
Diseases of the
COLON & RECTUM

Vol. 11

January-February, 1968

No. 1

Cancer of the Rectum:
Progress in Its Control*

MAUS W. STEARNS, JR., M.D.
New York, New York

DURING THE PAST 25 YEARS there has been definite improvement in the survival rate of patients with cancer of the rectum. This is demonstrated in Figures 1 and 2, which are based on the report of the Clinical Biometry Section, National Cancer Institute, for the End Results Group.¹⁸ Improvement appears to have been directly proportional to the increased resectability rate during this period. These improved operability rates were due primarily to improved preoperative and postoperative care, increased understanding of surgical physiology, improved anesthesia, and wider application of skillful surgical procedures by aggressive, well-trained surgeons who were the products of excellent surgical residency programs that came into existence after World War II. To what degree increased resectability rates were due to earlier diagnosis is difficult to determine but, as I will indicate later, probably this was of rela-

tively minor importance. The report of the National Cancer Institute also seems to indicate that when resectability rates failed to rise, presumably because technical limits of resectability had been reached, survival rates failed to improve further.

Evidently a number of surgeons believed that the results of accepted surgery, chiefly the Miles abdominoperineal type of resection, were not ideal and, consequently, they investigated various modifications. Their efforts took two main directions: 1) increasing the amount of tissue removed beyond that of the basic Miles resection, and 2) eliminating the permanent abdominal colostomy, thereby making life easier for those who survived. To discuss and evaluate all of the modifications would be beyond the scope of this presentation; therefore, I will limit my discussion to only a few that I consider significant.

Efforts directed at increasing the amount of tissue removed with the intent of improving survival rates took several forms: first, addition of meticulous abdomino-

* Presidential address given at the meeting of the American Proctologic Society, New Orleans, Louisiana, April 17 to 19, 1967.

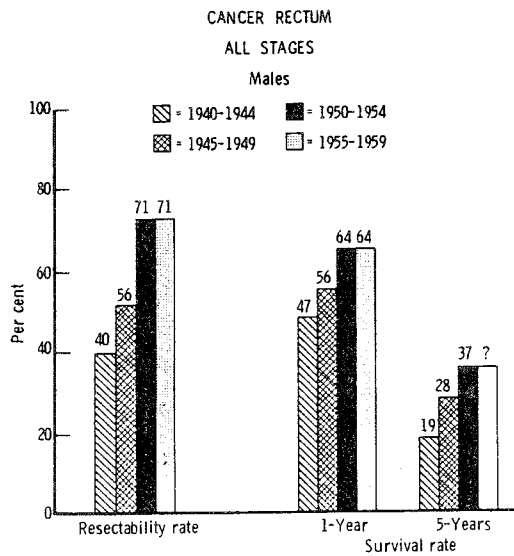


FIG. 1. One-year and five-year survival rates for all stages of cancer of rectum are indicated in two blocks of columns in center and on right. Improvement in these survival rates reflects directly increased resectability rates in sequential five-year periods indicated in column of blocks on left.

pelvic lymphadenectomy and, second, high ligation of the vascular supply providing for more extensive resection of the mesentery and its associated lymphatics. Results of abdominopelvic lymphadenectomy have been presented to this society by Bacon and associates¹ and by Deddish and me.¹⁵ Both reports indicated that abdominopelvic lymphadenectomy appeared to improve the survival rate by about 5 to 8 per cent. This, however, was not a statistically significant improvement. Bacon and co-workers reported no increased morbidity and believed that the procedure was worth while, and I believe he has continued to employ it. However, in our series, in many of the patients having operations by well-trained general surgical residents, there was a significant increase in morbidity, particularly in complications of the urinary tract. In our opinion these complications were sufficient to contraindicate addition of this measure as a routine in surgical management of cancer of the rectum, particularly because we were unable to demonstrate

significant improvement in the rate of survival.

Recently, Grinnell⁸ has reported his evaluation of patients at Presbyterian Hospital who had ligation of the inferior mesenteric vessels at the level of their origin. He could not prove that any patients had been salvaged as a result of this addition. However, he believed that it should be continued because it increased the safety margin for some patients and did not increase morbidity.

