[Special Lecture]

Current Concepts of the Treatment for Head and Neck Tumor in U.S.A.

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Although the overall cure rate for patients with squamous cell carcinoma of the head and neck has not improved appreciably in recent years, the approach in the treatment of such cancers has changed dramatically. Improvements in high technology such as CT scanning for diagnosis and the introduction of cobalt and electron beam irradiation therapy are examples of such advances. Emphasis has been placed upon the importance of factors such as early diagnosis, nutritional therapy, needle aspiration biopsy to help in more accurate staging, the introduction of the maxillofacial prosthodontist, neurosurgeon, and general and plastic surgeon to the management team, the change from pre-operative to post-operative radiation therapy for more advanced cancers and a better understanding of the biology of squamous cell carcinoma through many recent contributions to the scientific literature.

Most of the cancers that occur in the head and neck are squamous cell or epidermoid carcinomas. Over the years it has been recognized and emphasized that abuse of tobacco and alcohol are important etiological factors in the development of such cancers. It's been observed many times that patients with carcinoma of the larynx usually smoke a great deal, while patients with squamous cell carcinoma of the oral cavity, oral pharynx and hypopharynx are usually not only heavy smokers but also consume a great deal of alcohol. In the United States great emphasis has been placed on the relation between cigarette smoking and the development of lung cancer. This relationship is well known amongst the population of the United States, however, such publicity has not decreased the tobacco consumption.

Unfortunately, the relationship between cigarette smoking and the development of carcinoma of the larynx, as well as other sites in the head and neck and the lower aerodigestive tract has just not been emphasized. Even less emphasized, even amongst the medical profession, is the relationship with multiple primary cancers of the upper and lower aerodigestive tract. Any improvement in the cure rate in the future must depend upon early diagnosis, and until there is an awareness by both the medical profession and the lay population of the potential harmful effects of tobacco and alcohol upon the mucosa of the upper and lower aerodigestive

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tract no progress will be made.

Cancer of the larynx is the most common site of involvement for tumors treated by the Otolaryngologist. Treatment selection is most important because of the emotional climate surrounding the decisions involved in the treatment. The loss of voice and the ability to communicate is a very serious disability and one which many patients simply cannot overcome. The difficulty with communication and the presence of a permanent tracheostoma automatically sentences many patients who have undergone total laryngectomy to being confined to their home for the rest of their life. In recent years irradiation therapy and partial surgery have played an increasingly important role in early cancers of the larynx.

The introduction of a microlaryngoscopy has been very important in our field. The use of the microscope has allowed us to examine early lesions of the vocal cord much more carefully. This technique also allows for inspection and palpation of the vocal cords, laryngeal ventricles and subglottic space in detail, and also gives the opportunity to dissect the mucosa off the cords in such a way that it can be properly oriented and thoroughly examined by the pathologist. This is especially important in carcinoma-in-situ and microinvasive carcinoma.

In our Department, carcinoma-in-situ is treated by vocal cord stripping carried out through microlaryngoscopy. It is important to remove the entire mucosa of the affected vocal cord, in order to make certain that one is only dealing with carcinoma-in-situ, since carcinoma-in-situ often co-exists with squamous cell carcinoma. The treatment may be quite different in these two lesions. Although others have recommended the use of radiation therapy for carcinoma-in-situ, we have preferred repeated vocal cord stripping, a smoking cessation program and close followup as our treatment program.

Squamous cell carcinoma with microinvasion may be treated in one of two ways. This is ordinarily very superficial, limited carcinoma with small areas of invasion through the basement membrane. In the past, we have treated such patients with irradiation therapy similar to treatment of other T1 invasive squamous carcinoma of the vocal cord. Recently, Bailey has introduced the technique of repeat microlaryngoscopy vocal cord stripping for such patients with excellent results¹⁾. Our own patients, in the past, who have been treated with radiation therapy for this condition have all been long term survivors with no ill effects.

The use of the carbon dioxide laser in the treatment of carcinoma-in-situ, microinvasive carcinoma and T1 lesions of the vocal cord are under intense study in many parts of the world. In Japan this modality has been used for some years. In the United States there are also several in which this question has been under study. Strong and his colleagues at Boston University have been in the forefront in our Country of developing this modality further²⁾. At the moment we are not certain of the status or indications for the use of this modality in this country.

