numbered vials.

All operations were performed by resident surgeons under direct attending supervision. To maintain uniformity in the operative procedure, a standard operative protocol was followed. This included a 10 minute Iodophor® preparation, use of Steridrape®, right lower quadrant muscle splitting incision, minimal handling of the appendix, appendiceal stump inversion, glove change prior to closure, wound closure with absorbable (polyglycolic acid) sutures, and strict avoidance of both antibiotic irrigation and drainage. Primary skin closure was performed in all patients. Upon entering the abdomen, both aerobic and anaerobic cultures were taken of the appendiceal fossa, and the subcutaneous tissue of the incision at the time of closure.

Bacteriology and Sensitivity Testing

All organisms were cultured at the Clinical Microbiology Laboratories of the UCLA Center for the Health Sciences and identified by standard criteria.[1] The standard reference strains of *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27852 ("Boston" strain) and *Staphylococcus aureus* ATCC 25923 were used as internal controls with the facultative organisms. Two control strains of *B. fragilis* (UCLA #55973 and #55711) were tested simultaneously with all anaerobic isolates.

Antimicrobial susceptibility testing of facultative organisms was performed by the ICS-WHO agar dilution method.[2] The following ranges of drug concentrations were tested: cefamandole: 0.5–16 μg/ml and carbenicillin: 64–256 μg/ml. An inoculum of approximately 10^4 organisms diluted from broth cultures in the logarithmic phase of growth was used.

Anaerobic bacteria were tested by the agar dilution method, using Wilkins-Chalgren medium (pH = 7.2).[3] The following ranges of drug concentrations were tested: cefamandole: 0.5–16 μg/ml; clindamycin: 0.03–4 μg/ml; and carbenicillin: 64–128 μg/ml. An inoculum of 10^5 organisms was used after a 72-hour incubation on blood agar and an 18–24 hour incubation in Schaedler broth at 37 C. The plates were read after incubation at 37 C in a GasPak® jar (BBL Microbiology Systems, Cockeysville, Maryland) for 48 hours.

TABLE 1. *Reasons for Exclusion of Patients from the Study*

	Group I	Group II	Group III
Perforated appendix	7	10	10
Did not receive drug	6	9	5
Physician refusal	1	1	—
Preoperative exclusion	1	—	1
Intraoperative diagnosis other than appendicitis	—	1	1
Total	15	21	17

Patient Surveillance

All the patients were examined daily by the operative team, and carefully assessed for the development of wound, intra-abdominal or remote infectious complications. Upon discharge from the hospital, all patients were re-evaluated two and four weeks after operation for the development of late infection. A wound was considered to be infected when there was a collection of pus which was drained spontaneously or by incision. Appropriate aerobic and anaerobic cultures were taken from the infected wound, and aerobic and anaerobic isolates were tested for sensitivity to the prophylactic antibiotics, *i.e.* cefamandole and carbenicillin as described above.

In addition to monitoring septic complications, careful attention was paid to recording specific drug side effects, details critical to the general status of the patient and to the conduct of the operative procedure. Assessment was also made of the duration of postoperative hospital stay and the hospital cost incurred for each patient. Statistical analysis of the results by chi square analysis was conducted by the Biomedical Computer Center, University of California at Los Angeles. The study was approved by the Human Subjects Protection Committee and informed consent procedures were strictly adhered to in all cases.

TABLE 2. *Patient Population Summary: Distribution by Sex*

	Group I		Group II		Group III	
	No. Pts.	Per Cent	No. Pts.	Per Cent	No. Pts.	Per Cent
Male	31	68.9	25	55.6	33	73.3
Female	14	31.1	21	44.4	12	26.7
Total	45	100	46	100	45	100

TABLE 3. *Patient Population Summary: Age Distribution*

	Group I		Group II		Group III	
	No. Pts.	Per Cent	No. Pts.	Per Cent	No. Pts.	Per Cent
Under 3	0	0	0	0	0	0
3–14	7	15.6	8	17.8	9	20
15–25	21	46.7	22	48.9	16	35.6
26–35	15	33.3	12	24.4	12	26.7
36–45	2	4.4	3	6.7	3	6.7
46–55	0	0	0	0	2	4.4
56–65	0	0	1	2.2	2	4.4
Over 65	0	0	0	0	1	2.2
Total	45	100	46	100	45	100

Results

A total of 189 patients were entered into the study, and 136 were considered evaluable. Reasons for rejecting the 53 patients from final analysis are shown in Table 1, which indicates equal stratification of exclusion among groups. Of the evaluable patients, 89 were males and 47 were females (Table 2). The patients ranged in age from 4 to 75 years, with a mean of 23 years. The majority of patients in the three groups were in the second and third decades of life (Table 3).

