Options in the Management of Glottic Carcinoma
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Many options are available for treatment of glottic carcinoma. Open surgery and or tumorcidal irradiation are the common ones, and chemotherapy is becoming accepted as an adjuvant to them. Unconsidered usually are political, public health, transoral “minimalist” surgery options, and chemotherapeutic prevention of further cancers. The relative usefulness of each of these options depends on the nature of the disease, its location and aggressiveness, the ability of the host to resist the cancer, the ability of the therapy to eliminate or control the cancer, the skill of the therapist who is providing the therapy, the ability of the patient to undergo the therapy, the consequent morbidity and the patients willingness to accept the morbidity; it also depends on the bias of the patient and the bias of the therapist. With so many variables there can be no “cook book” recipe for management of glottic cancer; every case is different and all options should be considered in every patient.

Of the above variables, it is probable that the least important but most influential is bias. One can find literature support (statistics) for almost any therapeutic approach; however, the quality of clinical research in the field of head and neck cancer is such that statistics concerning therapeutic outcome are not very useful. They will be dispensed with generally in this discussion. What will be discussed are the author’s beliefs which have been developed by over thirty years experience in managing the Head and Neck Cancer service at the Boston VA Medical Center and through an almost as long exchange of ideas with valued colleagues, such as Julius Hicks and Laurence DeSanto. The three of us for many years have presented an American Academy of Otolaryngology- Head and Neck Surgery Course, Options in the Treatment of Early Glottic Carcinoma, and much of the material in this chapter is discussed in this course, where generally there is agreement in principle, and often in detail. But not always. We do disagree at times. My friends are not to be held accountable for all of the beliefs proposed here.

The first bias developed from this experience is that minimalist intervention should be the preferred approach. Since ever wider treatment margins have increased morbidity without improving survival, it now seems reasonable that, as much as possible, destructive
therapy should destroy only the cancer cells and leave all other cells undisturbed. A dry and
magnified surgical field make minimalist intervention possible. Minimalist intervention may
be repeated as often as necessary to control the sickest area(s) of the patients “sick mucosa”
while minimizing morbidity. Consistent with the minimalist approach is the concept that
simple is better. Each incision, flap, graft, suture line, each toxic chemical, each ionizing
electromagnetic wave has the potential to complicate things and inhibit recovery, and will
do so given sufficient opportunity. In all areas of human endeavor, including cancer therapy,
those who make the fewer mistakes are the most successful.

Although these two concepts are emphasized in this chapter, our fundamental bias is that
the only appropriate therapy is that which fits the unique need of the patient. This therapy
may or may not conform with the cancer treatment bias of the therapist, but one way or the
other, we always treat the patient, who has a disease.

The nature of the disease.
Carcinoma of the glottis is almost always squamous cell carcinoma which develops from
exposure to carcinogens in tobacco. These carcinogens produce effects which are dose
dependent, additive, irreversible and require time for expression. If a carcinogen is widely
distributed, its effects are widely expressed since all cells exposed to a carcinogen become
unhealthy and given enough time will become cancerous. This is a common observation in
head and neck cancer so that the terms “sick mucosa” and "field cancerization" are
understood and accepted by most workers in this area.

Since the process of tobacco induced carcinogenesis is not reversible, an unhealthy
mucosa is not made healthy even though a mass of cancer cells in it is destroyed or
removed, no matter how wide the margin. Wider margins have increased morbidity, but they
have not improved survival. Should the mass of cancer cells be destroyed and the patient be
"cured", and should the patient live long enough following the “cure”, further cancers are
expected in this sick mucosa. XRT cannot "sterilize" sick epithelium and prevent further
cancerization nor can chemotherapy, nor does stopping smoking reverse the process of
carcinogenesis in the glottis.
The glottis

The glottis consists of the true vocal folds (cords) and the anterior and posterior commissures (6). Unfortunately there is not agreement on the definition of these structures. Ogura stated that the glottis extends to a line 1 cm. inferior to the free edge of the vocal fold, but do we all agree where the free edge of a curving structure is? Kirchner and Som stated that the vocal fold extends to the superior border of the cricoid cartilage, a structure not easily seen, even at direct laryngoscopy. The UICC does not define cordal limits at all; while the AJC Manual for Staging of Cancer, third edition, makes a poor attempt: "The lower boundary [of the glottis] is the horizontal plane 1cm. below the apex of the ventricle". The upper boundary of the glottis is the same apex of the ventricle. Unfortunately, it does not suggest a way to find the apex of the ventricle in the living larynx; therefore, the lower and upper limits remain obscure to those following the AJC. In Europe the ventricular surface of the fold is considered supraglottis; in the USA it remains a part of the glottis.

In this chapter we consider the true vocal folds to be bounded anteriorly by the point of the anterior commissure, posteriorly by the posterior commissure and to include the vocal process and the free edge of the arytenoids between the cordal muscle and the posterior commissure, (even though the arytenoids are specifically defined by the AJCC-TNM staging system, 1987, as a part of the supra-glottis ... more confusion, but almost never important), bounded superiorly by the horizontal surface of the ventricle and inferiorly by the line of transition between respiratory and stratified squamous epithelium, the inferior arcuate line, which may be arbitrarily selected by the examiner. This line, of course, will curve, starting at the point of the anterior commissure, it extends about 0.5 cm. caudal at the midpoint of the vibrating portion of the cord and continues along the inferior surface of the vocal process.
Fig 1. Cross section AP and lateral views of the glottis. The stripped areas indicate the glottis, as defined in this chapter.

