Current Practice

Carcinoma of the Larynx

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The larynx is in many ways a unique structure, combining the primitive functions of respiration and deglutition with the phylogenetically more recent acquisition of speech. Impairment of the voice has long been recognized as an early symptom of laryngeal cancer, yet the management of neoplasms of this organ presents special problems to the laryngologist, since satisfactory rehabilitation after treatment requires, wherever possible, an adequate means of communication. The psychological importance of the voice varies with different ethnic groups, but on no occasion must its preservation be allowed to jeopardize effective eradication of disease, a policy which unfortunately is not universally practised.

Incidence and Possible Aetiological Factors

It is estimated that laryngeal cancer represents less than 2% of all human neoplasms and is therefore relatively uncommon. Considerable difficulties may be experienced when attempting comparisons of incidence rates originating from various parts of the world, for in some countries deaths from laryngeal cancer may be included in the figures for all respiratory neoplasms. Current estimations, however, give an incidence figure of between three and four per 100,000 population and a sex ratio of 10:1.

It is difficult to be certain whether there has been any real increase in incidence over the past decade, for most results are based on mortality rates. Since improvement in treatment and earlier diagnosis have resulted in a considerable improvement in survival rates this may conceal any real increase in incidence. Only comparisons of morbidity rates would disclose the true position, and where such information is available there does appear to have been an increase in laryngeal cancer in recent years—though not as dramatic an increase as that found for lung cancer.¹ Nevertheless, the sex ratio of this predominantly male disease has remained virtually unchanged since the figures of Felix Semon were published in 1907.²

As in the case of cancers elsewhere in the body chronic irritation is believed to be an important aetiological factor. Conclusive evidence was provided in 1956 by Wynder *et al.*³ of an association between smoking and laryngeal cancer, though again not so striking as that found between smoking and lung cancer. Only one of their 209 patients with cancer of the larynx was a non-smoker. Both pipe and cigar were also incriminated in this study, but the data showed quite conclusively that the risk of laryngeal cancer increased with the amount of tobacco smoked rather than the technique used.

It is not difficult to visualize the harm that might be caused to the laryngeal mucosa by repeated exposure to hot, carcinogenic tobacco smoke. It is harder to envisage similar changes resulting from ingestion of alcohol. Environmental studies have shown that heavy alcohol consumption, particularly of whisky, also plays an important part in the aetiology of laryngeal

cancer—brewers and publicans being particularly susceptible. Many patients, however, are heavy smokers and drinkers, and it is possible that the alcohol acts primarily as a promoter, while the tobacco initiates the neoplastic change in the larynx.

Premalignant Conditions

According to current nomenclature "pre-malignant" implies a condition which may either be reversible or may eventually result in frank malignancy. There is considerable disagreement about the frequency with which chronic laryngeal keratosis progresses to invasive carcinoma. Figures for patients developing cancer after periods of between six months and seven years vary from 3 to 40%.

Despite lack of agreement regarding prognosis and management, all agree that chemical irritation, particularly smoking, is an important factor in the aetiology of the keratotic condition. Prolonged irritation from chronic upper respiratory infection or industrial exposure to wood and metal dust may also result in hyperplasia of the laryngeal mucosa. Some of these cases will inevitably progress to carcinoma and might perhaps explain the occasional development of a laryngeal cancer in a non-smoker.

Anatomical Divisions of Laryngeal Cancer

In 1879 Krishaber⁴ first suggested the terms "intrinsic" and "extrinsic" to describe the anatomical sites at which laryngeal cancer occurs. These terms were universally adopted, but in recent years it has become apparent that they permit too variable an interpretation to allow accurate assessment of tumour site and they have been largely replaced by the terms supraglottic, glottic, and subglottic.

By definition the supraglottis comprises the posterior surface of the epiglottis, the false cords, and the ventricles. The glottis includes the upper surface and edges of the vocal cords together with the anterior and posterior commissures. The subglottic region is limited above by the inferior surface of the vocal cords and below by the lower border of the cricoid cartilage. Agreement about the anatomical limits of these sites is essential in any classification designed for international acceptance. In 1962 the International Union Against Cancer (U.I.C.C.) accepted the TNM system for the larynx for a trial period until 1972. This is now used by most laryngologists, though slightly modified in the U.S.A.

