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CANCER OF THE TONGUE: ITS NATURE AND THERAPY

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INTRODUCTION

The American Cancer Society estimates that 1,550 people will die in 1963 from cancer of the tongue. This tumor is the most frequent intraoral malignant lesion and is also one of the first cancers of any type to be treated surgically. Ever since Marchetti performed the first surgical excision of lingual cancer in 1664, physicians have held divergent views as to the most effective form of treatment. The purpose of this paper will be to review the evolution of thought regarding this malignancy during the past three hundred years, but first a résumé of general information.

Description of the Tumor

Histologic Classification

In a series of 1,554 patients from the Head and Neck Service of Memorial Hospital, approximately ninety-seven per cent of the tumors were squamous cell carcinoma; and adenocarcinoma, which arose from the mucous glands, composed most of the remaining lesions. Sarcomas were quite rare, as there were only nineteen cases of primary lymphoid tissue involvement, one rhabdomyosarcoma and one lymphangiosarcoma. Over ninety per cent of these lesions were grade one or two malignancies.

Site of Origin

The majority of tongue cancers arise on the lateral and ventral surfaces anterior to the circumvallate papillae; however, twenty-five per cent occur posterior to this structure. Tumors of the dorsum of the tongue are uncommon, and midline tumors are rare.

Metastatic Spread

Early and numerous metastases have been the reasons for making tongue cancer difficult to cure. Between forty to seventy per cent of the primary lesions have distant metastases^{2,3} by the time the patient is first hospitalized. The majority spread by lymphatics leading to the deep cervical lymph nodes or by direct extension to neighboring structures. An important factor in therapy is that metastases are usually to many nodes and not just a few large ones.² Depending on the report, bilateral lymph node involvement varies from one to ten per cent.

Age and Sex Incidence

Although tongue cancer has been reported in patients from nineteen to ninety-one years of age, four-fifths occur in the sixth through the eighth decades, with an average age of sixty-two years.^{1,4,5} All accounts agree the occurrence is eight to ten times more frequent in males, although an increasing incidence in females is attributable to a greater

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consumption of cigarettes and alcohol.

Presenting Clinical Symptoms

The chief complaint of patients with cancer of the tongue is usually trivial. Three-fourths of the patients in one series who had malignancies of the anterior or visible portion of the tongue complained only of a large but often painless mass. However, persons with tumors posterior to the circumvallate papillae commonly reported dysphasia or a sore throat and were treated for pharyngeal infections. Because of their lack of easy visualization and significant symptoms, tumors of the posterior tongue were frequently over-looked and were not discovered until hard lymph nodes were palpated in the neck. 1

Etiology

Many theories of origin have been described, but there is little factual knowledge as to the direct causation of squamous cell carcinoma of the tongue. Poor oral hygiene and neglected teeth have often been associated with cancer of the lateral border of the tongue. Such lesions occur much less frequently in persons with good dentition that is regularly maintained. 6

The American Cancer Society urges dentists to perform yearly follow-up examinations of individuals with dentures to ascertain if bone atrophy and subsequent changes in pressure and friction may have developed and consequently formed a focus of chronic irritation.

Recent clinical investigation has demonstrated that certain systemic and metabolic disorders probably play an important role in conditioning the oral epithelium so that it reaches a stage of cellular change in which it is more susceptible to carcinogenic stimuli. Because tongue cancer is approximately four times more common in luetics, Boyle and Goslin³ state there is probably a positive correlation between carcinoma of the tongue, especially of the dorsal surface, and syphilitic glossitis. Grantly Taylor⁶ reported a series of patients with oral cancer and found that fifty per cent of these individuals had clinical evidence of liver cirrhosis. Systemic diseases associated with atrophic glossitis, such as pernicious anemia and Plummer-Vinson Syndrome have been implicated as a background factor for cancer of the tongue. Leukoplakia signify a change in the epithelium from any of several causes and should be regarded as malignant until proved otherwise.