This confusion of nomenclature reinforces the idea that a picture is worth a thousand words. All tumors are best described with tumor maps.

Fig 2. Glottic tumor maps. Ours are representational in order to clearly describe important landmarks such as (A) the vocal process of the arytenoid, (L) the thyroglottic and vocal ligaments, the conus elasticus and (E) the pre-epiglottic area.
An early glottic cancer (T1) is defined by the AJCC as that tumor which is limited to vocal cords (may involve anterior or posterior commissures) with normal cord mobility. The T1 classification implies that the tumor has not invaded the underlying muscle, and thus does not interfere with mobility or expose the lymphatics; instead it is limited to the mucous membrane and perhaps the underlying loose connective tissue of the vocal fold cover. Kirchner, in fact, states: "T1 Lesions associated with normal vocal cord mobility do not penetrate the conus elasticus, nor do they invade the underlying thyro-arytenoid muscle". His collection of cordectomy, hemilaryngectomy and total laryngectomy whole organ serial sections contains about a dozen specimens of T1 glottic cancer, half of which are verrucous tumors. None trespass the thyroglottic or vocal ligaments. However, our (unpublished) experience from attempting excisional biopsies has shown that over 20% of T1 glottic squamous cell cancers (with normal cord mobility) invade the ligament or beyond, sometimes far beyond.

A wide spectrum of tumors are included in the glottic T1 stage, from very tiny to rather large. The presumption of a uniform therapy for each results in over treating some and under treating others.

Some microscopic tumors barely invade the subepithelial tissue and are small enough to be completely removed with the cup forceps biopsy. Others may involve the entire surface of one or both cords but are confined to the surface epithelium. Some apparently confined to the anterior commissure may invade the pre-epiglottic space and represent T2 (or is it T3?) cancer; or if they pass through the thyroid cartilage and escape the larynx they are T4 cancers. Those that invade the glottic musculature have an increased potential to enter the lymphatic system. Biologically, such tumors should behave similarly to those which produce cordal fixation (T3 cancers). (We have no statistics to prove or disprove this and know of no practical way to obtain them).

Micro invasive tumors, tumors involving part of one cord, all of one cord, both cords, crossing the anterior commissure, tumors invading the musculature, tumors escaping the glottis to the pre-epiglottic space, or through the thyroid cartilage may all be staged, accurately or not, as TI, early glottic cancer.
**T2 cancer** of the vocal fold “extends to supraglottis and or subglottis, and or with impaired mobility”, but rarely will several observers agree on the extent of “cordal mobility”. This is an uncommon classification in our experience, fortunately, since it includes a disparate group. Although few surgeons agree on what constitutes subglottic extension, most agree that cancers that do extend subglottically are difficult to control locally, while those cancers that extend to the ventricular bands without fixing the fold typically are rather superficial and easy to control locally.

**T3 cancer** of the vocal fold is “limited to the larynx with vocal cord fixation”. However, we consider cord mobility, including fixation, to be a useless criteria. We continue to use it, but only for purposes of documentation.

**T4 cancer** of the vocal fold “invades through thyroid or cricoid cartilage and or extends to other tissues beyond the larynx.” This too, may be a disparate group. A cancer limited to the anterior commissure but invading through the thyroid cartilage is a T4 cancer (and admittedly rare); however, it does not require the same management as does the cordal cancer that escapes the paraglottis.

**DIAGNOSIS:**

A diagnosis more specific than that provided by the TNM staging system is essential to the selection of the appropriate treatment option. The initial step is to understand the patient who is bearing the cancer.

**Patient evaluation**

Most patients with head and neck cancer are in poor general health and are older than their calendar age. As the evaluation develops, many specialty services may need to be
consulted, most frequently: cardiac, pulmonary, endocrine (diabetes), gastroenterology and genital-urinary. Any organ system may be malfunctioning and adversely affect the management of the patients' cancer. Extensive evaluation and reevaluation is mandatory throughout the course of the disease.

1.) HISTORY

The history details completely all past medical and surgical events, with particular reference to any prior cancer. At the Boston Veterans Administration Medical Center, of 11,005 patients accessioned to the Tumor Registry from 1964 through 1983, 1,159 (10.5%) developed subsequent primary cancers; of these, 263 (23%) developed in the head and neck area. In 1,796 patients with primary head and neck carcinoma, there occurred 401 (28%) subsequent primary tumors of which 218 (12%) were in the head and neck area. Our early Tumor Registry figures are not accurate, being understated; therefore, these figures indicate minimal occurrences. In 1983, of 752 cancers accessioned, 150 (20%) occurred as synchronous or metachronous multiple primary carcinoma.

Prior treatment for cancer is carefully detailed. If radiation therapy has been utilized the exact dosage and treatment fields must be known if there is any potential for overlap. Chemotherapeutic agents, dosage, schedules and effects are recorded.