The second line of endeavor has been to eliminate the abdominal colostomy as a necessary part of all curative procedures. The most important of these modifications are the abdominoperineal proctosigmoidectomy, or "pull-through" operation, and anterior resection with primary anastomosis, both of which are too well known to require elaboration. Fortunately, the lower limits of the tumor considered amenable to these procedures had been established early by intelligent consideration of anatomic factors and lymphatic drainage patterns. In consequence, no great effort has been made to employ these operations for lesions situated less than 7 or 8 cm from the anal margin. During the last ten years, it has been established that, within the prescribed limits, these procedures yield as good survival rates as does the Miles type of resection and colostomy, when employed for patients with tumors situated at the same level and with a comparable extent of disease.

The attempt to avoid unnecessary colostomy has led a number of surgeons to conclude that not all cancers of the rectum require radical resection and that, in selected cases, local excision provides an equally good chance of cure. Fansler⁵ and Jackman¹⁰ have written on this subject.

Jackman presented a follow-up study of 252 patients with histologic diagnoses of carcinoma of the rectum, of whom 211 were treated conservatively and were ob-

served for periods of eight to 18 years. The survival rate was 96.2 per cent—very convincing evidence of Jackman's ability to select patients for conservative treatment. Unfortunately, on occasion, Jackman's paper is quoted out of context, without giving it the thoughtful, considered study it deserves; and the mistaken impression is conveyed that all types of cancer of the rectum should be treated by local coagulation rather than resection. Jackman encountered these 251 patients during a ten-year period, January 1943 through December 1952. He does not reveal how many patients with cancer of the rectum were seen at the Mayo Clinic during this period, but his series must represent a small fraction of the total. He reported, in detail, the factors that should be considered when selecting patients for conservative treatment, and I urge those interested to read this portion of his report carefully. Among the criteria listed were the gross appearance, protuberant tumors being considered acceptable for local treatment, whereas flat or craterlike lesions with puckering or distortion of the adjacent normal-appearing mucosa would require radical resection. The smaller the lesion, the more serious would be consideration of local removal. An indication for radical resection is lack of mobility or the presence of firmness in the tumor, as determined by palpation. His criteria prove that he does not advocate treating clinically-infiltrating carcinoma by conservative methods, but, rather, he selects, very carefully, lesions that are classified histologically as carcinoma, but bear no evidence clinically that they are infiltrating carcinoma.

My reason for devoting so much time to Jackman's report is that I have been disturbed to hear of a number of surgeons, some of them members of this society, who claim that conservative treatment of cancer of the rectum (particularly coagulation) is

an acceptable method of treatment in patients in whom radical procedures are not contraindicated. I was also disturbed to hear one of my highly-respected colleagues, at a meeting of an influential surgical society, advocate coagulation as the "primary and preferred method" of treating cancer of the rectum. He presented no adequate supporting data of his own, either in numbers of patients treated or length of the follow-up period. In support of his thesis, he quoted Jackman's paper and the work of Strauss and co-workers,^{16, 17} who have been advocating coagulation as the treatment of choice in cancer of the rectum since the early 1930's. Strauss reports a survival rate of 75 per cent. As far as I can ascertain, Strauss and associates have not published clinical data to support their claims, being content to issue brief statements to the effect that they have treated more than 400 patients with a five-year rate of cure of 75 per cent. Wide acceptance of coagulation and such palliative methods as the preferred method of treatment of cancer of the rectum, on the basis of such claims, in my opinion, would nullify any progress that has been made in the control of cancer. I would like to repeat that improvement in the survival rate during the past 25 years has been directly proportional to increased resectability rates. It should be recalled that, in the days when fewer patients underwent resection, many were treated by coagulation, and results were improved only when resection became the treatment of choice. Furthermore, if resection is not performed for the usual cancer of the rectum, at least 40 per cent of patients will have unremoved lymph-node metastases. At present, our five-year survival rate, for patients who undergo resection and in whom there are metastatic lymph nodes, approximates 35 or 40 per cent. The argument that coagulation of rectal cancer produces an immunologic response sufficient to control metastases has

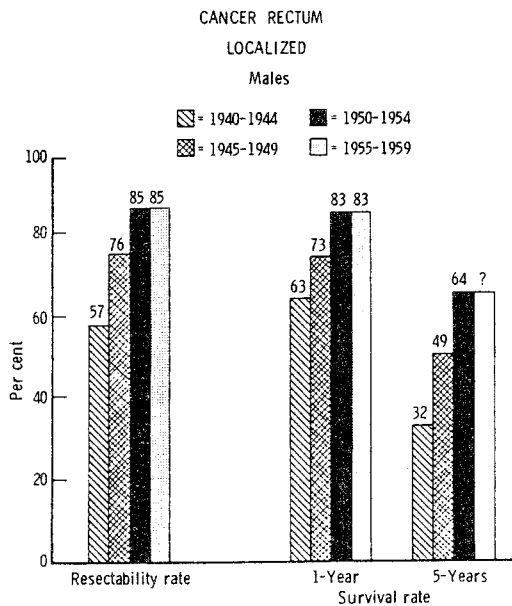


FIG. 2. One-year and five-year survival rates of patients with localized cancer of rectum are indicated in two blocks of columns in center and on right. Improvement in survival rates reflects directly the increased resectability rates in sequential five-year periods indicated in column of blocks on left.

not been proved, and it is indeed a dangerous assumption.