HISTORY OF THE DEVELOPMENT OF TREATMENT

Historically speaking, one of the first cancer operations was for tumor of the tongue. Prior to the seventeenth century, however, there is a curious lack of any specific mention of lingual cancer in the medical literature. "Butlin and other writers interpreted this negative historical evidence as indicating that cancer of the tongue was relatively rare until the beginning of the seventeenth century." ⁷ D'Arcy Power believed the characteristic symptoms of lingual cancer, and especially the late complications, would have made recognition easier if it occurred as frequently as today. Importance has also been attributed to the fact that several etiologic factors which are thought to be of some significance today, did not appear in Europe until the fifteenth and sixteenth centuries; namely, syphilis, tobacco and alcohol. If, however, one accepts the premise that lingual cancer has always been a disease of late middle or old age, the failure to mention this disease in early literature may be attributed to the low average length of life. Life expectancy in the first few centuries A.D. ranged from twenty to thirty years of age, and by the eighteenth century in Europe, it had only increased to forty years. Only two patients in the series of sixty-four at the University of Nebraska had lingual cancer before age forty. Therefore, this

disease probably existed as it does today, but the infrequency of persons attaining old age resulted in a paucity of recognized lingual cancers.

Although the first definite published report of a case of lingual cancer was made by Alexander Reade, in 1638, many of the ancient references to diseases of the tongue allude to cancer although this disease is not specifically mentioned. Certain portions of the Ebers Papyrus (about 1500 B.C.) have been interpreted as including directions for the treatment of "eating ulcer of the gums" and "illness of the tongue" which may refer to cancer.⁷ Hippocrates (460-370 B.C.) probably refers to tongue cancer in his Prorrhbeticon when he states that chronic ulcers of the tongue are common at the edge and urges that an inspection be made to find any sharp teeth irritating the ulcer. Celsus, 178 A.D., observed that ulcers arising on the side of the tongue last the longest, "and it must be looked to whether some tooth opposite the ulcer is too pointed, in which case the tooth must be smoothed down."⁷ Avicenna (980-1037 A.D.) in his Canon of Medicine may be mentioning cancer when he describes "apostema dura" a hard sore of the tongue. Then, Riverius, in 1589-1655 A.D. is possibly alluding to cancer when he describes a case of ulcer of the tongue "which proceeded from the grating of the teeth whereupon it rested."⁷

Since the beginning of man, the tongue has been associated with speech and any affliction of this organ, be it natural or man made, was usually described as divine punishment. As a result of such beliefs, excision of the tongue was often considered suitable for those who dissented from established religious opinion. A famous example is that of sixty Christian confessors in North Africa whose tongues were excised by order of the Vandal King, Hunneric, in 484 A. D. Immediately after this procedure, several observers noted the "miraculous" return to the power of speech by the majority of the victims, and "it is highly probable that the recoveries from these excisions of the tongue paved the way for early attempts at glossectomy in the treatment of disease of the tongue."⁷

From the time of Hippocrates to the sixteenth century, tongue cancer was observed with awe and not considered treatable. Abulcasis (1013-1107 A.D.) describes the use of cautery for external cancer, and warns that in the treatment of ranula, one must be certain that the tumor is neither "livid and black" nor "hard and painless", for "if it is, do not touch it, it is cancer."⁷ A similar statement was made by Guy de Chauliac (d. 1368 A.D.) when he said that "if the growth in the tongue is hard or cancerous, don't touch it to cure it."⁷

During the latter part of the seventeenth century several

surgeons published reports of attempts to excise lingual cancer. Marchetti, in 1664, using hot iron cautery, was probably the first to attempt the extirpation of cancer of the tongue. Then, in 1676, Wiseman reported two cases in which he utilized cautery, but the patients subsequently died of metastases.

Partial or total glossectomies were rare until the French surgeon, Louis, 1774, proclaimed that speech was not terminated - a fact noted in 484 A.D. when Hunneric excised the tongues of the Chrisitans. Louis advised surgeons to be more courageous, to perform more and earlier glossectomies when indicated, and chided Morgagni for advising against the operation by stating that "il n'est pas exerce par des hommes timides." ⁷ Then, in 1799, Richter ⁷ supplied a further stimulus to surgeons by declaring the knife was the most reliable therapeutic approach.

Hemorrhage was a prominent complication of early glossectomies and several procedures were devised to cope with it. Hot iron cautery was the earliest but not wholly satisfactory procedure. As early as 1759, Louis ligated vessels proximal to where they entered the tumor in order to control local ⁸ bleeding. In 1805, Home described a technique for slow strangulation and necrosis of the tumor area with the intention of preventing hemorrhage. His method consisted of drawing the tongue from the mouth and piercing it several times around the tumor with a needle threaded with a double ligature. (Fig.1).