A recent history (within six months) of myocardial infarction may preclude surgical intervention under general anesthetic, and any history of cerebral vascular occlusion prohibits the use of cisplatinum as a chemotherapeutic agent.

The family, work and social history discovers the amount of family support available, both emotional and financial. Monetary costs related to the management of head and neck cancer can be considerable. They are discussed openly so that the appropriate locale for treatment may realistically be selected, be it a private institution or a publicly supported one such as a VA Medical Center. The patient's work environment (if any) is also understood, should it require cosmetic acceptance and/or a voice with specific quality. Exposure to carcinogens and co-carcinogens (tobacco and alcohol) both past and present are discovered.
The present history details not only the "what, when and where" of the head and neck cancer, but also inquires carefully about the general condition of the patient and the specific function of the numerous organ systems that are important to successful chemotherapy, radiation therapy and surgery. This includes discovery of the patient's attitudes towards his disease and any bias he may have towards a specific therapeutic modality.

2. PHYSICAL EXAMINATION:

The physical examination includes the usual evaluation of the cardio pulmonary, renal, gastrointestinal, hepatic and metabolic systems. Special attention is also directed to factors important to the patient with head and neck cancer:

Mental capabilities, emotional status and attitudes: An organic, "Chronic Brain Syndrome" and Korsakoff's Psychosis are common in those who abuse alcohol. Any treatment that requires excellent patient cooperation is impossible in these circumstances. Rehabilitative efforts also require intelligent responses. Depression is common in these patients. Its' origins should be investigated; a central nervous system etiology is not uncommon and is treated when found.

Dental evaluation. Often the dental condition of patients with head and neck cancer is the result of total neglect. Dental caries, apical abscess, and periodontal diseases are the rule and are treated prior to the institution of surgical and/or radiation therapy.

A speech therapist evaluates any patient whose vocal and articulator systems may be disturbed by treatment of the cancer. Rehabilitation is initiated prior to definitive therapy and is continued afterwards.

Auditory function is documented prior to the use of chemotherapeutic agents, such as cisplatinum, which are toxic to the cochlea and to the kidney. 24º creatinine clearance is obtained also.
Esophageal form and function can affect treatment outcome and speech rehabilitation. Patients are routinely treated for gastro esophageal reflux (GER) prior to and after glottic trauma resulting from XRT or surgery.

Tumor evaluation

Tumor evaluation requires a tissue diagnosis and determination of the exact location and extent of the cancer(s) and a careful search for metastases and for synchronous primaries.

In evaluating a glottic tumor, the classic diagnostic techniques of indirect visualization, radiologic evaluation and random biopsy are inadequate and often are misleading. Especially misleading is the condition of vocal cord "fixation." In most instances of possible fixation, a group of observers will express some disagreement at indirect examination. The differentiation of normal movement, of impaired movement, of fixation and of generalized movement in the area of the glottis is not easy. More importantly, “fixation” does not correlate well with extent of invasion. Our experience in endoscopically exploring tumor limits has shown that cancer that invades cordal muscle, especially anteriorly, does not affect cordal movement significantly unless there is massive cancer, often transglottic and frequently invading cartilage. These cancers, as often as not, later are found to be T4. Harrison has found that 50% of T3 cancers escape the larynx (T4 cancer). At the other extreme, we also have observed superficial (T1) but exophytic cancers that have “fixed” the cord because of their bulk. Since immobility may occur in cancers of any stage, we believe cordal mobility to be a useless observation, even if all observers should be in agreement. Glottic cancer should not be managed according to the presence or absence of cordal fixation.

Radiologic evaluation, including computerized axial tomography, of thyroid cartilage invasion is unreliable because of the unpredictable pattern of ossification of the thyroid cartilage. Nor have we found a positive correlation between the soft tissue image seen on CAT/MRI scans and the cancer margin found at surgery. Typically, the scan implies a much larger cancer than that found at surgery.
Misleading also are random biopsies unless they fortuitously represent the most severe area of atypism.

Endoscopy provides the most reliable pre-operative information. It includes a search for other disease and we include esophagoscopy whenever possible. While it is true that air contrast Ba swallow examination will reveal most esophageal cancer, it will not show the very early T1 esophageal cancers, which are really the only ones that may be curable.

Endoscopic evaluation must include microlaryngoscopy, unless the patient is otherwise too ill. Complete exposure of the glottis; including the anterior commissure and the ventricles, is fundamental to this effort. A difficult laryngeal exposure is made easier by placement of the patient's head and neck into the Boyce - Jackson "sniffing position" and then flexing both further as necessary to improve exposure, by selection of a laryngoscope appropriate to the patient and to the triangular glottic shape (a laryngoscope with triangular distal end), by placement of the laryngoscope along the path of least resistance, by use of a true suspension device (such as the BU Suspension, rather than a laryngoscope holder such as the Lewy) in order to apply the laryngoscope force towards the larynx and away from the teeth and gums, and by allowing time for the force to work. With these techniques, an easy exposure is made almost perfect. The true vocal folds are exposed from vocal process to anterior commissure without the need for external pressure, the endotracheal tube remains out of sight between the arytenoids and there is no risk to the teeth, gums and cervical spine.

