Past Progress

Since its rudimentary beginnings in the 1950s, treatment of head and neck cancer with combined surgery and postoperative radiation therapy has been optimized, and many patients benefit from it. Nevertheless, in a substantial group of patients, especially those who present with advanced local or regional disease, therapy fails because of progression or relapse either at the primary site in the neck or in distant organs. Many studies have corroborated the principles espoused in the 1960s, and in this issue Bhadrasain Vikram, MD, summarizes his experience with the state of the art of combined treatment for head and neck cancer.

With the advent of microvascular reconstructive surgery, considerable strides were made in the recovery of form and function, significantly improving our ability to treat patients with advanced disease. Among the remarkable accomplishments of microvascular surgery are prompt postoperative recovery of patients after mandibular replacement, major soft tissue reconstruction, and reestablishment of pharyngoesophageal continuity. Microvascular surgery laudably complements previous surgical techniques and prosthetic rehabilitation.

Although full functional recovery sometimes may not meet the expectations of patients, they can go on to postoperative adjuvant therapy promptly, before local tumor cells can repopulate. Further improvement in surgical techniques is unlikely to result in significant gains in locoregional control. The same can be said, however, for the presently available modalities of postoperative therapy. Normal tissue tolerance and the potential for severe complications from combined treatments continue to be the limiting factors in delivery of treatment to cancer-bearing organs and tissues.

Over the years we have witnessed many changes in the way squamous cell carcinoma of the head and neck is treated, but the overall survival after therapy has not improved substantially. The vicissitudes of multimodality treatment have produced some tangible results and have raised a significant number of questions that deserve further research. In particular, the use of chemotherapy (either systemically or through the vascular supply of a tumor) has added new dimensions to our ability to treat squamous cell carcinoma of the upper aerodigestive tract.

Many treatment options and variations of combined treatment are available. The leitmotif for these combination treatments is an attempt to preserve function, improve locoregional disease control, and reduce the incidence of distant metastasis. Different strategies are used for these purposes.

In spite of aggressive therapy, local failure remains a significant problem in
advanced squamous cell carcinoma of the upper aerodigestive tract. We have some evidence that use of chemotherapy at the time of definitive treatment may delay the symptomatic appearance of distant metastases. Concomitant treatment with chemotherapy and irradiation remains a promising area for future investigation.7,8

Better therapy for advanced head and neck cancer necessarily includes a reduction of morbidity as well as mortality. Image-guided gastrostomy has facilitated the nutritional support of patients in whom significant acute effects develop in normal tissues. We need to find ways to reduce this acute insult and improve the therapeutic ratio of our treatments to reduce delayed sequelae.

For the large number of patients in whom cure is still not possible, the relentless progression of disease calls for renewed palliative efforts.9 Although many of these patients may be enrolled in phase I and II studies, other avenues exist to aid in symptom management. Proper pain control and relief of other symptoms by supportive care alleviate suffering and make the end of life more bearable.

Over the years, head and neck surgeons and radiation therapists have developed a variety of techniques to eradicate disease in affected organs, especially the larynx, and still preserve function. The techniques used by surgeons include open surgery and endoscopic surgery, especially with the assistance of laser technology. Radiation therapy has succeeded in preserving function, although some of its accomplishments often seem to be forgotten in our current multimodality treatment schedules.10-13

The article in this issue by John F. Carew, MD, and Jatin P. Shah, MD,14 describes well the use of chemotherapy either as a neoadjuvant or combined with radiation therapy in organ- and function-sparing protocols. Variations of this theme have been applied to the paranasal sinuses, the oropharynx, the oral cavity, and other areas with mixed success.

Recently published reports have shown some benefits from the use of chemotherapy. Different protocols are accruing patients through the cooperative groups in an attempt to establish whether neoadjuvant chemotherapy before radiation or concomitant radiation and chemotherapy is significantly better than radiation alone in function-preservation strategies for different tumor sites. Combined therapies that include conservation surgeries in the treatment plan also deserve further evaluation. The data suggest that nonsurgical strategies may be most beneficial in locoregional control and survival when used concomitantly.

We have learned that the addition of chemotherapy to radiation is not without morbidity, and it certainly adds cost to the treatment. Promptly obtaining answers to these questions through existing randomized studies is important.15-19

Organ function can be preserved in approximately two-thirds of surviving patients with advanced carcinoma after chemotherapy–radiation therapy protocols. We need to identify more effective regimens to achieve a higher complete response through either modulating chemotherapy or innovative radiation therapy schedules. Patients with nonlaryngeal squamous cell carcinoma of the head and neck should be enrolled in organ-sparing protocols. For these sites, not enough data exist for combined chemotherapy–radiation therapy to be considered the standard treatment.

**Future Promise**

Public education and implementation of preventive measures, especially the elimination of tobacco usage, should reduce significantly the incidence of squamous cell carcinoma of the upper aerodigestive tract.

Research indicates that soon we will be able to recognize populations at risk and define them through genetic map-
ping. These populations should be enrolled in screening programs and undergo intervention by molecular manipulation at a precancerous state. Research in this field has been a tangible by-product of ongoing chemopreventive trials. Removal of target tissue in the premalignant phase may be an option. As research in molecular epidemiology intensifies, the interaction between the genetic makeup of an individual and the influences of the environment will become clearer and novel programs will be developed, aimed at reversing the carcinogenic process at the preinvasive phase.20-24

Knowledge of the molecular biology of cancer has expanded logarithmically, and the information available on the genotypic and phenotypic characterization of malignant tumors has increased significantly.22,25-27 Numerous genes and their mutations now can be identified and measured quantitatively. In the future, the genetic fingerprints of a tumor and host will be used to refine our diagnostic and staging capabilities.

The standard TNM classification has been available for many years. It has withstood the test of time, but in its present format it is somewhat rudimentary. Although it is a standard means of describing with consistency the extent of measurable neoplastic disease in different organ systems and anatomic locations, further refinements and additions seem to be needed. The proposed clinical severity staging system may add value, but it needs to be corroborated through prospective studies before it can be established as a measurable dimension.28

The identification of molecular events will make possible prognostic grouping and will permit selection of therapy on a less empirical and more scientific basis. Targeted treatments aimed at growth factors, genotypic molecular events, and enzymatic pathways are the therapies of the future.29-33

Multidisciplinary disease management pathways are being developed for patient care. To the extent that they assist us in giving quality care at optimum expense, they should be used. Such an organized approach allows us to perform prospective outcome research studies to evaluate the true benefit of our therapeutic interventions.34,35

We have come a long way and have made progress. The future is exciting and promising. We should learn from every patient, offer our best available treatments, and be open to the knowledge acquired in basic science and clinical research endeavors.

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