The needle was then cut off and the ligatures tied so as to strangulate a wedge shaped area containing the tumor. If the ligatures were adequate, a slough usually resulted in seven to nine days.⁷

Because the ligature method was sometimes uncertain and usually required several days to be effective, a newer method of strangulation by ecraseur (crusher) was introduced by Bell. The apparatus consisted basically of a chain or wire forming a running loop at the end of a shaft equipped with a powerful screw by which the chain could be drawn tight. (Fig. 2). The part of the tongue to be excised was encircled by the loop; and by gradually increasing the tension, the tissue was strangulated and cut. (Fig.4). Middeldorpf modified the ecraseurs by the use of a galvanic battery which heated the wire loop, and thus combined the advantages of cautery with the crushing action of the ecraseur. (Fig. 3).

During the two centuries succeeding Marchetti's first attempt to cure lingual cancer, numerous innovations and increased interest had developed regarding this disease; however, a somber note was added by Richards in 1852. He stated that at that time there was no authentic report of a cure of lingual cancer in all of the literature. Pemberton agreed with this statement in 1867 and suggested the "only means of arresting the progress of cancer of the tongue consists of

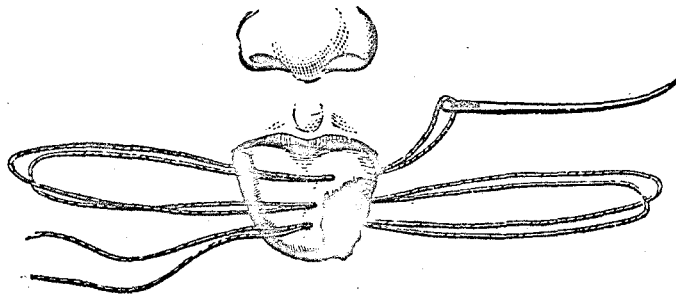


FIG. 1. Application of ligature for removal of cancer of the tongue (Erichsen). By cutting off the needle and cutting through the loops, the ligatures could be tied separately so as to encompass the entire diseased portion which, according to reports, sloughed off eight to ten days later.

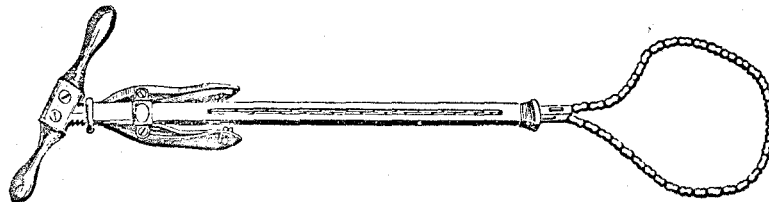


FIG. 2. The chain ecraseur (Holmes). This instrument, an elaboration of the principle of the ligature, used either a cord, a wire, or a chain which could be drawn tight by means of a screw, and provided for the more rapid strangulation and cutting through of the diseased portion of the tongue. (See Figs. 4 and 5.)

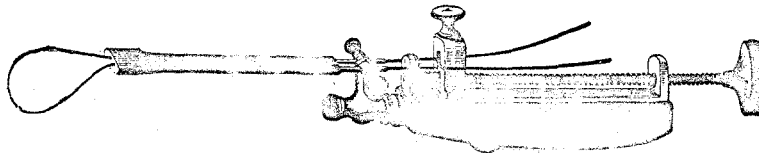


FIG. 3. The galvanic ecraseur (Erichsen). In this instrument the wire loop was heated by an electric battery, thereby combining the cautery with a crushing action. Judging from the rather infrequent mention of the instrument, it is probable that its use was more theoretical than practical.

Drawings reproduced from; The History of Lingual Cancer, by H.E.Martin, Am. J. Surg., 48:703-716 (June) 1940.

