Prophylactic and Preventive Antibiotic Therapy

Timing, Duration and Economics

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Previous studies have demonstrated that administered antibiotics must be active against major anticipated pathogens and must have reached sufficient concentrations in the tissue or body fluid at risk by the time of bacterial challenge if prophylactic therapy is to be maximally effective in reducing the infection rate of potentially contaminated surgery. The need for continuing antibiotic prophylaxis beyond the day of operation, however, has been uncertain. In a prospective, randomized, double-blind study of 220 patients undergoing elective gastric, biliary or colonic surgery, perioperative administration of cefamandole plus five days of placebo was compared to perioperative plus five days of postoperative antibiotic therapy; no significant difference was found between the groups in the rate of infection of wound (6 and 5%, respectively), peritoneum (2% each) and elsewhere (6% and 5%). In another prospective, randomized, nonblind study of 451 determinant cases of 1,624 patients undergoing emergency laparotomy, cephalothin was instituted preoperatively but after peritoneal contamination had occurred (*i.e.*, abdominal trauma, etc.); continued postoperative antibiotic again failed to reduce further the wound and peritoneal infection rates, as noted on comparing perioperative therapy alone (infection rates 8 and 4%, respectively) with perioperative plus 5–7 days of postoperative treatment (10% and 5%, respectively). Analysis of these data, as well as of the extra expenses incurred by 463 patients because of infection in a previous prophylactic antibiotic study, revealed an average additional expenditure of $2,686.00 for each instance of postoperative infection of the wound and/or peritoneum; whereas savings of $300.00 per patient at risk were obtained whenever appropriate prophylactic antibiotic had been given.

THE VALUE OF PARENTERAL ANTIBIOTIC as prophylaxis against postoperative surgical infections has been substantiated both in the animal laboratory[4,9] and in scientifically controlled clinical studies.[5,8,10,12,15,17] However, preoperative administration is exceedingly important, for without adequate concentrations of antibiotic in the tissues and/or body fluids at risk prior to the time of contamination, the incidence of infection has appeared to be almost as great, if not the same, as when antibiotic has been withheld altogether.[15] Animal experiments by Burke have suggested that a three hour delay following a given bacterial challenge may be the upper limit, beyond which initiation of parenteral antibiotic therapy consistently fails to reduce the incidence and severity of subsequent wound-related infection.[4] Maximal benefit, nevertheless, can be obtained only when antibiotic has been administered before the time of inoculation.[4,14,15] Antimicrobial treatment begun prior to contamination is therefore referred to as being prophylactic; if not instituted until after inoculation, preventive therapy is probably a more descriptive term.

Hospital surveillance will reveal which patients and which operations warrant prophylactic or preventive antibiotic therapy.[7,12] The two basic criteria are 1) when postoperative infection is common but seldom fatal (*i.e.*, elective gastric, biliary and colonic surgery) and 2) whenever postoperative infection, although rare, carries an unacceptably high mortality rate (*i.e.*, open heart surgery and peripheral vascular reconstruction).[8,15] The same surveillance methods, in conjunction with data from the hospital clinical laboratory, can also identify which bacterial pathogens are the most likely offenders, as well as which antibiotics can be relied upon to control such microbial contaminants.[7]

Thus, it would appear that only two major questions remain to be answered. How long after operation should prophylactic and preventive antibiotic therapies be continued? And do monetary savings gained by a lowered rate of infection further justify the additional expenditures incurred by a program of routine pro-

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TABLE 1. *Patient Statistics*

	Preoperative Cefamandole and Postoperative Placebo	Preoperative and Postoperative Cefamandole	Preoperative Cephaloridine and Postoperative Placebo
Patients	110	110	110
Av. age (yrs)	50.6	49.6	48.3
Race (W/B)	25/85	24/86	12/98
Sex (M/F)	47/63	49/61	45/65
Av. height (cm)	164.1	171.5	165.5
Av. weight (kg)	67.0	67.0	67.3
Diabetes mellitus	18	10	14
Steroid/radiation	1/1	0/0	1/1
Died	4	3	2
Septic death	1		

phylactic and/or preventive antibiotic therapy for a given population at risk?

