

costs.¹ Granted, those patients in whom complicating postoperative infection carries a significant mortality (*i.e.*, in open heart surgery and use of vascular prostheses⁸) 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 antibiotic 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 infection 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.

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 trials 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 in-

fection 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

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significantly so. In the remaining 23 clinical trials a statistically significant reduction in the incidence of infection was observed in those patients who received an antibiotic, compared with those who received none.

Although these collected reports do not speak with unanimity, they contain sufficient hard data to formulate a policy of prophylaxis that is discriminating in its application. Simplistically stated, antibiotics are justified when the probability of infection is high or the consequences of infection, should it occur, likely to be grave.

Conversely, certain risks preclude routine or indiscriminate use of these valuable agents. These risks include the possibility of adverse reactions, superinfection, or the development of resistant pathogens. Moreover, these same risks should limit the duration of drug administration whenever a prophylactic antibiotic is used.

And finally, to stress the obvious, antibiotic prophylaxis is not an option that permits relaxed standards of antisepsis or asepsis, nor is it a substitute for careful surgical technique.

DR. JERE W. LORD, JR. (New York, New York): Two years ago I had the opportunity of presenting a paper before this Association on the use of intraoperative antibiotic lavage. The technique is simply to irrigate the wound from time to time throughout the entire operative procedure employing a 50 ml bulb syringe containing a solution of normal saline in which is dissolved 1 g of Kanamycin and 1 g of Cephalothin. Some 500–1000 ml are used.

Our data at that time consisted of 434 cases of arterial surgery with no hospital and only one infection five months later in a patient with a femorofemoral prosthetic graft. There were also 226 clean cases of major general surgery and no infections were noted early or late. To date the total number is 800 with no hospital infections and no late infections except the one mentioned.

In regard to the clean contaminated cases, in seven years 79 operations on the biliary, gastrointestinal tract and colon were lavaged in similar fashion and there was only one wound infection, involving the subcutaneous region with *E. coli* following a colon procedure. There were no intraperitoneal infections.

I believe that there is a valid reason for the virtual elimination of postoperative wound infection with antibiotic lavage. Dr. Stone, in a previous paper, showed that he could reduce the incidence of postoperative wound infection in clean-contaminated cases from approximately 16 to 4% by the preoperative administration of Cefazolin parenterally. In his study he found the average concentration of antibiotics in the tissues of the abdominal wound to be 9.8 μg whereas our level of antibiotics is 1000 μg , approximately 100 times stronger.

Yesterday I had a discussion with Dr. Stone and he persuaded me that the wisest thing to do was to go home and stop these anecdotal things and start a prospective, randomized, double-blind study using antibiotic lavage and saline without antibiotics.

DR. WATTS R. WEBB (New Orleans, Louisiana): I have just two questions.

I think it's been established without shadow of doubt that utilization of antibiotics in colon surgery, and most abdominal injuries, is of value, even though the antibiotic regimen is not totally protective against all the bacteria that might be present.

I was interested that Dr. Stone would study antibiotics that primarily affect only aerobic Gram negative organisms. The cefamandole, I realize, has a slight effect against the anaerobes, but not sufficient, and I wonder if it wouldn't be better if he would study an antibiotic regimen that would be effective against most of the bacteria that are present in this particular situation.

Second, I was wondering, even though a prospective, double-blind study is good, how many patients do you have to study before you find out whether it's worthwhile or not? As was pointed out "a difference, to be a difference, must make a difference." And if it takes 200 or 300 patients to find out that it's going to be of statistical significance of 1 or 2 or 3%, then this cannot possibly be of any clinical significance whatsoever, and be of value to us.

DR. HIRAM C. POLK, JR. (Louisville, Kentucky): As has been so frequently necessary in recent years, I rise to try to explain to the audience the obscure words of my associate, Dr. Stone. Now, this

is particularly important this year, because there are three important areas that are worthy of emphasis, and I want to delineate them clearly for you.

Dr. Stone was very kind to point out, of course, that this work follows by only 9½ years the studies that Dr. Lopez-Mayor and I shared with the Society of University Surgeons while we both had the privilege of working for Dr. Warren at Miami some years ago.

Now, notwithstanding that, the next point that needs to be addressed is the fact that Dr. Stone has made another major contribution in an area in which all of us have been baffled. He has been able to address the duration of therapeutic antibiotic use in this study better than has been possible in any study in the English literature over the whole life of antibiotics. He has shown, contrary to most of our concern, and, I think, to all of our appreciation, that the short course of therapy that we have all appreciated in prophylaxis also applies in the therapeutic situation. This is a unique first-time observation, and probably has great and broad meaning for all of us in the practice of surgery.

Now, the third point is, I think, an equally important one. Without mentioning by name, Dr. Stone has implied that there is not prophylactic equivalency in the use of multiple drugs and multiple antibiotics. In a paper to be published in the *American Journal of Surgery*, probably in January or February, Dr. Condon will show that in a survey of learned surgeons who do a great deal of work in gastrointestinal surgery, the great majority of those surgeons use Keflin, by trade name, for their prophylactic agent, and continue it for several days after operation. I think Dr. Stone has put to death the concept of continuing it for several days after operation.

What perhaps is more important is some unpublished work from our laboratory now that explains, I think, the lack of unanimity in Dr. Sandusky's discussion. Keflin has never been shown to be of value in any randomized prospective study of prophylaxis of operative wound infection; and the reason it doesn't is that Keflin disappears so rapidly from the operative wound that no one of you, no matter how skilled you are, can finish an operation at such time that Keflin, administered systemically, is still present in the wound in a high enough concentration to be effective.

This is why drugs such as cefazolin and cephaloridine, which have long wound half-lives, have been uniformly effective, and why Keflin has been uniformly ineffective.

So I think these are two very major contributions that will stand the test of time and mean a great deal to all of us, not only in reducing cost, but, I think, reducing morbidity.

Dr. Stone, I think the one point that you need to clarify in discussion is the presumed absence of the use of topical antibiotic in the course of these particular trials.

DR. H. HARLAN STONE (Closing discussion): Dr. Sandusky, I think you have brought up an issue that is most important. Certainly we cannot relax our standards just because there is a circulating anti-infectious agent in the blood. It was found out shortly after the second World War, when penicillin was administered indiscriminately, that indeed disaster would strike if we did not maintain as clean an environment as possible within the operating room.

Dr. Lord, I am glad to know that I have convinced you to do that randomized study. It would indeed be well to document the difference as to how efficiently the antibiotic can be delivered to the wound via an irrigation solution versus the cardiovascular system.

Dr. Webb, with respect to anaerobes, the good Lord gave us oxygen which effectively kills off these organisms. Several years ago in a prospective, randomized, but, unfortunately, not blinded study, it was found that it did not matter whether you used an agent primarily directed against anaerobes or an agent specifically for aerobic organisms. The subsequent infection rate was the same. It is the bacterial synergy that is all important. If just one partner of the synergy can be eliminated, then the symbiosis cannot develop and accordingly you dramatically reduce the virulence of that particular set of organisms.

In an iron-clad fashion (that is, an outstanding prospective, double-blind, randomized study) Dr. Polk documented that these benefits of prophylactic antibiotic in the animal were real and could have clinical application. His work has probably had more impact on our practice than almost anything else.