The following diagnostic techniques are helpful during microlaryngoscopy:

1.) Visualization: We use 6x to 10x magnification with 20x oculars. Mirrors and telescopes also are used to examine areas not visible directly, such as the subglottis or the depths of the ventricles. It is easy to bend or twist the larynx using external pressure with one hand while the other uses a blunt probe or "cord roller" to expose subglottic cord or the ventricle. Should the lateral margin of the ventricle remain obscured by the false fold, the false fold may be excised without difficulty. Although keratosis and even erythroplasia often
are less obvious when the cords are stretched by the suspension technique, a supra vital stain (Toluidine Blue-O) helps delineate these lesions. When stained, keratosis appears whiter and erythroplasia appears more purple than its surrounding tissue. Supravital stains however are low in specificity and sensitivity for cancer. Mucous and ulceration from any cause is stained, whereas cancer underneath keratosis or otherwise intact epithelium is not stained.

2.) **Movement:** The tumor and the mucous membrane are grasped with a dull forceps and an attempt is made to move the superficial tissues over the underlying thyroglottic ligament, vocal ligament and vocalis muscle. Fixation implies invasion of the body of the fold.

3.) **Palpation:** A probe is used to palpate the soft tissues for the presence of a mass or fixation

4.) **Staining:** Supravital staining has not been as helpful for glottic lesions as it has been for those in the oral cavity. For expression of dysplasia, the stain must be exposed to excess nucleic acid. Since glottic cancers tend to develop below a layer of keratosis, they do not demonstrate supravital staining unless there is ulceration, and ulceration is usually easily seen, unstained, with the aid of the microscope.

5.) **Excisional biopsy:** An enbloc excision of the entire specimen is obtained, if possible, as follows:

   **Informed consent**

   The patient must understand the advantages and disadvantages of the excisional biopsy approach. While excisional biopsy can involve nothing more than removal of a few mm of epithelium, it also can result in a complete cordectomy, or something in between. The morbidity of excisional biopsy differs significantly over such a range of options. The patient must clearly desire any limitations that are agreed upon.
Frozen section

With early lesions that are confined to the vocal fold “cover”, complete excisional biopsy is often the only way that the most severe expression of the lesion can be determined. Biopsy for the purpose of frozen section evaluation prior to excisional biopsy of questionable lesions distorts the specimen and should not be performed. On the other hand, there should be a reasonably firm diagnosis of cancer prior to undertaking an “excisional biopsy” that extends well into focal fold muscle. Here experience helps. If the tumor looks like cancer, is large and obviously invasive, it very likely is cancer. Not many conditions today mimic a deeply invasive squamous cell cancer. Even so, we advocate that frozen section biopsy be obtained and be evaluated by the surgeon together with the pathologist prior to any extensive, “curative” excisional biopsy; if doubt remains, await the permanent sections.

Submucosal injection

Polypoidal degeneration of the vocal folds is often found on the ventricular surface of the vocal folds of patients with head and neck cancer, and cordal cancer almost always originates on the same ventricular surface. This is fortuitous because the subepithelial fluid associated with the polypoid degeneration increases the depth of the subepithelial “space”, thereby increasing the distance between the cancer on the “cover” and the underlying “body” of the fold. This offers some protection to the body of the fold during excisional biopsy and makes the dissection easier. If, in the case being investigated, there is no edema or but minimal edematous degeneration of the fold being evaluated, it is helpful to produce it by injecting the ventricular submucosal “space” with a dilute solution of epinephrine (Xylocaine® with epinephrine 1/100,000 is convenient). If the entire lesion elevates along with the mucosa, it suggests that the lesion is superficial, it has not invaded the dense connective tissue overlying the muscle and it may be dissected off of the fold easily. The injection also reduces bleeding so that visualization is improved, and by increasing the distance between the mucosal lesion and the underlying thyroglottic ligament and vocalis muscle, the process of excisional biopsy is made easier and safer, particularly if the CO2 laser is used for the resection.
Fig. 3. In this illustration, there is polypoidal degeneration of the vocal fold on the right. A similar cancer involves both vocal folds. However, that on the left side invades the body of the fold, while that on the right does not because of the increased distance between the surface and the thyroglottic ligament. The cancer on the right fold can be excised with preservation of the thyroglottic ligament and the post operative voice will be improved. Excision of the cancer on the left will result in loss of a significant amount of fold muscle and the post operative voice will be poor. An early glottic cancer that lifts with the surface upon injection of fluid into the subepithelial space usually is similar to the cancer on the right; it too can be excised with preservation of the thyroglottic ligament and improved post operative voice.

**Technique for excision**

The mucosal limits of the resection are established by incisions one or two millimeters from the margin of the lesion. We prefer to use a sickle knife or an upturned scissors. The CO2 laser may be used, but if the patient margin is not enlarged, then the histologic margins will always be reported as positive, which tends to upset the tissue committee. The lesion is grasped with a blunt forceps, put on tension and bluntly dissected along the underlying dense connective tissue (thyroglottic ligament, vocal ligament, conus elasticus).