Duration of Prophylactic Therapy

During the 16 month period between June 1, 1976 and September 30, 1977, all patients admitted to the general and pediatric surgical services of Grady Memorial Hospital became candidates for study if an elective gastric, biliary or colon operation was planned. There was an automatic exclusion in cases of pregnancy, breast feeding, allergy to cephalosporins and antibiotic therapy within 2 weeks prior to operation. Permission for study participation was obtained in writing from an informed patient, parent or guardian.

Appropriate records of age, race, sex, presence of other disease entities, state of nutrition, primary clinical and pathologic diagnoses, operative procedure carried out, complications, other significant events in the hospital course and, finally, outcome were carefully kept. Specific function studies were run on the kidneys (routine urine analysis, serum creatinine and creatinine clearance), liver (serum bilirubin and various hepatic enzymes) and bone marrow (complete blood count with white cell differential and scrutiny of the blood smear for platelet adequacy). During operation aerobic and anaerobic cultures also were taken of the organ contents, peritoneal cavity and surgical incision prior to closure. Subsequent wound and intraperitoneal infections were similarly cultured. Aerobic bacterial isolates were speciated and tested, by both disc and tube dilution methods, for susceptibility to the two study antibiotics, cefamandole and cephaloridine.[2] Anaerobes were merely categorized routinely as to genus and occasionally as to species and subspecies.

Three distinct antibiotic regimens were given in a prospective, randomized, double-blind fashion according to the following format:

Group 1: cefamandole, 1 g/dose, intramuscularly, 1 hour prior to operation, intravenously during operation and intravenously in the recovery room plus diluent as placebo every 6 hours, intramuscularly, for 5 days postoperatively.

Group 2: cefamandole given perioperatively as in Group 1 plus cefamandole, 1 g/6 hr, intramuscularly for 5 days.

Group 3: cephaloridine, instead of cefamandole, given perioperatively as in Group 1 plus diluent as placebo every 6 hours, intramuscularly, for 5 days.

Vials of antibiotic and placebo were identified only by patient number and were marked as to which should be reserved for postoperative administration. Cefamandole was chosen because of documented effectiveness in treating peritonitis[13] and significant excretion of the drug in bile.[11] Cephaloridine served as a control, since several studies had previously demonstrated its effectiveness as a prophylactic agent.[5,10]

Results

There were no significant differences in the three groups of 110 patients each with respect to age, race, sex, weight, immune deficiency states and eventual outcome, categorized as survival, death and cause of death (Table 1). No adverse drug reaction occurred in any patient.

There were no differences in rate of infection between the various groups. More importantly, the incidences of infection within the surgical incision (Table 2) and the abdomen (Table 3) were essentially the same with cefamandole given perioperatively only (6 and 2%, respectively) as with perioperatively plus 5 additional days following operation (5 and 2%, respectively). The likelihood of sepsis in other areas also was similar, being 13 and 12%, respectively (Table 4). Results obtained from the use of cephaloridine were identical to those obtained with perioperative plus postoperative cefamandole. No significant differences among the three groups were evident with respect to the specific types of operation, *i.e.*, gastric, biliary and colonic.

Tabulation of bacterial culture results demonstrated that 89% of the aerobic organisms initially isolated were sensitive to the antibiotic administered, while only 58% of such later isolates from complicating infections—be they from wound, peritoneum or other area—were susceptible (Fig. 1). Infection occurred only in those instances in which at least one major contaminating pathogen was resistant to the antimicrobial agent given.

Comment

These data accumulated from a prospective, randomized, double-blind study demonstrate that the ef-

TABLE 2. *Postoperative Infection Within the Surgical Incision*

Area of Operation	Preoperative Cefamandole and Postoperative Placebo		Preoperative and Postoperative Cefamandole		Preoperative Cephaloridine and Postoperative Placebo	
	Patients	Infection	Patients	Infection	Patients	Infection
Stomach	25	0	29	0	25	1 (4)
Biliary tract*	36	2 (6)	40	0	45	0
Colon	54	5 (9)	47	5 (11)	44	2 (5)
Totals	110	7 (6)	110	5 (5)	110	3 (3)

* Cholecystectomy plus colectomy or gastrectomy in 15 patients.
Numbers in parentheses indicate per cent.

ficacy of cefamandole as a prophylactic antibiotic is equal to that of cephaloridine. In addition, antimicrobial therapy continued beyond the day of operation was neither a benefit nor a detriment to the subsequent hospital course or, more specifically, to any risk for development of a postoperative infection within the wound and/or abdomen proper.