Adjuvant Therapy

We must face the fact that evidence, to date, does not indicate that any truly significant improvement in the over-all control of cancer of the rectum is forthcoming from extensions of currently-accepted surgical procedures. Much remains to be done to provide the best type of surgical management for all patients with cancer of the rectum. Some years ago, a number of surgeons recognized that adjuncts to surgery should be sought if we expected to improve management of cancer of the colon and rectum. In view of considerable enthusiasm for chemotherapy after World War II, chemical agents were employed in treatment of cancer of the colon and rectum.

Cole and his collaborators,^{3,12} at the University of Illinois, instituted a program in

which nitrogen mustard was used as an adjunct to surgery in the management of cancer of the colon and rectum. After reading their recent articles, it is my impression that they no longer use this method routinely.

The Veterans Administration Surgical Adjuvant Cancer Chemotherapy Study Group used Thio-Tepa as an adjunct. In a progress report in 1965,¹⁹ they admitted that it produced no beneficial effect. Subsequently, they began a study of FUDR as an adjunct, but results of this experience have not been published.

Curreri and Mackman⁴ reported, in 1966, their experience with the "second look" in patients who had been treated with fluoropyrimidines. They claim that an unusually high proportion of these patients were free of recurrence after prolonged use of these agents. This work should be followed with interest.

Rousselot and his collaborators^{2, 13} used nitrogen mustard initially, and subsequently substituted 5-FU, administered intraluminally, in isolated segments of the colon. In their preliminary reports, they claim that there was improvement in the survival rate. This work also should be observed with interest.

Our group at Memorial Hospital has reported to this society our experiences with preoperative irradiation.¹⁴ In this report it was indicated that prognosis after resection in patients with cancer of the rectum and metastasis to lymph nodes was significantly better if small doses of irradiation were given prior to operation. Comparison was made with patients with similar cancer who were not given this type of preoperative treatment. This report was based on a retrospective study of a large number of patients with primary, previously untreated cancer of the rectum, seen during a 13-year period. We are now engaged in a prospective, controlled alternate case study of the effect of preoperative

irradiation, but with the advent of Medicare and Medicaid, it appears that this investigation will be severely hampered because of steadily decreasing numbers of patients with primary untreated cancer of the rectum.

Fletcher, Allen and Dunphy⁶ have been using a much higher dosage of x-ray preoperatively than we have employed. Their published results should contribute to further evaluation of this scheme of management.

The Veterans Administration is also engaged in a study of preoperative irradiation, and when its report is published, it should be informative.

I believe the group at St. Mark's is engaged in evaluation of postoperative irradiation in patients with metastasis to lymph nodes. Results of this study should provide another contribution to the problem.

These observations bring into focus a problem common to all who are interested in modifying accepted methods of treatment. How can a new or resurrected procedure be evaluated to obtain maximum information in the shortest time possible with the least risk to the patient? Aside from the moral question of informed and understanding consent by patients, how can numbers sufficient for proper evaluation be correlated in the shortest possible time to provide for early employment of procedures of value and abandonment of those that are harmful? To me, it seems obvious that only by use of some central clearing organization can results from relatively small numbers of patients be utilized quickly as a part of a significant whole. An example of such a cooperative effort is the End Result Group. The Veterans Administration has provided another admirable example of coordinated effort to evaluate adjuvant therapy in the management of cancer. Unfortunately, patients encountered in the Veterans Administration are not representative of the normal popula-