The duration of the operation, in minutes, and the pathologic classification of the appendix, two factors which would influence the eventual development of postoperative infection, were assessed. There was no significant difference in the duration of operation among the three groups (Table 4). Similarly, classification of the appendix according to gross and microscopic appearance into the categories: normal, acute, suppurative, and gangrenous revealed no significant differences among the three groups (Table 5).

Aerobic and anaerobic cultures of the appendiceal fossa were obtained in all patients. This demonstrated an increase in positive cultures as the appendicitis progressed from acute inflammation through suppuration to gangrene. There were equal numbers of positive aerobic and anaerobic cultures in the acute and suppurative cases of appendicitis; however, anaerobes were approximately 1.5 times more frequent than aerobes in the gangrenous appendix (Table 6). A similar analysis was conducted of subcutaneous tissue cultures obtained on closing the abdomen, and this revealed similar findings with a greater number of positive cultures as the inflammation progressed (Table 7). An analysis of peritoneal cultures obtained at the time of appendectomy demonstrated that there was an equal distribution of positive cultures among the three groups in the study, indicating similar frequency of potential bacterial contamination which would influence the infection rate (Table 8).

TABLE 4. *Duration of Operation*

	Minutes		
	Group I	Group II	Group III
Range	25–100	35–100	25–120
Mean	56 ± 17	61 ± 20	60 ± 23

TABLE 5. *Pathology of Appendix*

	Group I		Group II		Group III	
	No. Pts.	Per Cent	No. Pts.	Per Cent	No. Pts.	Per Cent
Normal	6	13.3	5	10.9	7	15.6
Acute	15	33.3	15	32.6	15	33.3
Suppurative	21	46.7	22	47.8	21	46.7
Gangrenous	3	6.7	4	8.7	2	4.4
Total	45	100	46	100	45	100

The majority of aerobic bacterial isolates recovered from the peritoneal fluid was *E. coli*. Viridans streptococci and enterococcus were second and third in frequency, respectively. With the exception of enterococcus, greater than 95% of aerobic isolates were sensitive to cefamandole at concentrations of less than 16 μg/ml. *B. fragilis* and *Eubacterium sp.* were the predominant anaerobic organisms cultured at the time of operation. These anaerobes were resistant to cefamandole at a concentration of 16 μg/ml, however, 90% were sensitive to carbenicillin at a concentration of 128 μg/ml.

Postoperative Infection

A total of seven postoperative infections occurred, for an overall incidence of just over 5%. There were six infections in Group I (placebo), one infection in Group II (cefamandole) and zero infections in Group III (cefamandole plus carbenicillin). The incidence of wound and intra-abdominal infection was significantly lower ($p < 0.05$) for both Groups II and III, compared with Group I (placebo) (Table 9). There was no significant difference in infection rate between Group II

TABLE 6. *Positive Peritoneal Cultures*

Appendix Pathology	Aerobic		Anaerobic	
	Number	Per Cent	Number	Per Cent
Normal	1/15	6.6	5/15	33.3
Acute	3/43	7.0	3/42	7.1
Suppurative	9/55	16.4	11/54	20.4
Gangrenous	4/9	44.4	6/9	66.7

TABLE 7. *Positive Subcutaneous Tissue Cultures*

Appendix Pathology	Aerobic		Anaerobic	
	Number	Per Cent	Number	Per Cent
Normal	1/15	6.6	5/15	33.3
Acute	5/43	11.6	11/41	26.9
Suppurative	8/53	15.1	16/52	30.7
Gangrenous	3/9	33.3	5/9	55.6

TABLE 8. *Positive Peritoneal Cultures*

	Group I		Group II		Group III	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
Aerobic	7/43	16.2	4/39	10.2	6/40	15.0
Anaerobic	10/43	23.2	9/39	23.0	6/38	15.7

No statistical difference between positive aerobic or anaerobic cultures among groups ($p > 0.1$).

(cefamandole) and Group III (cefamandole plus carbenicillin) ($p > 0.3$). A summary of each of those patients who developed postoperative infections is shown in Tables 10 and 11. In Group I (placebo), there were three subcutaneous wound infections, two wound infections extending subfascially and requiring suction drainage, and one wound and intra-abdominal abscess, which required abdominal exploration and drainage. In Group II, (cefamandole) one subcutaneous wound infection occurred.