Duration of Preventive Therapy

During the 18 month period between October 1, 1976 and March 31, 1978, patients for study of preventive antibiotic therapy were those admitted to the trauma and pediatric surgical services of Grady Memorial Hospital for surgical care of an acute abdominal condition. Emergency laparotomy was carried out on 1,624 patients, although only the 773 who had sustained some form of abdominal trauma were considered to be valid study candidates.

Details recorded were age, race, sex, mode of injury, alcoholism, preexisting disease states, presence and severity of hemorrhagic shock on admission, interval between injury and admission as well as operation, most contaminating intraperitoneal wound, operative procedure, postoperative complications, including infection, hospital course and duration and final outcome as defined by survival, death and cause of death. Cultures of subsequent infections, especially those of the surgical incision and abdomen, were processed for aerobic and anaerobic growth. Speciation of all pathogens was routinely accomplished, although only aerobic isolates were tested, by disc and tube dilution methods, for susceptibility to cephalothin.[2]

Parenteral antibiotic therapy was determined by the last digit in the previously randomly assigned hospital number. An odd-numbered final digit dictated intravenous cephalothin at a dosage of 2 g/6 hr for no less than three and no more than four administrations. An even final digit prescribed a continuation of such therapy for at least 5, yet no more than seven, additional hospital days. No other parenteral antibiotic was to be administered concomitantly, although a change in antimicrobial regimen could be made after the third postoperative day whenever overt sepsis so warranted.

Results

Of the 773 total trauma patients, 179 were excluded because of a significant deviation from the established antibiotic protocol. Another 143 patients were eliminated from consideration due to an inadequate follow-up. The remaining 451 patients were thereby distributed in a random, prospective, nonblind fashion (according to last digit of their hospital number) into two specific groups. Cephalothin was given only perioperatively to 213 patients, while 238 others received cephalothin both perioperatively and for 5–7 days postoperatively.

No significant differences were noted between the

TABLE 3. *Postoperative Infection Within the Abdomen*

Area of Operation	Preoperative Cefamandole and Postoperative Placebo		Preoperative and Postoperative Cefamandole		Preoperative Cephaloridine and Postoperative Placebo	
	Patients	Infection	Patients	Infection	Patients	Infection
Stomach	25	0	29	1 (3)	25	0
Biliary tract*	36	1 (3)	40	1 (3)	45	0
Colon	54	2 (4)	47	1 (2)	44	2 (5)
Totals	110	2 (2)	110	2 (2)	110	2 (2)

* Cholecystectomy plus colectomy or gastrectomy in 15 patients.
Numbers in parentheses indicate per cent.

TABLE 4. *Postoperative Infection Outside the Incision and Peritoneum*

	Preoperative Cefamandole and Postoperative Placebo (110 Patients)	Preoperative and Postoperative Cefamandole (110 Patients)	Preoperative Cephaloridine and Postoperative Placebo (110 Patients)
Infections	16	15	17
Patients	14	13	15
Infection rate	13%	12%	14%
Area of infection			
Urinary tract	9	10	12
Pulmonary	6	2	1
Intravenous site	0	1	1
Septicemia	1	2	3

two groups with respect to age, race, sex or mode of injury (Table 5). There also were no significant differences in incidence of immune impairment (diabetes mellitus and renal disease), alcoholism, presence and severity of shock on admission, volume of intravenous crystalloid and colloid required for fluid replacement, interval from injury to time of admission and to time of operation and total number of days in hospital. Frequencies of contamination among the major sites of wounds, *i.e.*, colon, rectum, stomach and esophagus, were similar for both groups (Table 6).

The incidences of infection within the surgical incision (8 and 9%) and peritoneum (4 and 5%) were not significantly different between those patients who received cephalothin perioperatively only and those whose antibiotic therapy was continued for 5–7 days postoperatively (Table 7). The likelihood of infection developing elsewhere and mortality rates also were relatively equal.

Since not all complicating infections were adequately cultured, bacteriologic data were not considered to be truly representative and therefore were not analyzed in great detail. Nevertheless, only 31% of the aerobic bacteria isolated from postoperative infections were susceptible to cephalothin at a disc concentration of 30 μg.