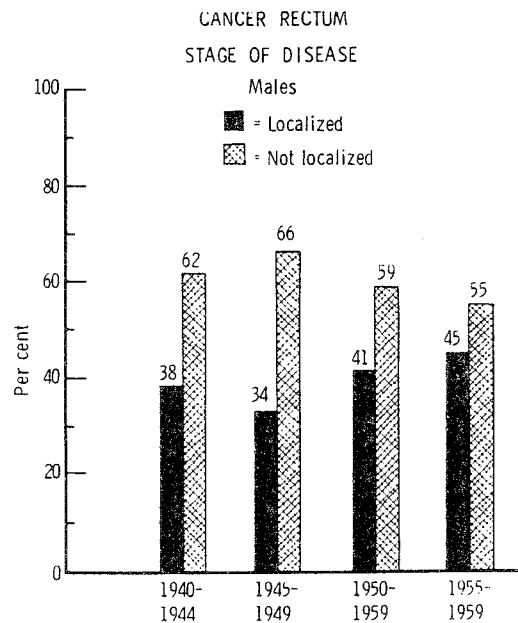


FIG. 3. Relative proportion of male patients who underwent surgery for localized as opposed to metastatic disease during sequential five-year periods has not varied significantly during 20 years of this study.

tion, being considerably older males. That this is a limiting factor in drawing conclusions from such statistics is suggested in their verbally reported operative mortality rates of 10 and 20 per cent, which exceed anticipated improvement.

Research, mutually agreed upon and conducted by members of this society, might prove more flexible than that of conservative institutional research departments, and might be expected to accomplish useful investigations with a less formidable operative mortality rate. Is it not possible that members of this society, working through regional programs of cancer, heart and stroke agencies, might effect progress toward establishing central clearing organizations and organizing cooperative research programs?

Early Diagnosis

In Figures 3 and 4, which I have prepared from the report for the End Results Group,¹⁸ it is evident that, during the

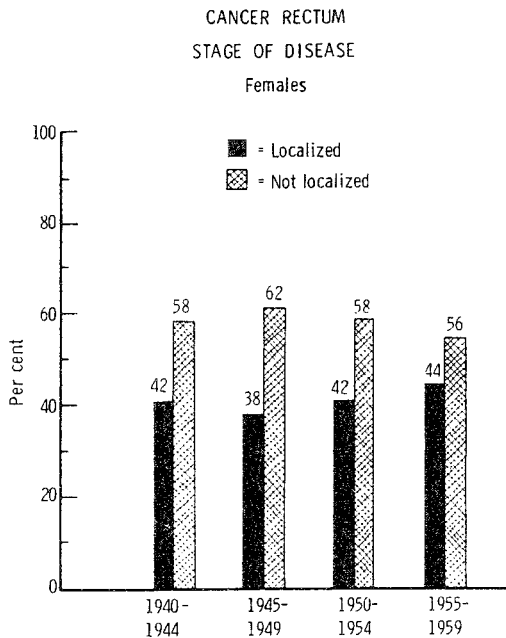


FIG. 4. Relative proportion of female patients who underwent surgery for localized as opposed to metastatic disease during sequential five-year periods has not varied significantly during 20 years of this study.

years under study, no significant increase in the number of patients with localized disease who underwent surgery could be demonstrated. In other words, it would appear that after symptoms bring the patient for examination, and cancer of the rectum has been diagnosed, essentially the same proportions will have localized and disseminated disease.

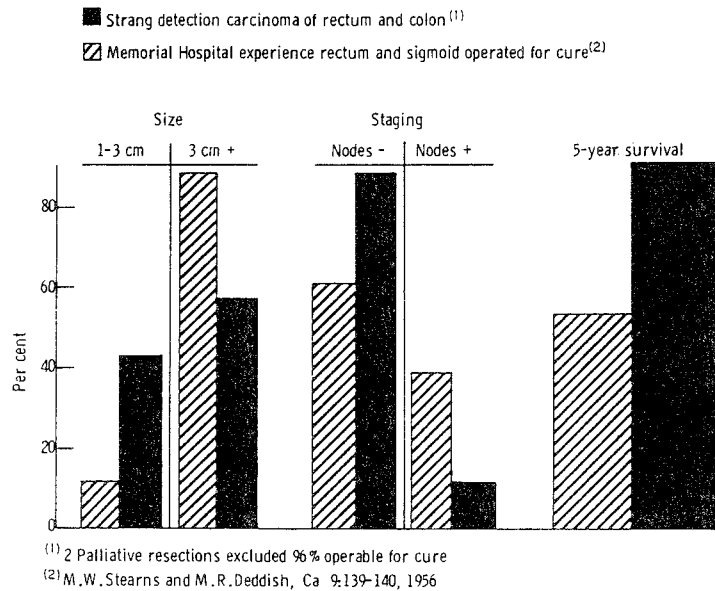
Hertz and his collaborators⁹ have shown that, in patients with cancers detected in the asymptomatic stage, there is a substantially higher proportion of localized disease (Fig. 5). Also, they found that a much higher proportion of patients treated during the asymptomatic stage survived five or more years after resection. That this represents an increased curability rate is not proved. It may simply reflect the time element involved. Nevertheless, until it is disproved, a working assumption is justifiable that it represents an improved curability rate and that diagnosis and treatment

of cancer in the asymptomatic period is desirable.