Should the cancer invade the dense connective tissue, or the vocal muscle, it is carefully excised at the appropriate depth to separate the cancer from the patient. Here the CO2 laser is the ideal instrument. If the cancer is found to be too large to remove by this approach the procedure is terminated and the patient is later managed according to this important new information.
**Search for residual cancer:**

The cordal wound is examined under 16x - 25x (with 20x oculars). Cancer aggregates as small as 100 cells can be detected easily in the dry wound resulting from a laser excision. An inflammatory response in the residual muscle also is cause for suspicion. These areas are checked with frozen section biopsies. Further excisions are performed as necessary, stopping only when it is felt that all tumor has been removed or that it cannot be removed endoscopically.

**Mapping the lesion.**

The location of the cancer and the lines of the resection are recorded on a tumor map (see above).

**Processing the excisional biopsy specimen.**

A carrier substance is used to orient the specimen properly for histologic processing (the white meat of a cucumber is cut into 15mm x 15mm x 1mm slices, dehydrated by 3-24 hour passages through 95% alcohol and then stored in alcohol. To use the cucumber as a carrier, place it in a petri dish and then press out and absorb the alcohol with a sponge. A drop of glue (egg white or benzoin) is placed on the surface and the excisional biopsy specimen is flattened onto it making certain that all edges are uncurled. The petri dish is gently flooded with formaldehyde fixative and covered for transportation to the histology laboratory. After fixation, the entire specimen including the cucumber is imbedded in paraffin and multiple sections perpendicular to the surface and along the long axis of the specimen are obtained.

**Evaluating the specimen.**

All excisional biopsy specimens must be examined by the surgeon together with the pathologist. Each will have knowledge that the other may need to arrive at the correct diagnosis.
OTHER CONSIDERATIONS:

Needs and abilities of the patient: All patients differ in their attitudes towards themselves, their disease and life in general; this and medical problems, especially recent myocardial infarct or the presence of mental deterioration ("chronic brain syndrome", Korsakoff's, Alzheimer's, etc.) or deterioration in their physical age and general ability to undergo any form of treatment (Karnofsky scale), and some abnormalities of body configuration can make some treatment options impossible to carry out.

Patient bias: Medical sophistication is now common in many patients; often they have known or read about others with similar cancers, how they have been treated and the outcome. They have developed strong opinions as to the form their own treatment should take. It is wise to respect such bias whenever possible.

The ability of the physician(s) to provide every option with equal skill is rare. The most skillfully utilized option usually is the most successful.

TREATMENT OPTIONS AND CONSEQUENCES:

A.) POLITICAL:

Through the political process one could, in theory, outlaw growing, importing, selling and using tobacco, i.e., abolish a $16 billion per year industry with incidental health costs estimated at a further $37 billion per year. This notion is so impractical that it merits no further comment except to say that even if successful we would still be faced with 20 or 30 years of management of those head and neck squamous cell carcinoma already induced by tobacco exposure.

B.) PUBLIC HEALTH:

Public Health measures include many already in use: avoidance of tobacco exposure, maintenance of a healthy lifestyle including proper diet, reduced alcohol intake, etc.
(Physicians of course, should provide good role models and so guide by example as well as by precept). Unfortunately, these simple measures are for many impossible.

C.) MEDICAL:

Gastroesophageal reflux disease: The relationship between chronic irritation and the development of cancer has long been noted in many and varied locations in the body. In the larynx, both tuberculosis and syphilis once were implicated; more recently, gastroesophageal reflux disease (GERD) has been associated with glottic cancer. Morrison, Ward and Hanson have reported GERD in cases of laryngeal cancer developing in non-smokers.

GERD should be investigated in all patients with glottic cancer and treated when present. Further, we routinely employ anti-reflux therapy in all patients undergoing glottic surgery. Although we have no experimental evidence to support this therapy, we believe it to be more beneficial to the healing process than is voice rest.

D) BIOCHEMICAL:

Biochemical modification of the biologic response to the carcinogens of tobacco may be possible. Vitamin A analogs appear to inhibit the process of head and neck carcinogenesis, but unfortunately they are impractical in the high doses that have been shown to be beneficial. It is our experience that the associated skin reactions of severe scaling and itching are not tolerated indefinitely, and if the medication is stopped, the atypia reappears. A multi-institutional evaluation of low dose cis-Retinoic Acid was initiated in 1992.

At present there is no proven chemotherapeutic agent suitable for use as the primary treatment of squamous cell carcinoma of the head and neck, including the glottis, even though many uncontrolled studies and occasional anecdotal experiences suggest that agents such as cisplatinum combined with 5FU may provide long-term control. We have occasionally seen "life-long" resolution of a synchronous "mini" cancer in patients undergoing adjuvant chemotherapy for other and larger cancers.
Neo-adjuvant chemotherapy has excited many with its promise. The preliminary results of a Veterans Affairs Cooperative Study, prospectively comparing, in T3 and T4 glottic squamous cell carcinoma, surgery plus irradiation to cis platinum / 5FU induction chemotherapy plus irradiation have shown a comparable early survival rate in the two study arms. The long term outcome remains unknown, as does the contribution of chemotherapy (and surgery, as well) to the outcome compared to that of radiotherapy alone. We believe that this therapy remains investigational and should be utilized only as a part of an organized research study.

