Hormonal manipulation, chemotherapy, radiation, and surgery are the major modalities used to treat breast cancer. A number of effective hormonal agents and approaches are now available to treat all stages of breast cancer. Furthermore, the ability to measure hormone receptor levels in tumors allows us to select patients likely to respond to hormonal manipulation. Patients with metastatic breast cancer are initially evaluated for obvious complications like hypercalcemia, unstable bone lesions, central nervous system metastases, and pain, as well as the extent of disease, and metastatic sites. Patients with so-called visceral crises who have extensive liver involvement or lymphangitic lung metastases usually receive chemotherapy immediately. These patients are not likely to respond to hormonal therapy and may die before a response is obtained; chemotherapy is more effective and works faster in this setting.

Patients without visceral crises or those who have stabilized after treatment for visceral crises are evaluated for hormone receptor status. Those with positive or unknown receptors are often treated with hormonal therapy, whereas those with negative hormone receptors usually receive chemotherapy. Some patients with negative receptors may be candidates for hormonal therapy by virtue of a long disease-free interval or a chronic and indolent course. Many options exist for hormonal therapy. Nevertheless, the response frequency for most hormonal maneuvers is similar, with the exception of androgens and, perhaps, estrogens, which tend to have lower overall response rates.

Several factors determine the use of hormonal therapy. Premenopausal patients are still treated in many centers with oophorectomy, or ovarian ablation with irradiation. Since antiestrogens and progestins have been shown to be effective in premenopausal patients, these agents are now being used initially, perhaps with oophorectomy later. This subject is controversial, however, and therapeutic decisions must be individualized. If initial therapy does not produce a response, we often proceed with chemotherapy.

Hormonal therapy for postmenopausal patients begins usually with an antiestrogen or progestin. Responding patients are maintained on the same therapy until recurrence. At that point, an alternative hormone is used. Patients taking an antiestrogen as adjuvant therapy receive a progestin after recurrence. Third-line hormonal maneuvers, which include aminoglutethimide or other aromatase inhibitors, estrogen, androgen, luteinizing hormone releasing hormone (LH-RH) analogues, or experimental agents, can be used at the time of progression. New antiestrogen, antiprogesterone, and antiaromatase compounds as well as somatostatin and LH-RH analogues are under investigation. Systemic chemotherapy is used when hormonal options have been exhausted. Combinations of hormones and combinations of chemotherapy and hormonal therapy have not increased efficacy.
In the past few years, a great deal of excitement has been generated for the use of both antiestrogens and progestins in different clinical situations. Tamoxifen has been widely used as therapy for advanced breast cancer and as an adjuvant. Currently, trials to test this agent as a chemopreventive in patients at high risk for breast cancer are under way. However, a number of questions arise with this approach. The potential risk of endometrial cancer, symptoms of estrogen deprivation (which can affect quality of life, especially in the premenopausal age group), effects on the heart and bone (which can be favorable), and uncertainty about long-term side effects are subjects of current debate. These issues are being addressed by the current National Surgical Adjuvant Breast and Bone Project (NSABP) placebo controlled chemoprevention trial, which is expected to accrue 1,600 women.

Dose-response studies of progestins have demonstrated a number of expected and some unexpected effects. One such unexpected effect is the marked increase in appetite and weight gain seen initially in patients with breast cancer and later in those with a variety of other malignancies. The mechanisms of these effects seem to be related to both behavioral and metabolic responses.

The role of hormonal therapy in the management of weight loss and poor appetite in patients with cancer and acquired immune deficiency syndrome (AIDS) is a subject of great importance, especially in the areas of nutrition and quality of life. More recently, a reversal of multidrug resistance has been described in certain cell tumor models with the use of progestins. The effects of megestrol acetate on appetite, food intake, and weight in addition to antitumor efficacy, offer new opportunities for intervention to the oncologist, nutritionist, surgeon, radiotherapist, and others who care for cancer patients. This new therapeutic option can be of benefit to cancer and AIDS patients in combination with other modalities like patient education and dietary supplements and other nutritional support. Further studies may also offer an opportunity to evaluate not only the mechanism of action of megestrol acetate but of other compounds as well. In addition, we may be better able to understand the mechanisms of weight regulation, storage of energy, and related metabolic pathways as they pertain to cancer and other disease states.

2
Tchekmedyian
Hormonal Therapy in Advanced Breast Cancer