All aerobic organisms which were cultured from postoperative infected wounds from patients who received placebo were sensitive to cefamandole at a concentration of <16 μg/ml. In the one infection which occurred in the cefamandole group, Enterobacter was cultured from the blood and wound and this organism was resistant to cefamandole at a concentration of >16 μg/ml. In addition, this latter patient developed a wound hematoma secondary to systemic administration of heparin for a pulmonary embolus which occurred on the fifth day after operation, that may have contributed to the infection. The addition of prophylactic use of carbenicillin in this patient would not have been beneficial since neither the Enterobacter nor the *B. fragilis* were sensitive to carbenicillin.

Noninfectious postoperative complications were infrequent in this study. The most frequent among all three groups was a transient elevation of the SGOT and alkaline phosphatase levels, occurring in three patients, and a wound hematoma (three patients). There was no decrease in the likelihood of postoperative respiratory or urinary tract infections by the administration of prophylactic antibiotics. No patient developed a drug allergy. With the exception of the one patient mentioned above, who developed an infection with Enterobacter, emergence of resistant bacterial strains causing superinfection did not occur by administering antibiotics prophylactically.

Cost Analysis

The number of postoperative days spent in the hospital for each of the groups is summarized in Table 12. The average postoperative stay was 3.8 days for Group I (placebo), 2.9 days for Group II (cefamandole) and 3.2 days for Group III (cefamandole plus carbenicillin). Calculation of the total cost per patient of hospitalization including per diem rate, cost of therapeutic antibiotic for infection and cost of prophylactic antibiotic is shown in Table 13. The use of prophylactic antibiotics resulted in a substantial savings ($247.99 per patient) for those patients who received cefamandole compared with those patients who received a placebo. The use of cefamandole plus carbenicillin also resulted in a saving, but this was decreased to $95.53 per patient.

Discussion

In the present study, the prophylactic administration of cefamandole or cefamandole plus carbenicillin were equally effective in significantly reducing the rate of wound infections following appendectomy for acute nonperforated appendicitis when compared with the administration of a placebo. The use of prophylactic antibiotics in nonperforated appendicitis has been questioned by some authors[4] because of the relatively minor degree of bacterial inoculation in these patients and the relatively low incidence of infection. However, a large number of reports[5–9] indicate that, despite a positive peritoneal culture in less than 20% of these patients, the infection rate is significant, and ranges from 10–20%. In a previous retrospective study reported from our institution, the incidence of infection in patients who received no prophylactic antimicrobials for nonperforated appendicitis was 10.2%. This is comparable to an infection rate of 13.3%, which was found in the placebo group of the

TABLE 9. *Postoperative Infections*

	Number	Per Cent
Group I	6/45	13.3
Group II	1/46	2.2
Group III	0/45	0

Group II vs. Group I—$p < 0.05$.
Group III vs. Group I—$p < 0.025$.
Group II vs. Group III—$p > 0.3$.

TABLE 10. *Infections in Group I (Placebo)*

Patients	Pathology of Appendix	Surgery Duration (Min)	Peritoneal Culture		Infection Type	Wound Culture		Same Organism as Peritoneal Culture?	
			Aerobic	Anaerobic		Aerobic	Anaerobic	Aerobic	Anaerobic
40 yr. m	acute	80	negative	negative	wound	negative	negative	—	—
10 yr. m	suppurative	25	*E. coli*	*B. fragilis* *B. melaninogenicus* *Fusobacterium* *Peptostreptococcus* *Eubacterium*	wound and subfascial	*Enterococcus*	same as peritoneal	no	yes
12 yr. m	suppurative	55	not done	not done	wound	*E. coli*	*B. fragilis*	—	—
28 yr. m	suppurative	45	*e. coli* *Pseudomonas*	*B. fragilis* *B. melaninogenicus*	wound	*E. coli* *Pseudomonas* Viridans strep	no growth	yes	no
15 yr. m	gangrenous	55	no growth	*B. fragilis* *Peptostreptococcus* *Eubacterium*	wound and intra-abdominal	*E. coli* Viridans strep	*B. fragilis* *Peptostreptococcus* *Fusobacterium*	no	yes
27 yr. m	suppurative	50	no growth	no growth	wound and subfascial	Viridans strep *E. coli*	no growth	no	no

present study, underscoring the magnitude of the problem of postoperative infection after appendectomy for nonperforated appendicitis. Based on the guidelines which have been proposed for appropriate preventative antibiotic usage,[10,11] an incidence of wound infection of approximately 12% in nonperforated appendicitis is of sufficient magnitude to justify prophylactic antimicrobial administration.