Techniques designed to strengthen the natural immune system include the use of substances which block prostaglandin synthesis, plasma apheresis to remove immune "blocking" factors, interferon to add natural immune substance, etc. Again, these adjuvants are exciting but unproven.

E.) RADIATION THERAPY:

Radiation therapy has been the treatment of choice for early glottic carcinoma in the North American continent. Its proponents claim that it works, that it is easier on the patient than surgery, and that it leaves a normal voice. While there is some truth here, there is also myth.

Does it work? Control rates for T1 glottic carcinoma, reported by various radiotherapists usually range between 85% to 90%.

However, there is a source of uncertainty in every item in this sentence. First, the determination of control typically is made by the radiotherapists, the majority of which do not themselves examine the glottis before or after treatment. The T1 classification, as discussed earlier, is frequently in error, even when made by a laryngologist. Further, a significant number (about 10%) of patients referred to us for treatment of biopsy proven glottic carcinoma, upon re-examination by microlaryngoscopy and excisional biopsy, have demonstrated no evidence of cancer. Their tumors had been removed entirely by the first
diagnostic biopsy. If they had been treated further with radiation therapy the radiotherapist could claim credit for successfully treating these patients without cancer. Lastly, 25% of these elderly and sick patients die during the period of observation, for reasons other than cancer. In this population, control rates of greater than 75% are reportable only by use of relatively new statistical procedures involving “intent to treat”. Although these techniques have become widely accepted, they remain as much art as they are science. Moreover, they were not available when many of the often quoted reports were written. This is true, not just for reports by radio therapists, but for all reports of all approaches. All statistics involving head and neck cancer should be viewed with scepticism.

Is it easier on the patient? The early effects of XRT include burnt skin, mucositis with dysphagia and hoarseness, fatigue, malaise and loss of appetite. Although radiation therapy may "cure" the cancer, it makes a sick mucous membrane sicker. XRT cannot be repeated in the same area. Ionizing radiation does not prevent or reverse the process of carcinogenesis, does not "sterilize" premalignant atypia. It is, in fact, oncogenic. Metachronous cancers frequently arise in areas previously irradiated. Other long term effects of XRT include: edema, atrophy and fibrosis, and in 1-2%, necrosis. Although immediately not obvious as are the effects of surgery, the long term effects of XRT are inevitable, degrade vocal quality, and may be disabling. Failures are salvaged (85-100%) by surgery, usually total laryngectomy. These morbid costs of XRT are in addition to those of the diagnostic endoscopy, as are the monetary costs of the treatments which must include the loss of time and perhaps work during the six weeks of treatment.

Is the voice better? One of but many determinants of vocal quality is the similarity of movement of the mucous membrane cover of the vocal folds as subglottic air flows between them. Treatment of any tumor large enough to extend into the glottic musculature produces scar tissue that fixes the mucous membrane cover to the muscle. The resulting asymmetry of cover movement produces a hoarse voice. While scarring and fixation are expected from surgical excisions that extend into cordal muscle, scarring and fixation also occur with XRT of cordal tumor with similar extension, and the voice remains similarly poor. Moreover, the long term effects of irradiation, e.g., mucosal atrophy, loss of mucous secretion, and muscle atrophy and fibrosis, also impair vocal quality, even in those whose cancer was limited to the vocal fold cover.
fig 4  a) the normal waves occurring in the cover of the vocal fold during voicing, b) an “early” glottic cancer that invades the muscle of the vocal fold body, c) following treatment of any sort, scar tissue binds the cover to the body and disturbs the vocal wave.

Do we use radiation therapy? Indeed we do. It is an option available to every patient and should it fit the needs of the patient, it is provided. Most commonly it is used for management of extensive T1 cancers, those involving both vocal folds or demonstrating field cancerization throughout the larynx, or those whose deep margins are uncertain following an attempt at excisional biopsy. Occasionally it is used because patients prefer it, or because the patient is not suitable for suspension microlaryngoscopy.

For advanced glottic carcinoma, radiotherapy as the primary treatment has the potential advantage of sparing the larynx, but it does so at the risk of increased morbidity and decreased survival. We advocate this option when the patient prefers it, when the patient is unable to undergo the stress of surgery, or when the cancer is “unresectable”. These are uncommon events. Most commonly, radiotherapy is employed as post operative adjuvant therapy in those patients with metastasis to more than two cervical nodes, or with extracapsular spread.

F.) SURGICAL OPTIONS:

LARYNGO-FISSURE AND CORDECTOMY : Laryngo-fissure or thyrotomy splits the thyroid cartilage at or near the midline to provide exposure to the glottic interior. It is one
of the earliest laryngeal operations. Pelletan, a French surgeon, used it to remove a piece of impacted meat in 1778. It was used in 1863 by H.B. Sands of New York to remove a carcinoma, perhaps successfully. The patient died of other causes two years later. Solis-Cohen, in 1867 claimed the first cure of laryngeal cancer by laryngo-fissure, his patient surviving another twenty years.

**Cordectomy** removes all of the fleshy part of the true vocal cord. Many surgeons remove the false cord as well, but we prefer the minimalist approach and remove the cancer with but a few mm of margin. A tracheotomy protects the postoperative airway.