In our Department, we have utilized partial verticle laryngectomy as primary treatment of cancers of the vocal cord which extend either to the anterior commissure or to the vocal process of the arytenoid, and which do not have more than one centimeter of subglottic extension. We know from our own experience, and that of others, that cancers

treated by irradiation therapy which involve these structures have a high rate of failure. The radiation therapy literature indicates that with early lesions of the vocal cord the cure rate is upwards of 90%. However, a closer evaluation of the literature reveals that many patients who are irradiation failures who are treated by salvage surgery are included in this group²⁹. Rather than to put the patient through two separate and distinct therapeutic modalities, we tend to utilize primary surgery on those whose possibilities for failure, because of involvement in the anatomical sites, are high.

The use of radiation therapy for glottic cancers is reserved for that group of patients who have a lesion of the mobile vocal cord without involvement of the anterior commissure, arytenoid or subglottic area. These patients do very well indeed with irradiation therapy and the cure rate is very high. Irradiation therapy is also utilized in those patients who do not have involvement of the above mentioned anatomical site and yet refuse surgery.

We prefer to treat patients whose cancers are limited to the supraglottic area with primary surgery. The experience with radiation therapy for such lesions has not been gratifying³⁰, and the recurrence rate has been high enough to allow us to utilize the same general concepts as we do for glottic cancers and to operate on those patients whose possibility for recurrence is high. Such surgery may be curative and it preserves the voice. In my own practice, I reserve horizontal supraglottic laryngectomy for those patients whose cancers are limited to this area. I have found that extending the surgery to include patients with involvement of structures, such as the base of the tongue or the pyriform sinus, has not been a good modality for cancer control and extending the operation out of the supraglottis inflicts considerable additional functional disabilities upon the patient.

Unfortunately, many of the patients that we see with supraglottic cancers, which may be ideally located for surgery, are excluded from consideration from conservative supraglottic surgery because of inadequate pulmonary reserve due to chronic lung disease or generalized debilitation based on other medical factors. Such patients are treated by total laryngectomy. Irradiation therapy for supraglottic lesions has been limited to those patients who refuse surgery, for those patients whose lesions are so advanced that they are treated for palliation alone. Irradiation therapy is also utilized as an adjunct to surgery.

Since 1876, when Billroth introduced total laryngectomy, the operation has been the mainstay in treatment of more advanced cancers of the larynx. We utilized this operation for T3 and T4 lesions of the glottis, as well as for transglottic lesions, infraglottic lesions and those supraglottic lesions in which patients do not qualify for supraglottic laryngectomy.

Unfortunately, the total laryngectomy is debilitating to the patient since it deprives him of the ability to communicate verbally, which is one of the qualities that sets the human being apart from the rest of the animal kingdom. We have utilized mechanical means of a laryngeal speech such as the Cooper-Rand device and the Western Electric Vibrator. These are both battery driven and provide a monotonous although understandable form of speech. Lowry⁴¹ has recently introduced a vibrator placed in a denture to accomplish similar mechanical means of speech.

Esophageal speech remains overall the most satisfactory means of voice rehabilitation, but is a technique that can be mastered by very few individuals.

Phonatory rehabilitation through surgery is by no means new. Professor Asai⁵⁾ introduced an operation which produced a tracheo-esophageal fistula enabling people to speak. This is a complex operation, and in the era of heavy use of irradiation therapy requires multiple stages and patients sometimes had difficulty with healing.

This subject, therefore, has been under intense study in our Country, and the most attention recently has been made by puncture technique to form a tracheo-esophageal fistula and insert a small valve. The introduction of the Singer-Blom and Panje valve has been the most recent innovations. These are very simple procedures, and the introduction of the valve rather than having the patient have to close the tube manually has been a great improvement.