Comment

From this prospective, randomized, nonblind study, it is apparent that preventive antibiotic therapy in patients with significant wound and peritoneal contamination was not made more effective in reducing the incidence and severity of infection within the incision and abdomen by continuation of the therapy beyond the day of operation. Such results mimicked those obtained in the above reported study, in contradistinction to what might have been expected in cases of established wound and/or peritoneal infection.

Economics of Prophylactic Therapy

A previously reported, double-blind, prospective, randomized study of 400 patients undergoing elective operations on the stomach, biliary tract and/or colon was extended by the addition of 63 similarly managed patients.[15] Cefazolin or placebo was administered

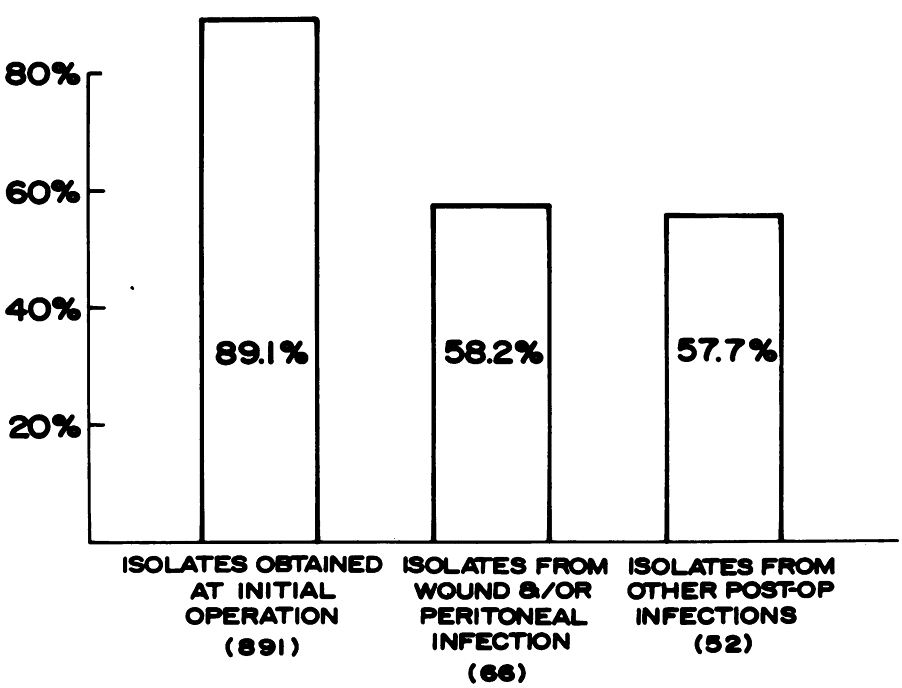

FIG. 1. Antibiotic susceptibility of aerobic pathogens as determined by sensitivity disc testing. Agent used was cefamandole, 30 μg.

TABLE 5. *Patient Statistics*

	Cephalothin Perioperatively Only	Cephalothin perioperatively and 5–7 Days Postoperatively
Patients	213	238
Average age (years)	29.6	31.5
Race (white/black)	42/171	50/188
Sex (male/female)	175/38	201/37
Gunshot	91	121
Stab	98	99
Shotgun	1	3
Blunt	23	15

intramuscularly 8–12 hours prior to operation, 1 hour preoperatively, in the recovery room after operation, on the morning following the day of surgery and on that same afternoon (Fig. 2). The study was so designed that antibiotic was begun 8–12 hours preoperatively, just 1 hour prior to operation, shortly after operation or not at all.

Patient classification was revised so as to distribute cases into one of two groups, either 1) those receiving antibiotic preoperatively or 2) those receiving only placebo prior to operation. Rates of infection of the surgical incision were 4% and 14%, respectively, and were significantly different statistically ($p < .01$). Incidences of postoperative peritoneal infection, 2 and 6%, respectively, also were significantly different but not to the same level of confidence ($p < .05$).

Analysis of infections related to the surgical incision and/or peritoneal cavity revealed that 11 of 232 patients receiving preoperative cefazolin and 36 of 231 given only placebo prior to operation developed such infections (Table 8). Overall, almost two extra hospital days per patient were required by those individuals denied preoperative antibiotic, with such excess being due entirely to potentially avoidable surgical infections.