Laryngo-fissure and cordectomy has become the treatment of choice in much of the continent of Europe and occasionally in areas of North America as well. It is another option, but a rare one in our hands. Suitable candidates are those patients:

1. with tumor limited to one mobile cord and that does not involve the anterior commissure or the vocal process
2. who are young and should not be irradiated
3. whose anatomy prohibits transoral excision
4. whose extent of tumor is in doubt
5. who will be difficult to follow
6. who prefer cordectomy
7. who following failure of XRT fit above criteria #1,3 or 6.

(All criteria need not apply to every patient.)

Laryngo-fissure and cordectomy is a technically easy procedure, quick to perform and with little peri-operative morbidity (an external incision and a tracheotomy) so that the post-operative hospital stay is short. It provides an excellent specimen for histologic evaluation to determine the adequacy of treatment. Follow up is easy. The post-operative voice is poor and remains so. "Cure" rates of 90% or better are reported.
TRANSORAL RESECTION (Excisional biopsy):

Transoral resection is not a new idea. Lynch, in 1920, reported his first nine cases of transoral cordectomy. He eventually accumulated a series of thirty-nine patients. An occasional report by others described the continued usefulness of this approach in carefully selected patients. New and Dorton in 1941 reported a 90% cure rate for patients with early cordal cancers treated by transoral excision of the cord with surgical diathermy. In 1946, Lejeune described the following advantages of transoral resection using the Lynch suspension:

1.) simplicity of operation
2.) no external excision
3.) preservation of continuity of the thyroid cartilage
4.) better post-operative phonation
5.) shorter hospitalization
6.) good prognosis

Lillie and DeSanto in 1973 reported a series of 290 patients with early glottic carcinoma treated at the Mayo Clinic. Of these, fifty-seven with invasive carcinoma and forty-one with in situ carcinoma of the true vocal cords were treated transorally by means of suspension laryngoscopy. None of the ninety-eight patients so treated died of laryngeal carcinoma. One required laryngectomy eight years after treatment. Four patients were retreated by transoral methods. The authors also noted that the technique of suspension laryngoscopy and transoral excision was “generally unappreciated, not considered, unknown or rejected as unsound”. However, Strong, Vaughan, DeSanto, Kaufman, Motta, Steiner and others have continued to develop the method for selected patients. We have referred to it as "excisional biopsy". The procedural details have been described in the section on endoscopic evaluation, page.......
Excisional biopsy is an endoscopic, en bloc resection of the entire lesion for serial sectioning and histologic review. Criteria for attempting glottic excisional biopsy include:

1. Cordal cancer with normal or impaired (not fixed) cord mobility, as confirmed at endoscopy. Cancer may involve the anterior commissure and may have been treated previously.
2. Medical suitability for suspension microlaryngoscopy

Since the stage of the lesion, as determined by clinical evaluations such as indirect laryngoscopy, CAT and MRI often is inaccurate, we do not use the information from these studies to determine treatment. We find that the process of excisional biopsy provides the only accurate determination of the extent of the cancer. It is for this diagnostic purpose, largely, although not entirely, that we attempt excisional biopsy in those whose cancers involve the anterior commissure or have been treated previously.

Unsuitable for an attempt at excisional biopsy are

1. Patients with severe mucosal atypia over the entire glottis
2. Patients who request radiation therapy because of its purported superior vocal quality (however, see discussion of voice quality, above. "Unsuitability" in this instance results from the unproven but conventional claim to better voice with XRT. Defensive medicine may not be best, but it is often prudent)

Excisional biopsy can be considered to result in a curative resection if all of the following criteria are met:

1. The lesion can be seen in its entirety;
2. Following removal of the lesion, there is no evidence of tumor in the wound on examination with the surgical microscope at 25x,
3. Histologic examination of the excised specimen shows the margins to be free of cancer.
At the Boston VA Medical Center, attempts at excisional biopsy have been carried out since 1972. On several occasions we also have attempted to describe this experience in statistical terms, but have found this to be impossible because the phenomenon of field cancerization results in imprecision in both numerator and denominator. Over time, many of our patients develop multiple glottic cancers. We do not believe that a cancer appearing at some future time on an opposite vocal fold is a recurrent cancer; indeed, a cancer appearing on the same fold in a different location, or many years later, may not be a recurrent cancer. This is a subjective call, obviously prone to bias, and it is common in our patient population. As an extreme example, one of our patients, following XRT, underwent excisional biopsy 13 times for new and or recurrent glottic cancer over a span of 12 years before finally succumbing to lung cancer. His glottis remained functional, and we believe, as did the patient, that the management of his glottic disease was successful. But we do not know how to describe this patient, and other similar patients, statistically; we can offer no “cure rate”. However, it is our impression that true recurrence is a rare event in those patients who met the three criteria above.

This example also illustrates the fact that should a new cancer develop or should the old cancer recur, excisional biopsy may be repeated as often as necessary.

In those who do not meet criteria 2 and/or 3, above, excisional biopsy provides unequivocal evidence of the extent of the disease and of the need for further therapy as appropriate. This may be started without delay, as following any other biopsy.