The factors which are operative in the development of wound and intra-abdominal infection after appendectomy are multiple. These include, lack of excellence in surgical technique, impairment of local or systemic host defenses and, most importantly, the presence of significant peritoneal bacterial contamination. All of these factors must be considered and controlled in evaluating any antimicrobial regimen which is proposed to decrease the infection rate. Although similar studies[4,6,7,12] testing systemic antibiotic prophylaxis in acute appendicitis have been reported, some of these factors have not been controlled, thus, diluting the direct effect of the antimicrobial prophylaxis as the cause of a decreased infection rate. The present study was carefully designed to control these factors in that: appendectomy was performed according to a standard protocol by surgical residents under attending surgeon supervision in one university hospital; no topical antiseptics or antibiotics were used; no drainage was employed; and the degree of peritoneal contamination as determined by the number of patients who had positive peritoneal cultures was identical in each group. Therefore, we consider the reduced infection rate noticed in the

TABLE 11. *Infections in Group II (Cefamandole)*

Patients	Pathology of Appendix	Surgery Duration (Min)	Peritoneal Culture		Infection Type	Wound Culture		Same Organism as Peritoneal Culture?	
			Aerobic	Anaerobic		Aerobic	Anaerobic	Aerobic	Anaerobic
41 yr. m	suppurative	75	*E. coli*	*B. fragilis*	bacteremia and wound	blood and wound: *Enterobacter* wound: *E. coli*	wound: *B. fragilis* *Eubacterium*	yes	yes

groups which received cefamandole or cefamandole plus carbenicillin to be a direct effect of antibiotic prophylaxis.

Post appendectomy infections are, in the majority of patients, caused by a polymicrobial flora consisting of facultative aerobes and obligate anaerobes. *E. coli* is the most frequently cultured aerobe from both contaminated peritoneal fluid and from infected wounds.[6,7,13] Of the anaerobes, *B. fragilis* is the most common pathogen, and, in one study,[14] was cultured from the appendiceal fossa in 37% of the patients undergoing appendectomy and in 78% of the patients where bacteria were isolated from this sight. Our study supports this finding of the prevalence of *E. coli* and *B. fragilis* contamination in acute appendicitis. A positive peritoneal culture in our study yielded *E. coli* in 93% of the patients and *B. fragilis* in 62%. In addition, there was a direct correlation with the degree of appendiceal inflammation and the percentage of positive peritoneal and subcutaneous tissue cultures.

Although a wide variety of antimicrobial agents, both singly and in combination, have been used for antimicrobial prophylaxis in acute appendicitis,[4-9] a cephalosporin alone appears to be best suited for this role. The reasons for this include: the low incidence of toxicity; favorable pharmacokinetic properties which allow rapid equilibration between blood, interstitial fluid and tissue that results in bactericidal levels when the drugs are administered 30–45 minutes prior to surgery; and excellent spectrum for facultative pathogens. An additional factor which is most important is that the cephalosporins are not routinely used in the treatment of established intra-abdominal infections, a condition which would preclude their use prophylactically.

In this study, cefamandole was chosen over the other cephalosporins because of its extended Gram negative aerobic spectrum and because its pharmacokinetic properties are similar to cefazolin and cephaloridine, two drugs which have been proven to be effective prophylactically.[10,11] Carbenicillin was chosen because of its added coverage of *B. fragilis* and the absence of severe toxicity, which is associated with clindamycin and chloramphenicol, the two other antibiotics used commonly to cover *B. fragilis*.

Although it would seem appropriate and necessary to administer antibiotic prophylaxis against both aerobic and anaerobic contaminants, the evidence to support this point is quite controversial.[4,8,10,15] In one study, lincomycin, an agent with activity against *B. fragilis* but not Gram negative aerobes, was tested prophylactically in acute appendicitis. The incidence of wound infection was significantly lower (6%) in the antibiotic group than in the control (17%). However, in this study, an agent effective against aerobes was not tested for comparison, and wound drainage was used which may have had an adverse effect on infection formation. Metronidazole has been compared with ampicillin in prophylaxis of acute appendicitis, but only showed superiority in patients with gangrenous and perforated appendices.[4] The infection rate of the metronidazole group was 47% versus 16 for those receiving ampicillin. On the other hand, Fine and Busuttil[5] reported no difference in infection rates after nonperforated appendicitis when gentamicin and clindamycin were compared with a variety of single agents which do not possess an anaerobic spectrum. In a well designed double-blinded clinical trial, Foster and O'Toole[8] demonstrated that prophylactic cephaloridine significantly decreased the rate of postoperative wound infections, compared with a placebo. The infection rate in the group treated with cephaloridine was only 1.4%, and it is highly unlikely that the addition of anaerobic coverage would significantly reduce this incidence of infection.

