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if distant metastases have occurred, the disease is too far advanced to warrant surgical attack on the primary lesion. Operation is almost never attempted in the face of incontrovertible evidence of distant spread. The situation is altered, however, if incurability is determined only at the time of operation. Resection of the primary lesion is often indicated under such circumstances, since considerable symptomatic benefit may be obtained by removal of a large, obstructing, bleeding, infected carcinomatous mass. Palliative removal of a lesion in the lung, stomach, or large intestine frequently adds much to the comfort of the patient and possibly prolongs life. Palliative operative procedures, such as gastroenterostomy, in which the primary lesion is not removed, are much less effective and have generally proved to be unsatisfactory. It is sometimes beneficial to remove a late-appearing solitary metastatic lesion of a growth which characteristically metastasizes only sporadically.

Surgical procedures on the nervous system for relief of intractable pain are indicated when the course of the disease is apt to be long. Procedures, such as rhizotomy, prefrontal lobotomy, and topectomy, have definite, though limited, indications in the treatment of patients with cancer.

#### SUMMARY

In the face of new therapeutic methods and repeated recommendations for alterations in existing surgical technics it is desirable to review the principles underlying the surgical treatment of cancer. Curative treatment depends on extirpation of all neoplastic tissue. The limits of practical surgical endeavor are set by knowledge of the pathologic extension of the neoplastic disease and the expected postoperative health and comfort of the patient.

Treatment of patients early in the course of the disease is possible only by prompt referral of the patient with symptoms, and determined efforts to detect cancer when it is still asymptomatic. Vigorous application of well considered radical surgical procedures at this stage results in the most effective control of cancer.

## HORMONES IN CANCER THERAPY

ALBERT SEGALOFF, M. D.

NEW ORLEANS

My predecessors on this symposium have referred to methods which offer varying degrees of hope for the cure and eradication of cancer. At least at present hormonal therapy has nothing to offer which could be classified as cures or eradication. Rather we must speak in terms entirely of palliation, regression, increased survival times, and comfort. Although the future may hold some hope of attainment of cure through hormonal agents, it is better to deal with the present realities.

The current glamorous agents of endocrinology, cortisone (compound E) and ACTH (the hypophyseal adrenocorticotrophic hormone), have, of course, been tested for their effects on neoplastic disease and have indeed shown promise in some types of malignancy. For practical purposes ACTH and cortisone will be considered as a single entity since the adrenocorticotrophic hormone has its effect in various diseases by stimulating the adrenal to produce either cortisone or cortisone-like substances. Except in an occasional instance it has not been possible to differentiate between the actions of these two agents. Although there is evidence that the administration of ACTH leads to the secretion by the adrenal of predominantly compound F, its actions can still not be readily distinguished from that of cortisone.

Some years ago Dougherty and White<sup>1</sup> described the lympholytic effect of excess adrenal hormone, either administered exogenously or from the animal's own adrenal under stimulation with ACTH. Essentially the same effects have been described for the increased adrenal secretion associated with the general adaptation syndrome of Selye.

Presented at meeting of the Orleans Parish Medical Society, Oct. 9, 1950.

From the Department of Medicine, Tulane University School of Medicine and the Endocrine Research Laboratories of the Alton Ochsner Medical Foundation, New Orleans.

It was, therefore, logical that these agents be tried in patients with leukemia as well as those with malignant lymphomas. In acute leukemia the response to cortisone or ACTH has often been extremely dramatic. Striking remissions have been attained rapidly in a large percentage of such patients. However, unfortunately, the duration of these remissions has been all too short. In the vast majority of cases eight to twelve weeks is the maximum length of a remission. Somewhat less dramatic remissions have been seen occasionally in patients with chronic lymphatic leukemia. Of the malignant lymphomas a favorable response seems to have been obtained in Hodgkin's disease and reports indicate that at least in several cases it has been possible to attain a rather prolonged remission by repeating the course of therapy. To date, therapy with either cortisone or ACTH in other types of malignancy shows no promising results.

The field of cancer therapy which seems to be most amenable to hormonal agents is that of advanced cancer of the mammary gland in both sexes. This subject is now under extensive study in a large cooperative clinical investigation under the Research Committee of the American Medical Association, formerly the Therapeutic Trials Committee. It has been known for many years, in fact almost a century, that remissions can be obtained in young women with advanced mammary cancer by oophorectomy. As many as one third of the patients castrated have shown regression of lesions, sometimes lasting as long as two years. More recently, it has become apparent that castration is an even more efficacious therapeutic maneuver in males with cancer of the breast. Fifty per cent or more of patients so treated showed exceedingly dramatic regression of lesions.