Another obstruction to progress in the control of cancer of the rectum is engendered by the polyp-cancer controversy. Owing to insistence by highly-respected members of the profession that there is no direct relationship between polyps and cancer, many claim that there is no prophylactic value in detecting and removing polyps. Some physicians even see no particular value in advocating sigmoidoscopy in asymptomatic persons. This opinion has been advanced recently by Moertel, Hill and Dockerty,¹¹ who speak of the extremely small number of cancers discovered in asymptomatic individuals by sigmoidoscopy—probably not more than 0.1 per cent.

My personal opinion, which is shared by my associates on the Rectal and Colon Service of Memorial Hospital, is based on our examination by sigmoidoscopy, during the past 20 years, of many thousands of patients in the cancer age group. During these examinations we have found literally thousands of polyps, hundreds of which have contained microscopic evidence of adenocarcinoma. We have biopsied a great many excrescences, 2 to 3 mm in diameter, none of which has contained microscopic evidence of carcinoma. It seems impossible to escape the conclusion that the great majority of cancers of the terminal portion of the colon have their origin in polyps and few arise *de novo* from the mucosa. If this theory is correct, we are forced to believe that removal of polyps, before infiltration and invasion develops, constitutes true cancer prophylaxis. A recent report by Gilbertson,⁷ on the experience at the Cancer Detection Center at the University of Minnesota, indicates that this is actually true. He reveals that, in a follow-up study of more than 45,000 annual recheck proctosigmoidoscopic examinations, there was not a single death in patients re-examined because of cancer of this region. I would

FIG. 5. Comparison of pathologic findings and five-year survival rate of a group of asymptomatic patients who had cancer of the bowel (Strang group) with group of patients who had cancer of bowel and who were considered to have had curative surgery indicates higher proportion of smaller lesions, less frequent occurrence of metastases and higher five-year survival rate in asymptomatic group.⁹



urge all "doubters" to read his report carefully. Also, I urge that we stop playing games of semantics and numbers and devote our considered attention to that which clinical experience appears to make obvious. This should be done before the widespread effort to have more asymptomatic persons examined by sigmoidoscopy has been defeated.

A most effective study of the polyp-cancer problem could be effected by establishment of a central clearing organization where unlimited data, derived by sigmoidoscopy, could be accumulated and evaluated during a period of 15 to 20 years.

Future Progress

While I have no intention of attempting to envisage whence true progress in the control of cancer of the rectum will come, I would like to suggest certain lines of exploration for members of this society, either in laboratories or in cooperative efforts coordinated through centers such as I have mentioned.

Chemotherapy, undoubtedly, will offer substantially more toward the control of cancer of the rectum than it does at pres-

ent. The problem is to find new agents. New, fresh approaches certainly are needed.

Cancer immunology is a field that is just beginning to open up for clinical investigation. Developments within this entire field undoubtedly will have application in the management of cancer of the rectum. Of more immediate interest is the fact that, recently, methods have been developed which appear to make possible more satisfactory determinations of antigen-antibody responses in man.

A number of clinical observations, made in regard to preoperative irradiation, suggest that some immunologic phenomena have been operative. The immunology department of the Sloan-Kettering Institute is now studying our patients who have preoperative irradiation to determine if any evidence can be detected that it stimulates an immunologic reaction.

One possible contribution from treatment of cancer of the rectum by coagulation might accrue from a study of the immunologic response. If coagulation induces the antibody reaction that is claimed, it might be utilized as a preliminary treatment prior to resection.

Undoubtedly a number of observations and problems regarding rectal cancer require exploration. For example, what is the significance of the consistently better survival rate in women as compared to that of men after treatment of rectal cancer? Why is the incidence of cancer of the rectum higher in the northeastern urban populations than in rural populations of the south? Why does the incidence of rectal cancer among the Japanese increase rapidly when they migrate to the United States? The solution of these and similar problems may contribute to progress in the management and control of rectal cancer.