In our Department, early cancers of the oral cavity are treated by primary surgical excision with or without reconstruction. The treatment of small superficial cancers in this way leads to very high cure rate. The hospitalization for such operations is usually relatively brief, the rehabilitation is very satisfactory and the patient experiences very few side effects. The alternative to this method of treatment is irradiation therapy, which, although it has a high cure rate, usually has more undesirable side effects than surgery, including xerostomia and loss of the sense of taste. Another reason for the use of surgery, rather than radiation, is that there is at least a 15% incidence of second primary cancers arising in the upper aerodigestive tract. If one treats the early lesions surgically with good possibilities for a cure, then irradiation therapy may be left to a later date for treatment of future primary cancers.

Our Department has been very interested, over the years, in the treatment of superficial cancer of the floor of the mouth. Such lesions are treated by 3-dimensional excision with or without marginal mandibulectomy and are rehabilitated by the use of a split thickness skin graft⁶⁾.

For patients having advanced cancer of oral cavity and oral pharynx, major surgical ablative therapy including radical neck dissection, is still the keystone of treatment followed by adjunctive radiation therapy. Most patients with cancer of the oral cavity present in a more advanced stage and are mostly patients with T3 and T4 lesions. The adequate ablation of such cancers, particularly those involving the tongue and the retromolar trigone, often makes segmental resection of the mandible necessary in order to gain adequate exposure and to be able to include pterygoid muscles as an additional margin of resection. This creates problems for the patient, in that it down-grades speech, chewing and swallowing. Most patients with major ablative surgery must retrain their swallowing act in order to accommodate to this.

The methods of reconstruction in the oral cavity have changed remarkably in the past two decades. In our Department, the split thickness skin graft is most commonly used for reconstruction. It has the advantage of being very quick and dependable in its healing, does not require a second surgical incision and tolerates post-operative radiation therapy very nicely⁷⁾. The pectoralis major myocutaneous flap⁷⁾ has also been a major step forward in reconstruction. This flap may be transposed non-delayed into the oral cavity and does not require a second stage to release the flap. The donor site may be closed primarily by wide

undermining. This flap also has the advantage of supplying bulk in the oral cavity when this is necessary. It is also helpful cosmetically in decreasing the concavity produced by segmental resection of the mandible as well as radical neck dissection.

In the last 10 years we have utilized post-operative radiation therapy in patients with advanced cancers of the head and neck, particularly those in the oral cavity and hypopharynx, particularly those patients with palpable neck nodes. Preoperative radiation therapy provided a substantial problem, in that it interfered with the proper healing of the wounds. However, the use of post-operative radiation therapy depends upon quick healing of the wounds and placing patients in irradiation therapy promptly, since most radiation therapists feel that adjunctive radiation therapy is not useful if it is applied more than two to three months following the resection. The earlier, less expeditious methods of reconstruction such as deltopectoral flaps often did not allow for patients to be placed in radiation therapy in a timely way. Therefore, the use of skin grafts and pectoralis major myocutaneous flaps has been a considerable advantage, in that the patients heals very promptly and can be placed in irradiation therapy in a timely way.

The loss of a segment of mandible in such patients still remains a problem both for comesis, and to a lesser extent, function. We had not made any effort to carry out primary reconstruction following segmental resection of the mandible. We have, however, utilized several means of reconstruction in patients who have had the loss of the anterior segment of the mandible, which is quite debilitating to them. We've utilized titanium mesh implants with and without the use of cancellus bone. We have also had recent experience with the use of osteocutaneous free grafts taken from the iliac crest with overlying skin and reconstructed with microvascular anastomosis.

Cancer of the hypopharynx remains a major problem for us even today. Most of these patients present with cancers advanced enough so that the patient is nutritionally depleted. It has long been recognized that these patients tolerate surgery poorly and have major problems with wound healing, pharyngocutaneous fistula and loss of cervical flaps. In the past, attempts have been made to improve the patient's nutrition and place them in positive nitrogen balance with the use of enteral feedings by utilizing nasogastric tube or gastrostomy. These methods are somewhat slow, and high calorie tube feeds are often poorly tolerated.

The introduction of intravenous hyperalimentation by Dudrick and his colleagues⁸⁾ has provided a means by which patients can be promptly and conveniently placed into positive nitrogen balance so that they heal well following surgery. The need for fast healing is also quite apparent in this group of patients, since all patients with advanced cancer of the hypopharynx treated in our Department are also treated with adjunctive irradiation therapy.