Cost of each postoperative infection of the wound and/or abdomen was tabulated on the basis of certain readily available and easily identifiable additional

TABLE 6. *Most Frequently Contaminated Wounds*

	Cephalothin Perioperatively Only	Cephalothin Perioperatively and 5–7 Days Postoperatively
Patients	213	238
Colon-rectum	35	39
Stomach/esophagus	23	27
Duodenum/small bowel	46	53
Liver/biliary tract	42	45
Urinary/renal	17	21
Pancreas/spleen/vascular	23	22
Negative laparotomy	27	31

TABLE 7. *Postoperative Infections and Mortality*

	Cephalothin Perioperatively Only (213 Patients)		Cephalothin Perioperatively and 5–7 Days Postoperatively (238 Patients)	
	Number	Incidence	Number	Incidence
Any operative infection	22	10.3%	36	15.1%
Incision, subcutaneous	16	7.5%	23	9.7%
Incision, muscular	5	2.3%	8	3.4%
Peritonitis	8	3.8%	11	4.6%
Drain tract	3	1.4%	4	1.7%
Other related infections	2	0.9%	4	1.7%
Deaths	8	3.8%	11	4.6%

charges (Table 9). Total excess hospital days were multiplied by the standard *per diem* of \$80.00. To this were added daily charges of \$170.00 whenever the infected surgical intensive care unit was used. Expenditures for extra medications, primarily antibiotics, and wound dressing supplies were determined by standard charges levied by the hospital pharmacy and central supply. Laboratory fees, especially for bacteriology and blood counts, were also calculated, as were charges from radiology for diagnostic studies ordered to locate pockets of intra-abdominal sepsis. Operating room and recovery room billings, as well as the cost of supplies used by the anesthesia service, were obtained from the hospital business office; while anesthesia and surgical professional fees were calculated from the California Relative Value Scale with a single unit based at \$60.00.[6] The extra medical expenditures caused by a single operation-related infection could then be determined.

PREOPERATIVE		OPERATION	POST-OPERATIVE		
PM	AM		PM	AM	PM
X	X		X	0	0
0	X		X	X	0
0	0		X	X	X
0	0		0	0	0

X = antibiotic 0 = placebo

FIG. 2. Design of study with respect to time of antibiotic and placebo administration.

TABLE 8. *Postoperative Hospital Stay (Relationship to Infection Within the Incision and/or Abdomen)*

	Preoperative Antibiotics		Preoperative Placebo	
	No Infection	Infection	No Infection	Infection
Patients	221	11	195	36
Average post-op hospital days	10.3	23.6	10.1	27.1
Average excess post-op days		13.3		17.0
Total patients	232		231	
Average post-op hospital days	10.9		12.8	
Average excess post-op days			1.9	

The average was $2,686.00 per infection, with minor variations between the two groups according to whether antibiotic or placebo had been given preoperatively (Table 9).

To the extra expenditures brought about by a postoperative infection, the cost of the prophylactic antibiotic was added to the total for that group which received such medication (Table 10). The difference was still more than $69,000.00 greater for the group given preoperative placebo and, when distributed equally among those same patients, amounted to almost $300.00 per patient at risk.

Postoperative Antibiotic Therapy

Since prolongation of prophylactic treatment beyond the day of surgery appears to offer no medical benefit

TABLE 9. *Additional Hospital Costs Due to Infection Within the Incision and/or Abdomen)*

	Preoperative Antibiotic	Preoperative Placebo
Patients with postoperative infection	11	36
Average excess hospital days	13.3	17.0
Total excess hospital days	146	612
Cost of excess hospital days	$11,680.00	$48,960.00
Postoperative days in infection ICU	13	35
Cost of excess ICU days	$2,210.00	$5,950.00
Extra medications/dressings	$4,126.41	$14,479.03
Added lab costs (bact., etc.)	$1,425.00	$5,170.00
Fees for extra diagnostic studies (x-ray, etc.)	$2,845.00	$9,305.00
O.R. and R.R. charges for complicating infection	$905.21	$3,667.94
Extra anesthesia (fees, supplies)	$1,354.82	$3,969.17
Added surgical fees	$2,448.00	$7,752.00
Total extra costs	$26,994.44	$99,253.14
Average cost/patient	$2,454.04	$2,757.03
Total average cost	$2,686.12	