Conclusions

Progress in the over-all control of rectal cancer can be accomplished in the following manner: by achievement of the highest possible resectability rate; by well-designed and executed surgical procedures; by employment of adjuncts available now and continuance of vigorous and imaginative efforts to find more effective agents; by ceaseless efforts to detect and remove polyps; by earlier diagnosis accomplished by full employment of means currently available and, hopefully, new screening methods; by clinical research in the field of immunology; by cooperative efforts to pool all types of data relevant to patients with cancer of the rectum; by long-term follow-up study of large populations subjected to examination for cancer of the rectum, and by epidemiologic studies of the population with regard to cancer of the rectum.

It is of equal importance to discourage regressive measures which threaten and even obstruct effective types of treatment which are available.

References

1. Bacon, H. E., F. Dirbas, T. B. Myers and F. Ponce de Leon: Extensive lymphadenectomy and high ligation of the inferior mesenteric artery for carcinoma of the left colon and rectum. *Dis. Colon & Rectum*. 1:457, 1958.
2. Cole, D. R., L. M. Rousselot and C. Grossi: Chemotherapy for colorectal cancer. *S. Clin. North America*. 45:1075 (Oct.), 1965.
3. Cole, W. H., S. S. Roberts and A. L. Graham: Carcinoma of the colon. *Arch. Surg.* 91:547, 1965.
4. Curreri, A. R. and S. Mackman: Reoperation in carcinoma of the colon following resection and adjuvant chemotherapy. *Surg., Gynec. & Obst.* 123:274, 1966.
5. Fansler, W. A.: A consideration of the surgical treatment of cancer of the colon and rectum. *Dis. Colon & Rectum*. 1:32, 1958.
6. Fletcher, W. S., C. V. Allen and J. E. Dunphy: Preoperative irradiation for carcinoma of the colon and rectum: A preliminary report. *Am. J. Surg.* 109:76, 1965.
7. Gilbertson, V. A.: The potentiality for survival enhancement by expeditious detection of neoplastic disease. Experience at the Cancer Detection Center, University of Minnesota. *Prog. Clin. Cancer*. 2:48, 1966.
8. Grinnell, R. S.: Results of ligation of inferior mesenteric artery at the aorta in resections of carcinoma of the descending and sigmoid colon and rectum. *Surg., Gynec. & Obst.* 120:1031, 1965.
9. Hertz, R. E. L., M. R. Deddish and E. Day: Value of periodic examinations in detecting cancer of the rectum and colon. *Postgrad. Med.* 27:290, 1960.
10. Jackman, R. J.: Conservative management of selected patients with carcinoma of the rectum. *Dis. Colon & Rectum*. 4:429, 1961.
11. Moertel, C. G., J. R. Hill and M. B. Dockerty: The routine proctoscopic examination: A second look. *Proc. Staff Meet., Mayo Clin.* 41:368, 1966.
12. Mrazek, R., S. Economou, G. O. McDonald, D. P. Slaughter and W. H. Cole: Prophylactic and adjuvant use of nitrogen mustard in the surgical treatment of cancer. *Ann. Surg.* 150:745, 1959.
13. Rousselot, L. M. and D. R. Cole: Intraluminal injection of nitrogen mustard as adjuvant chemotherapy in treatment of cancer of the colon and rectum. *Surg., Gynec. & Obst.* 114:409, 1962.
14. Stearns, M. W., Jr., J. W. Berg and M. R. Deddish: Preoperative irradiation of cancer of the rectum. *Dis. Colon & Rectum*. 4:403, 1961.
15. Stearns, M. W., Jr. and M. R. Deddish: Five-year results of abdominopelvic lymph node dissection for carcinoma of the rectum. *Dis. Colon & Rectum*. 2:169, 1959.
16. Strauss, A. A., M. Appel, O. Saphir and A. J. Rabinovitz: Immunologic resistance to carcinoma produced by electrocoagulation. *Surg., Gynec. & Obst.* 121:989, 1965.
17. Strauss, A. A., S. F. Strauss, R. A. Crawford and H. A. Strauss: Surgical diathermy of carcinoma of the rectum: Its clinical end results. *J.A.M.A.* 104:1480, 1935.
18. United States Department of Health, Education and Welfare, Public Health Service. End results in cancer. Report #2, p. 30.
19. Veterans Administration Surgical Adjuvant Cancer Chemotherapy Group: Adjuvant use of HN2 (NSC-762) and thiotepea (NSC-6396)—Progress report. *Cancer Chemotherapy Reports*. 44:27, 1965.