**Morbidity:**

Excisional biopsy is minimalist therapy. It attempts to separate, with the least possible injury to normal structure, the cancer from the patient; therefore, the morbidity following successful treatment of glottic cancer by excisional biopsy is less than with any other method, including, we believe, radiation therapy. This is true for form, function and monetary cost. Following recovery from anesthesia, patients may be discharged from the hospital and resume normal activity, except for voice precautions which are continued until
there is complete mucosal healing. Nothing further need be done, other than careful follow up.

**FAILURE of EXCISIONAL BIOPSY**

If excisional biopsy does not completely separate the cancer from the patient, further tumorcidal treatment is needed. If the margins are uncertain or if the residual tumor is minimal, radiation therapy is usually offered, with dosage and fields appropriate to the extent of invasion revealed. Cancer deep in cordal muscle, even with normal mobility of the fold, is treated with wide field radiotherapy, including the neck(s). If the cancer is found to escape the glottis or the larynx, appropriate open resection, including neck dissection, is recommended. The extent of the laryngeal frame work resection in the young and otherwise healthy patient varies according to the extent of the cancer. Unfortunately, most of our patients are not young or healthy; therefore, the extent of resection is determined by their ability to recover from the inevitable complications of function conserving procedures. A total laryngectomy provides the debilitated patient with the best chance of uncomplicated recovery and prompt access to post operative radiation therapy. This is our primary goal, and total laryngectomy with neck dissection is the procedure most often selected. Both necks are examined, suspicious nodes are sampled with frozen section evaluation, and selective node dissection is performed as seems necessary. Post operative radiation therapy is also offered if the deep cancer margin is less than 5 mm and or there are multiple cancerous nodes or extracapsular extension.

**AIRWAY MANAGEMENT:**

Algorithms for management of airway compromise depend upon urgency, with immediate obstruction requiring immediate cricothyroidotomy. However, we prefer to avoid incisions in the neck. Whenever possible, patients with a compromised airway are intubated initially: they are taken to the operating room, started on intravenous hydration, given dexamethasone 10 mgm iv, monitored by EKG and oxymeter, examined by indirect laryngoscopy or with a fiberscope and intubated while awake. Prior to attempting intubation
the anesthesiologist is made aware of the location and extent of the cancer, the patient’s anterior neck is infiltrated with a local anesthetic, and the following equipment is made available: a tracheotomy kit with knife at the ready, a tubed laryngoscope with a bore large enough to pass a 7mm OD endotracheal tube, a tube of this size, a rigid bronchoscope for “coring” out the tumor, if necessary, and double suction. If intubation is successful, the patient is admitted to the ward and evaluated generally and “tuned up” prior attempting staging endoscopy. During the staging endoscopy the airway may be improved by excising cancer tissue with the CO2 laser, or even with use of large basket forceps. Usually the patient may be extubated; however, if the airway remains inadequate, we prefer to leave the patient intubated until laryngectomy can be carried out. Tracheotomy is performed only if XRT will be the treatment of choice.

REHABILITATION:

Every patient with glottic cancer requires some rehabilitation, even those who are managed minimally. Post treatment, all patients are followed by the voice therapist and treated according to need. The most common problems are those related to voice and all undergo voice therapy of some sort, ranging from training in breath support to development of esophageal speech. Reasons for success or failure are not always clear. Motivation and intelligence are critical elements, but sometimes even the most ideal patient cannot master esophageal speech and only 8% of our patients are successful at this. Of the failures, about 35% are suitable candidates for tracheo esophageal shunt placement. We have abandoned the practice of creating the shunt at the time of laryngectomy, first, because of problems with the T-E fistula during post operative radiation therapy, but also because many of our patients simply are incapable of caring for the valve. Of those shunts placed in selected patients, about 85% are successful. The electrovoice is furnished to all laryngectomies in the immediate post operative period, and most (55%) continue its use indefinitely. Non vocal communication, such as writing, is used by 6%.

The most severe problems arise in those who have undergone some form of open, partial laryngectomy and are related to problems with aspiration on swallowing. This may take
several weeks of retraining to overcome. Here, a “swallow team”, is invaluable to the extent that if this therapy is not available, some other form of cancer management should be selected.

Smoking cessation programs are initiated in those who are willing to participate.

TREATMENT PLANNING - CHOOSING THE OPTIONS

There must be a primary physician who is responsible for managing the patient, and only one; however, management of a cancer patient requires a multidisciplinary approach that utilizes the complimentary skills of many health care professionals. A TUMOR CONFERENCE (or Tumor Board) formalizes this approach: The function of the Tumor Conference is:

1. to inform the primary physician of all pertinent facts regarding the patient and his disease
2. to act as a forum where the members of the team may discuss the advantages and disadvantages of various treatment programs including protocols.

The Tumor Conference cannot act as a decision making body regarding treatment because the patient and the patients family do not participate in the discussion. Common sense suggests and common law demands that the patient actively participate in the treatment process (informed consent). Management of head and neck cancer requires enormous work and dedication by both physician and patient and a cooperative attitude is achieved and appropriate treatment is selected only when the patient is an active member of the team and participates in all decisions regarding his care, including choosing his "option".

The best option is the one that best satisfies the needs of the patient.