TABLE 10. *Additional Hospital Costs Incurred by Prophylactic Antibiotic and Postoperative Infection Within the Incision and/or Abdomen*

	Preoperative Antibiotic	Preoperative Placebo
Total patients	232	231
Extra charges due to wound and/or intra-abdominal infection	$26,994.44	$99,253.14
Cost of preoperative and perioperative antibiotic	$3,125.04	
Net excess expenditures	$30,119.48	$99,253.14
Difference	$69,133.66	
Net excess cost/patient	$129.83	$429.67
Difference	$299.84	

to the patient, continuation of such therapy can be construed to be a wasteful practice. Calculation of these costs, then, must be based entirely upon expenditures for extra antibiotic, since the rates of infection are the same, as are the average durations of postoperative hospital stay. The above cited study using cefamandole has given objective data to support this belief.

Computation of extra expenditure for drug in the study using cefamandole as the prophylactic agent revealed an unwarranted pharmacy charge of $92.00 per patient when antibiotic was continued postoperatively (Table 11). Subtraction of this amount from the anticipated $300.00 per patient saving when perioperative antibiotic alone is given significantly reduces the overall economic gain to only $208.00 per case, a loss of almost one-third of what had been saved initially.

Similar waste could be demonstrated for patients receiving preventive therapy with cephalothin (Table 12). In that study reported above, an unnecessary $23,895.00 was spent for postoperative antibiotic. This averaged a little more than $100.00 per patient when distributed equally throughout the group treated with continued postoperative antibiotic.

Discussion

Ever since our appreciation of the germ theory and the realization of its determinant role in wound sepsis, surgeons have attempted to manipulate various com-

TABLE 11. *Cost of Prophylactic Antibiotic Course*

	Preoperative Cefamandole and Postoperative Placebo	Preoperative and Postoperative Cefamandole
Doses per patient	3	23
Costs ($4.60/dose)	$13.80	$105.80
Difference	$92.00	

ponents of the host–parasite relationship so as to eliminate postoperative wound infection. Progression from an antiseptic to aseptic technique has clearly minimized the bacterial challenge, while gentleness in handling tissues and avoidance of residual culture media such as clot or necrotic tissue have significantly limited the nutritional support offered to contaminating pathogens. Extremes of modern implementation of these two principles have been the "super-clean" room and sharp tissue dissection under tourniquet control. Still, infections do occur.

The majority of mammalian species are more resistant to bacterial infection than is man. For example, veterinary surgeons usually ignore the cardinal isolation rules which are so strictly enforced in our hospitals and operating rooms. The ideal would indeed be a human race possessed of the inherited bacterial resistance demonstrated by less-developed animals. Certain immunization programs could provide an answer, that is, if it were always possible to predict exactly which pathogens would colonize a given wound and if the unexpected contamination or emergency condition were to never arise. The success of such an active immunization program was dramatically demonstrated by the near total eradication of tetanus as a major threat to battle casualties of the Allied forces during World War II.[3]

Parenterally administered antibiotics offer an alternative and can serve as an instantaneous means of increasing the patient's resistance through provision of exogenously produced circulating antiinfectious compounds. However, appropriateness of antibacterial spectrum, timeliness of distribution in tissue, drug safety and cost are important considerations. The initial application of this concept was not uniformly beneficial, for bacterial resistance to the penicillin used became a frequent complication.[1] Similar experiences have been noted with other antimicrobial agents, especially if applied topically without wound or patient isolation.[16] As a result, prophylactic antibiotics at one time became a despicable term and often were incriminated as causing many more infectious problems than would have developed otherwise.