One of the most interesting phases of endocrine therapy of cancer of the breast is that the age of the host plays an exceedingly important role in the response to hormonal agents. Of course, it is interesting to speculate whether the cancer which arises in an older woman is different from that arising in a younger woman, or whether it

is the host itself in its effect upon the cancer that makes the difference. Nevertheless, the favorable response to massive estrogenic therapy is almost entirely confined to postmenopausal women. The longer the interval since the menopause the better the prognosis for regression following estrogen therapy. It does appear that as high as 50 per cent of women who have undergone the menopause five or more years before treatment will show objective regression of mammary cancer from estrogen therapy. At present there seems to be no reason for choosing one estrogen in preference to another. Both soft tissue and osseous lesions respond in this advanced age group.

In younger women, particularly of the premenopausal group, massive estrogen therapy may often lead to accelerations in growth of the tumor rather than regressions. Therefore, it would appear that estrogenic therapy should definitely be reserved for women who have undergone the menopause.

For younger women, the male sex hormone, the androgen testosterone, appears to offer some hope. Although the percentage response, that is, patients showing objective regression of the tumor, is less with testosterone therapy than with estrogens, it is nonetheless not inconsequential. Approximately 30 per cent of patients with advanced mammary cancer treated with testosterone in adequate dosage show objective regression of lesions for a varying length of time, probably not longer than one and a half to two years as a maximum. The results with testosterone are somewhat better for osseous metastases than for soft tissue lesions, but this question still must be settled by a study of large numbers of patients. Therapy with testosterone has additional advantages in that many of the patients experience tremendous subjective improvement even though the lesions may continue to progress. Most active researchers in this field have seen bedridden patients get up and go about their normal activities while there is objective evidence of continued expansion of the neoplastic lesion.

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To many people the side effects of testosterone therapy are sufficiently distressing to preclude its use. Although difficult to understand, it is nonetheless true that many women are unwilling to trade a deep voice and facial hair for months of comfort and life. A search, therefore, has been carried out for agents which have the beneficial effects of testosterone without the androgenic effect. Certain reports in the literature, somewhat premature we feel, refer to methylandrostenediol, a synthetic compound related to testosterone. This compound has in our hands, also shown some evidence of production of regression in metastatic cancer of the breast. It is too early as yet to say how well the percentage response correlates with that obtained with testosterone, although it does appear that a greater percentage of patients do respond to testosterone therapy than to therapy with methylandrostenediol. However, it is even more apparent that this agent does not have the ability of testosterone to produce the feeling of well-being mentioned previously. Indeed, many of our patients treated with this agent have complained of excessive lassitude and weakness. As already mentioned, much additional work must be done for final evaluation of the role of this compound. It is my own opinion that it is inferior to testosterone with respect to the production of regression of the tumor, as well as to subjective feelings, and should take only second place to testosterone for therapy of advanced mammary cancer.

There is an increasing amount of work on the hormonal therapy of uterine and cervical malignancies. However, as yet insufficient data are available to warrant their discussion.

The excellent results obtained with endocrine therapy in cancer of the prostate are so well known to all of you that it will be mentioned only in passing. The recent report of a large joint series<sup>2</sup> would make it apparent that the combination of castration and estrogenic therapy yields the best long term results.

It thus appears that at least at present in its own restricted field, hormonal therapy

does have something distinct to offer in neoplastic disease. Its sphere of usefulness may be expected to increase and we can hope that the future will bring greater promise.

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### TREATMENT OF CARCINOMA OF THE CERVIX AT CHARITY HOSPITAL

#### III. CUMULATIVE RESULTS AT THREE, FIVE AND TEN YEARS IN 1641 CASES.

MANUEL GARCIA, M. D.†

NEW ORLEANS

Results of the treatment of carcinoma of the uterine cervix at Charity Hospital have been reported to the Society on two previous occasions. Cases of the disease have continued to be referred in large volume, and bringing an appraisal of the results up to date may prove of interest. Hence this third report is submitted.

From April 1, 1938, to June 30, 1947, a total of 1641 authentic cases of carcinoma of the cervix were examined in the Department of Radiology. All had histologic confirmation; primary and recurrent lesions were included; and more than 99 per cent have been traced. The absolute survival rates observed are shown in Table 1. The

TABLE 1  
CHARITY HOSPITAL OF LOUISIANA  
PRIMARY AND RECURRENT CARCINOMA  
OF THE CERVIX  
RESULTS IN HISTOLOGICALLY VERIFIED CASES

| Period                    | 3 YEARS<br>1938-47 | 5 YEARS<br>1938-44 | 10 YEARS<br>1938-39 |
|---------------------------|--------------------|--------------------|---------------------|
| Cases Examined            | 1641               | 1159               | 286                 |
| No Treatment              | 70                 | 60                 | 11                  |
| Untraced                  | 9                  | 6                  | 4                   |
| Survivors                 | 674                | 347                | 67                  |
| Absolute Survival<br>Rate | 41%                | 30%                | 23%                 |

†From the Department of Radiology, the Charity Hospital of Louisiana at New Orleans.

\*Presented at meeting of the Orleans Parish Medical Society, October 9, 1950.