T relates to the tumour and indicates the different degrees of extension of the cancer based on clinical examination, endoscopy, and radiography.

N defines the state of the regional lymph nodes where amenable to examination.

M indicates the presence or absence of distant metastases.

In the larynx no account is taken of histopathology in this classification, but the system does allow combination of various degrees of the three components to be expressed as stages.

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No experienced surgeon believes that this or indeed any existing system of classification accurately reflects the true histological extent of the tumour. Yet the necessity for precise recording of the macroscopic extent of the disease is in itself worth while, and the universal adoption of one system does ensure that published results bear some comparison no matter in what country they originate.

Pathology

Laryngeal cancer is invariably of the squamous cell variety, though occasionally adenocarcinomas may arise from the mucous glands. Less than 2% of malignant neoplasms of this organ arise from connective tissue, fibrosarcoma being the most common. The majority of the squamous carcinomata are moderately well differentiated, but variations in the degree of differentiation are often found in various parts of the same tumour. This probably explains the lack of correlation between routine biopsy reports and prognosis. Both the treatment and the prognosis of laryngeal cancer are governed to a large extent by local anatomy. The cartilaginous framework of the larynx offers some temporary resistance to spread, though ultimately it is penetrated through the vascular foramina, the cancer then growing within the perichondrium (Fig. 1). An exception is the epiglottis, which offers no impedance, being rapidly penetrated by advancing tumour.

FIG. 1.—Serial section of laryngectomy specimen showing destruction of left thyroid lamina by extensive transglottic carcinoma.

A more favourable factor is the virtual absence of lymphatics in the true vocal cords, hence the rarity of lymph-node metastases from early tumours arising at this site. The remainder of the larynx, however, has a well-developed network of lymphatic vessels passing to the upper and middle deep cervical lymph nodes from the supraglottis, and to the lower deep cervical, paratracheal, and superior mediastinal lymph nodes from the subglottic region. The frequency with which these lymph nodes are invaded by metastatic cancer is of great importance in both the surgical and the radiotherapeutic treatment of laryngeal cancer.

Management of Glottic Cancer

The commonest site for laryngeal cancer in this country is the anterior half of the vocal cord. Provided the tumour remains localized to a mobile vocal cord (stage I) the five-year survival rate is at least 85%. This excellent figure is reduced to about 60% when the cord is fixed or when the neoplasm extends to the anterior commissure (stage II), and to 30% with hemilaryngeal involvement⁵ (stage III).

Involvement of the anterior commissure brings the danger of extension to the pre-epiglottic space, thyroid cartilage, and thyroid gland; while superiorly invasive growth may spread to involve the laryngeal ventricle and false cord—areas rich in lymphatic drainage. Though subglottic extension of glottic tumours is not uncommon, when associated with cord fixation the prognosis is considerably worsened.

The overall recurrence-free crude survival rate given by Shaw⁵ for 306 consecutive patients with glottic carcinoma is 62.1% and is in keeping with other published results. In view of the excellent prognosis for early cordal carcinoma it is disappointing that the average duration of hoarseness previous to diagnosis is usually six months, and it must be emphasized again that any patient with hoarseness persisting for longer than two weeks must have an expert examination of the larynx. Pain is never a symptom of early glottic cancer and occurs only when there has been invasion of cartilage.

Laryngeal cancer remains a serious disease, yet there has been an unfortunate tendency in recent years to view its management as a trial of strength between radiotherapist and surgeon—to the possible detriment of the patient. Despite the impressive statistical evidence produced by supporters of both modalities the fact remains that in many patients it is not possible to be absolutely certain of the true extent of the neoplasm and therefore individual series may not be strictly comparable. This may perhaps explain the surprising difference in published survival rates purporting to be based on the treatment of similarly staged tumours.

The principles of treatment outlined in this paper are based on my own personal experience of this neoplasm, knowledge of the techniques, and results of other experienced laryngologists, and on a critical evaluation of the more reliable world literature. I fully expect these views to be modified in the years ahead.

Where adequate external irradiation—in the form of cobalt-60 therapy—is available, the majority of small stage I tumours confined to the vocal cord are best treated by radiotherapy. This results in a normal voice and a five-year survival rate of at least 85%. Over one-half of the failures can still be salvaged by secondary surgery, which may only need to be some form of partial laryngectomy. Similar treatment is also effective in the early stage II neoplasms, provided the vocal cord remains mobile. Unfortunately, difficulty may be experienced in detecting minor degrees of impairment of mobility with consequent overoptimistic conclusions about the true extent of the growth.