The scientific basis for parenteral antibiotic prophylaxis was first documented by Miles et al.[9] and Burke.[4] From a set of carefully controlled experiments in laboratory animals, it was shown that time of drug administration, blood supply of tissue to be challenged and appropriateness of the antimicrobial spectrum were the three crucial factors. Delay in antibiotic administration beyond the third hour after bacterial contamination consistently failed to reduce the size of the control infectious lesion.[4] Greatest benefit was obtained only if antibiotic had been given prior to the time of bacterial inoculation.[4,14,15] The delivery of anti-infectious substances, whether autogenous antibody or exogenous antibiotic, was based upon the current state of the cardiovascular system in general and, more specifically, the blood supply of the local tissue being challenged.[4] Thus, administration of vasopressors uniformly increased the size of the control lesion and negated any potential benefit that may have accrued from even preinoculation antibiotic treatment.[4]

TABLE 12. *Antibiotic Costs (Cephalothin, 2 g/6 hrs, Intravenously)*

	Perioperative Only	Perioperative and 5 Days Postoperative
Antibiotic administrations (2 g each)	4	24
Total antibiotic given (g cephalothin)	8	48
Antibiotic cost ($2.51/g)	$20.08	$120.48
Difference/patient	$100.40	
Patients	213	238
Cephalothin expenditure	$4,277.04	$28,674.24
Perioperative expenditure only	$4,277.04	$4,779.04
Excess expenditure		23,895.20

Polk and Lopez-Mayor were the first to confirm these findings in a prospective, randomized, double-blind study of humans undergoing elective gastric or colonic surgery.[10] The rate of infection following colectomy was cut to one-fourth, that is, from 15 to 4%, by the preoperative administration of cephaloridine in comparison to a placebo control. Subsequent clinical studies constructed on the same prospective, randomized, double-blind basis have supported these initial observations.[5,8,10,15,17] In one clinical experiment, postoperative initiation of antibiotic therapy to patients undergoing surgery on the stomach, colon or biliary tract gave results identical to those obtained by use of a placebo in controls.[15] In the same study no difference in results was noted between patients in whom antibiotic therapy was begun 1 hour preoperatively and those in whom therapy was initiated 12 hours preoperatively. Failures could uniformly be correlated with either absence of antibiotic at bacteriocidal concentrations in tissues at the time of bacterial inoculation or resistance of major pathogens in the inoculum to the antibiotic given.

From the present report, the necessary duration of antimicrobial coverage appears to be quite brief. Certainly administration must be started prior to operation, yet continuation of antibiotic prophylaxis beyond the time in the recovery room has added nothing to prevention. Only unwarranted extra cost is incurred.

The indiscriminant administration of antibiotics prophylactically can only lead to the evolution of resistant strains and to an unjustified excess in medical costs.[1] Granted, those patients in whom complicating postoperative infection carries a significant mortality (*i.e.*, in open heart surgery and use of vascular prostheses[8]) or a high frequency of morbidity (*e.g.*, in colon resection[10,15]) are irrefutable candidates. Nevertheless, there are other patient conditions and specific operations that equally satisfy these two basic criteria. Only through a program of hospital surveillance can such risk factors be determined.[7,12]

Surveillance has demonstrated, for example, that not all patients undergoing gastrectomy warrant prophylactic anitbiotic therapy.[12] In cases of peptic duodenal ulcer disease, in which hyperacidity is the rule, stomach contents are usually sterile and thus operation-related wound and intra-abdominal sepsis is uncommon. However, if gastric ulcer or gastric cancer, conditions known to be associated with achlorhydria and hypoacidity, are the indications for surgery, cultures of the stomach are almost routinely positive for a mixture of pathogens, and the anticipated high incidence of postoperative infectin is accordingly noted. Similarly, better definition of patient susceptibility has been detailed in elective biliary tract surgery, in which the risk for infection in uncomplicated cholecystectomy without choledochotomy in patients less than 70 years of age is minimal and thus does not routinely warrant antibiotic prophylaxis.[5]

In the present report, the average additional cost of a postoperative wound and/or peritoneal infection has been calculated at $2,686.00. Nevertheless, this figure fails to reflect losses in income due to prolonged incapacitation, the additional discomfort and a recognized increase in mortality, particularly in instances of open heart and reconstructive vascular surgery.

Documented savings in health care expenditures can best be exemplified through a comparison of programs that use antibiotic prophylaxis with those that avoid it for patients undergoing similar surgical procedures. In colon surgery, the cost of a three-dose antibiotic course is approximately $15.00 per case. As many reports so confirm, the resultant reduction in infection rate is approximately 15%, that is, from 20% to 5%.[10,15] Thus, for 100 consecutive operations, an expenditure of $1,500.00 for antibiotic prophylaxis can potentially yield a $40,500.00 dividend.