In the present trial, our data clearly demonstrated that cefamandole, a cephalosporin whose spectrum is primarily directed at the facultative aerobes signifi-

TABLE 12. *Postoperative Days to Discharge*

	Group I		Group II		Group III	
	No. Pts.	Per Cent	No. Pts.	Per Cent	No. Pts.	Per Cent
2 days	22	48.9	21	45.7	22	48.9
3 days	2	4.4	8	17.4	4	8.9
4 days	12	26.7	16	34.9	13	28.9
>4 days	9	20.0	1	2.2	6	13.3
Total postop days	170		135		142	
Avg. postop days/ patient	3.8		2.9		3.2	

TABLE 13. *Cost Analysis of Hospitalization*

	Group I	Group II	Group III
Total patients	45	46	45
Total patients infected	6	1	0
Total postoperative days	170	135	142
Average postoperative days/ patient	3.8	2.9	3.2
Cost of hospitalization per patient (365.00/day)	1387.00	1058.50	1168.00
Cost of therapeutic antibiotic for infection per patient*	104.53	17.04	0
Cost of prophylactic antibiotic/patient	0	168.00	228.00
Net cost/patient	1491.53	1243.54	1396.00
Saving	0	247.99	95.53

* Cost of antibiotic for 7 days × patients infected ÷ total number of patients (cost of antibiotic for 7 days = $784.00).

cantly reduced the postoperative wound infection rate, compared with a placebo. This beneficial effect was seen despite a 23.0% incidence of anaerobic growth from peritoneal cultures, and despite resistance of *B. fragilis* isolates *in vitro* to cefamandole at a concentration of 16 μg/ml. The single infection occurring in the cefamandole treated group was caused by an Enterobacter resistant to cefamandole. Furthermore, this patient was administered heparin for pulmonary embolism, and developed a wound hematoma which could have afforded enhancement of bacterial growth.

The addition of carbenicillin, an agent which was active against 90% of the anaerobic isolates in this study, did not significantly reduce the incidence of infection despite the extended anaerobic spectrum which it offered. That carbenicillin was indeed active against the anaerobes is evident by the reduction of anaerobic bacterial growth in both peritoneal and subcutaneous tissue cultures from those patients receiving carbenicillin, compared with patients receiving cefamandole alone or a placebo. These findings strongly support the hypothesis that aerobic antibiotic prophylaxis in acute appendicitis is quite effective and that it is unnecessary to add specific anaerobic coverage.

With increasing demands being placed on physicians and hospital administrators for cost containment in health care, there are certain misgivings concerning the cost of prophylactic antimicrobial usage. Our study confirms the analysis reported by Stone,[10] in which appropriately used prophylactic antimicrobials are not only cost-effective but can also result in a substantial reduction in hospitalization time per patient, by decreasing the postoperative infection rate. In the present study, one postoperative wound infection increased the hospital cost by an average of $2400.00 and the hospitalization time by five days. These figures are conservative since they do not account for the disability and additional time lost from work incurred by those patients who develop a postoperative infection. A net savings per patient of $247.99 was found when single drug prophylaxis was used. If this saving is projected to the number of patients who undergo appendectomies in the United States, a significant financial impact on health care could be potentially realized.

Based on the results of this study, we recommend that single drug aerobic perioperative prophylaxis (no longer than 24 hours) be used for patients who undergo appendectomies for acute appendicitis. The drug should be administered 30–40 minutes prior to making the surgical incision. Specific anaerobic coverage is unnecessary and may be contraindicated, since injudicious use of anaerobically oriented antibiotics for prophylaxis may result in untoward side effects and will, undoubtedly, play a role in the development of resistant microbes which will preclude the use of these agents for later specific therapy.

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Addendum

In the 12 months following the termination of the study, 54 patients have undergone appendectomy for acute nonperforated appendicitis. These patients were managed with perioperative cefamandole as described in the study and the overall infection rate was one out of 54 or 1.8%.

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