More advanced glottic lesions are better treated by laryngectomy, with radical neck dissection reserved for cases with palpable cervical lymph nodes. Nevertheless, many patients with relatively advanced disease continue to receive primary irradiation. The management of these irradiated patients poses many problems to the laryngologist, for not only may the true extent of the residual or recurrent neoplasm be difficult to detect but there is often difficulty in obtaining the histological evidence necessary before recommending total laryngectomy. This delay in carrying out salvage surgery might seriously jeopardize the patient's prospects of long-term survival.

Supraglottic Neoplasms

With the exception of carcinomas arising from the tip of the epiglottis, supraglottic neoplasms invade surrounding structures

and metastasize to regional lymph nodes more rapidly than lesions occurring on the vocal cords. Staging of these tumours is difficult except for the early exophytic lesion, for extension into soft-tissue or pre-epiglottic space may be difficult to determine. Since early symptoms are minimal many patients seek attention only when their tumour is extensive and producing pain and dysphagia from ulceration and infiltration into the aryepiglottic fold or pyriform fossa. Dyspnoea and hoarseness may result from the sheer bulk of the exophytic tumour. In many patients the presenting symptom is an enlarged cervical lymph node and there is reliable histological evidence for supposing that metastatic deposits will occur in at least 50% of all patients with supraglottic cancer.

The early-stage tumour is invariably best treated by external irradiation, as in the case of the vocal cord. Unfortunately, most supraglottic cancers are more advanced when diagnosed—indeed, my own histological studies on serially sectioned laryngectomy specimens have shown that the true extent of these tumours is invariably greater than was clinically suspected. The five-year survival rates for both surgery and radiotherapy are unsatisfactory, though they are difficult to compare statistically because of inaccuracies inherent in present methods of staging. Published results, however, suggest that, provided surgical excision is combined with elective neck dissection, a 60% five-year crude survival rate may be expected. Primary irradiation for apparently similar cases yields 50%. Whether the loss of the larynx compensates for this increase in survival rate is not always easy to determine, particularly since some radiation failures will be salvaged by secondary surgery.

Modern techniques for preserving vocal cord function during the removal of the supraglottic cancer have resulted in survival rates similar to those obtained by total laryngectomy.⁶ Even better results have been obtained by combining preoperative radiotherapy with total laryngectomy, and the next few years will undoubtedly show considerable clarification of the real value of these various methods.

Subglottic Neoplasms

Subglottic extension of cordal neoplasms is not uncommon and is often associated with a poor prognosis. Tumours arising primarily in the subglottic region are rare, which is perhaps fortunate, because spread to the prelaryngeal and paratracheal lymph nodes occurs readily, being often undetected before surgical exploration. Most cases are best treated by total laryngectomy, thyroidectomy, and resection of the manubrium sterni, which allows dissection of the superior mediastinal lymph nodes.⁷ Palpable lymph nodes in the lower deep cervical chain necessitate neck dissection. As in the supraglottis, however, a programme of combined radiotherapy and radical surgery may improve the 62% first-year survival figures obtained by the above procedure.

Special Investigations

The larynx is readily accessible to both direct and indirect inspection, and traditionally the former has been carried out with the aid of a head mirror. The limitations of this procedure are well known, and present-day assessment of the macroscopical extent of laryngeal cancer is best determined by direct laryngoscopy with the Zeiss operating microscope.⁸ This technique allows the larynx to be viewed under excellent illumination and high magnification, but since endotracheal anaesthesia is essential the drug-induced relaxation does not permit accurate assessment of vocal cord movement.

Apart from lateral soft-tissue radiographs, every patient with suspected or proved laryngeal cancer will have a series of frontal tomograms. These allow the laryngeal structures to be seen free from the shadows of the cervical vertebrae and may show

unsuspected destruction of thyroid cartilage or subglottic extension of the tumour. More recently the Philips Polytome has allowed greater definition in these 0.5 cm. cuts (Fig. 2), but correlation between clinical and radiological findings is still essential, since surrounding oedema may cause confusion in determining the true margin of the tumour.