Conservation of health care funds appears to be similar for cardiovascular surgery. Although the amount of money saved in preventing a single infection is significantly greater, reductions in an already low infection rate are not so dramatic and therefore are based on only 2 to 3% of the population at risk. Still, elimination of even one avoidable death is something that will forever defy a dollar and cents label.

References

1. Altemeier, W. A., Culbertson, W. R. and Vetto, M.: Prophylactic Antibiotic Therapy. Arch. Surg., 71:2, 1955.
2. Bauer, A. W., Kirby, W. M. M., Sherris, J. D. and Turk, M.: Antibiotic Susceptibility Testing by a Standardized Single Disc Method. Am. J. Clin. Pathol., 45:493, 1966.
3. Boyd, J. S. K.: Tetanus in African and European Theaters of War, 1913–1945. Lancet, 1:113, 1946.
4. Burke, J. F.: The Effective Period of Preventive Antibiotic Action in Experimental Incisions and Dermal Lesions. Surgery, 50:161, 1961.
5. Chetlin, S. H. and Elliott, D. W.: Preoperative Antibiotics in Biliary Surgery. Arch. Surg., 107:319, 1973.
6. Committee on Relative Value Studies: 1969 California Relative Value Studies, 1974 revision. San Francisco, California Medical Association, 1975.
7. Cruse, P. J. E. and Foord, R.: A Five Year Prospective Study of 23,649 Wounds. Arch. Surg., 107:206, 1973.
8. Kaiser, A. B., Clayson, K. R., Mulherin, J. L. Jr., et al.: Antibiotic Prophylaxis in Vascular Surgery. Ann. Surg., 188: 283, 1978.
9. Miles, A. A., Miles, E. M. and Burke, J. F.: The Value and Duration of Defense Reactions of the Skin to the Primary Lodgement of Bacteria. Br. J. Exp. Pathol., 38:79, 1957.
10. Polk, H. C. Jr. and Lopez-Mayor, J. F.: Postoperative Wound Infection: A Prospective Study of Determinant Factors and Prevention. Surgery, 66:97, 1969.
11. Ratzan, K. R., Baker, H. B. and Lauredo, I.: Excretion of Cefamandole, Cefazolin, and Cephalothin into T-tube Bile. Antimicrob. Agents Chemother., 13:985, 1978.
12. Stone, H. H.: Gastric Surgery. South. Med. J., 70 (Suppl. 1):35, 1977.
13. Stone, H. H., Guest, B. S., Geheber, C. E. and Kolb, L. D.: Cefamandole in the Treatment of Peritonitis. J. Infect. Dis., 137:S 103, 1978.
14. Stone, H. H. and Hester, T. R. Jr.: Incisional and Peritoneal Infection after Emergency Celiotomy. Ann. Surg., 177:669, 1973.
15. Stone, H. H., Hooper, C. A., Kolb, L. D., et al.: Antibiotic Prophylaxis in Gastric, Biliary and Colonic Surgery. Ann Surg., 184:443, 1976.
16. Stone, H. H. and Kolb, L. D.: The Evolution and Spread of Gentamicin-resistant Pseudomonads. J. Trauma, 11:586, 1971.
17. Strachan, C. J. L., Black, J., Powis, S. J. A., et al.: Prophylactic Use of Cefazolin Against Wound Sepsis after Cholecystectomy. Br. Med. J. 1:1254, 1977.

Discussion

Dr. William R. Sandusky (Charlottesville, Virginia): I have completed a review, now in press, dealing with antimicrobial prophylaxis for surgical infection.

There are now at least 31 reports of prospective, controlled, randomized clinical trails that have evaluated the influence of parenterally administered antibiotics on the incidence of postoperative infection. In the review, infection is defined as sepsis in the operative incision or body cavity, but does not include infection in the pulmonary system or urinary tract. In each of these studies, either an antibiotic or, in control cases, a placebo was administered before—and I emphasize "before"—the beginning of the operation. These 31 trials involved 6864 patients undergoing a variety of operative procedures in cardiovascular, orthopedic, gynecological and general surgery.

Two reports in the collective review indicated that patients who received antibiotics indeed had a greater incidence of infection than those who did not. In six studies the infection rate with antibiotics was lower than that of the controls, but not