In an attempt to reconstruct patients in a timely way, the patients may now be reconstructed by the use of pectoralis major myocutaneous flaps, pharyngogastric anastomosis or free jejunal grafts. The pectoralis major myocutaneous flap is most useful as a one stage reconstruction for defects in the hypopharynx. It is particularly effective and useful in those cases in which there is not a circumferential defect. Those with circumferential defects reconstructed in this way often develop fistulas. The use of pharyngogastric anastomosis

following laryngopharyngoesophagectomy is useful. However, it is not appropriate for older or debilitated patients, since they may tolerate the abdominal surgery poorly. The introduction of free jejunal grafts reconstruct utilizing microvascular anastomosis has been very valuable. The patients seem to tolerate the abdominal portion of the surgery well, they are fed immediately through a jejunostomy tube and the free graft itself heals very well and tolerates post-operative surgery.

The introduction of CT scanning and craniofacial surgery has made for marked improvements in management of advanced cancers in the nose and paranasal sinuses. In the United States we see far fewer cancers in these anatomical sites than are seen in Japan. Most of our patients, at the time of the diagnosis, have far advanced cancers in this area. Radical maxillectomy, with or without orbital exenteration, is still the mainstay of treatment of cancer in this anatomical site.

With the advent of the CT scanner, we are now supplied with tremendous detail as to the extent of involvement of the nasal cavity, sinuses, cranial cavity, and adjacent structure such as the eye and the cavernous sinus. This then provides us with a basis for determining extent of resection. The addition of the neurosurgeon to the management team, to assist in the craniofacial approach to resection of tumors of the nose and paranasal sinuses which involve the anterior cranial fossa, has been a recent development. Through such an approach cancers may now be resected with great thoroughness, and it is hoped that long term cure rate will be improved in this way (Schramm & Myers). The use of the subarachnoid catheter and mannitol infusion to reduce brain volume and provide better exposure, as well as the galial-periosteal flap for reconstruction have been very excellent technical advances in this field⁹⁾.

Metastasis of squamous cell carcinoma to cervical lymph nodes remains a poor prognostic sign. In our Department we have reviewed many such cases¹⁰⁾ and have noted that the presence of extracapsular spread of cancer into the soft tissue downgrades the patient's prognosis markedly. This prognostic marker is a very important sign, as patients who have extracapsular spread of their cancer do poorly when compared to those groups who have either no metastasis or metastasis to the cervical lymph nodes which is still contained within the capsule. In our Department, all patients who have extracapsular spread of tumor are placed in a treatment program of full course irradiation therapy followed by an intensive six month course of chemotherapy utilizing methotrexate and 5FU. We are hopeful that this adjunctive chemotherapy will be helpful in reducing the development of distant metastasis in these cases.

Patients who have metastasis to the cervical lymph nodes with fixation of the mass to underlying structures (N3) are technically inoperable. In the past, such patients have been treated with pre-operative irradiation therapy and many have been made technically operable through shrinkage of the tumor and loosening of the tumor mass from the underlying structures. Such patients, however, following surgery have usually died relatively soon from either local recurrence or distant metastasis.

In a pilot project in our Department we have demonstrated that neoadjuvant chemotherapy consisting of cis-platinum and 5FU has had a beneficial cytoreductive effect. These tumor

masses have become much smaller and no longer fixed thus rendering these patients operable. Following surgery, such patients are treated with full course post-operative irradiation therapy following which they are placed into a course of maintenance chemotherapy. Whether some, or all of these patients, will be curable is not clear at present. What is clear, however, is that with the advent of agents active against squamous cell carcinoma adjuvant chemotherapy has become a part of our therapeutic program in selected patients. Many centers are now intensely studying the role of such chemotherapy in their own institutions, as well as in multi-institutional studies, and it is our hope that the National Cancer Institute will choose to fund these important clinical trials.

In the future early diagnosis, improved methods of surgery and reconstruction, improved forms of irradiation therapy and chemotherapy we hope will all be combined to improve the cure rate in patients with head and neck cancer.

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