FIG. 2.—Laryngeal polytome showing a soft-tissue swelling on both sides of larynx involving true and false cords and early subglottic extension of swelling on the right side.

FIG. 3.—Laryngogram showing filling defect in left pyriform fossa due to the presence of an extensive neoplasm.

Contrast laryngography, in which the cocainized larynx is coated with oily propyl iodone (Dionosil), enables the delineated larynx to be viewed under conditions of quiet respiration and phonation (Fig. 3). During the Valsalva manoeuvre contrast medium is forced against the undersurface of the closed vocal cords, outlining the subglottic space, and the use of this valuable radiographic technique provides yet another guide to the accurate assessment of laryngeal cancer. The procedure is uncomplicated, though requiring patient co-operation, but has yet to be universally accepted.

Variations in vocal cord movements are difficult to determine clinically, yet of great importance in evaluating tumour extension. Stroboscopy produces an optical illusion in which an object moving rapidly and periodically can be made to stand still or move very slowly. Synchronization of the illumination with the frequency of vibration results in an apparent stand-still of the object—in this case with the vocal cords in any desired position. Small variations in the rate of illumination will produce slow movements of the cords and highlight any variations from the normal. Unfortunately, the equipment to carry out this most useful investigation is expensive and available in only the more specialized hospitals.

Conservative Surgery

The evolution of the surgical treatment of laryngeal cancer has resulted in increased emphasis on conservation of function while attempting to maintain effective extirpation of the malignant tumour. Partial laryngectomy is certainly not new, for the first laryngofissure for cancer was performed in 1851, and this operation, together with a number of modifications, is still enthusiastically practised in many countries for glottic growths. In recent times most of the impetus for the development of "conservation" procedures has come from the Latin countries, where both the incidence of supraglottic cancer and the psychological need of a functioning larynx is perhaps greater than in other ethnic groups.

Although encouraging reports of these imaginative procedures have been published in which five-year absolute survival rates of 75% have been claimed for supraglottic tumour,⁹ there still remains some scepticism about the reliability of the horizontal supraglottic laryngectomy. Complication rates after previous irradiation are high, but there can be no real doubt that there is a place for these techniques as initial therapy. As laryngologists acquire the necessary skill to perform these operations and make judgement in deciding when they are applicable, there will inevitably be a more realistic approach to the management of supraglottic cancer.

Post-laryngectomy Speech

It is impossible to visualize the impact of total laryngectomy on any individual patient, though my own experience is that the Anglo-Saxon faces this operation better than any other ethnic group.

Full rehabilitation is dependent on many individuals, not least of whom is the speech therapist. In the skilled hands of

speech therapists the majority of male patients and many females will acquire a bucco-oesophageal voice adequate enough to enable them to integrate fully into society. There are, however, individuals who find this means of voice production distasteful or inadequate for their professional needs. The "electronic larynx" is no alternative, and in 1965 Asai¹⁰ published a technique designed to re-establish pharyngeal speech without the necessity of first swallowing air into the oesophagus. In essence, this procedure produces a deliberate pharyngotracheal fistula so designed as to minimize leakage of saliva into the trachea but which allows air to pass upwards into the pharynx. Several extremely successful results have been reported from the United States with the use of this method on patients unable to master oesophageal speech and who had previously received no irradiation.

Laryngeal Transplants

This brief account of the management of laryngeal cancer would perhaps be judged incomplete if mention were not made of the recent widely publicized "laryngeal transplant."

For many years attempts have been made to produce effective laryngeal homotransplantation in animals. If possible, then its application in restoring laryngeal function after laryngectomy or loss through trauma in man would be considerable. Unfortunately the survival of even the replanted excised larynx in the dog has proved to be virtually impossible, and this ignores the problems of immunological rejection and infection which would be met in homotransplantation.

The technical difficulties of re-establishing blood supply and motor and sensory innervation are considerable but essential if the new larynx is to function normally. An adequate post-operative airway must be maintained and the larynx replanted in its proper anatomical location—all without jeopardizing the effectiveness of the initial resection if it be for cancer.

Recent reports of a case in which a laryngeal homotransplant was purported to have been performed have indicated that not only was the initial resection for a laryngeal cancer inadequate but no attempt was made to revascularize or innervate the transplanted larynx. It is difficult to comprehend the value of such experimental procedures whether in animal or man.

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