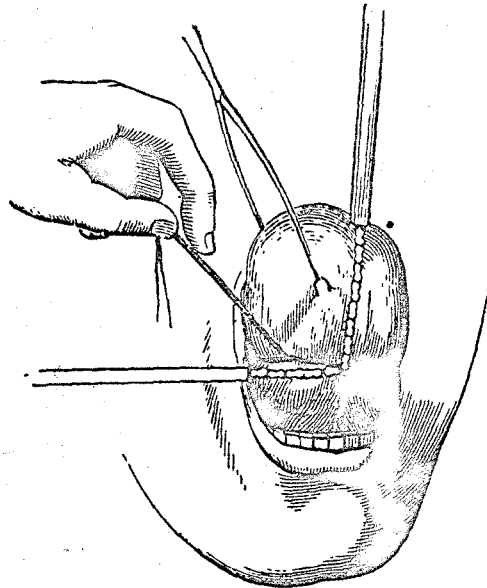
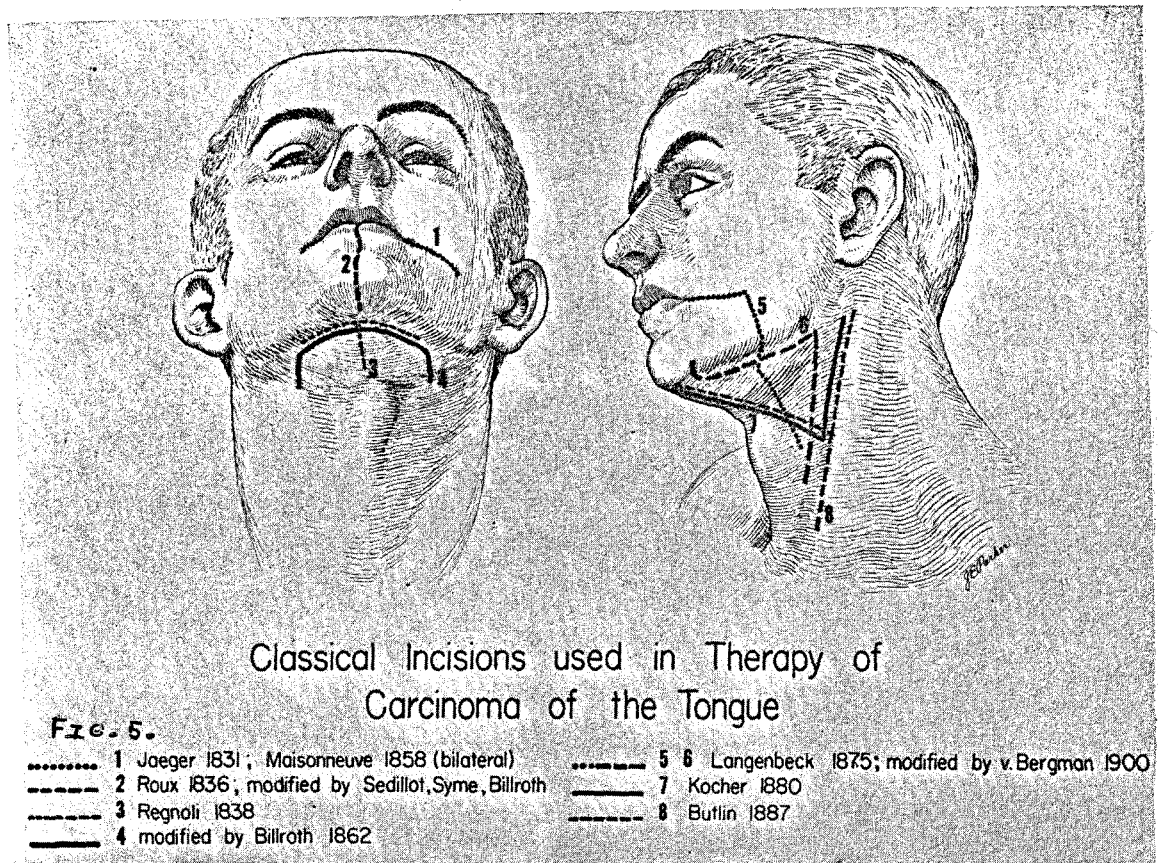


FIG. 4. Removal of the anterior portion of the tongue by the application of two ecraseurs (Erichsen). The ligature in this case was used both for traction and to prevent the ecraseurs from slipping forward.



Top drawing reproduced from; *The History of Lingual Cancer*, by H.E.Martin, *Am. J. Surg.*, 48:703-716 (June) 1940.

Bottom drawing reproduced from; *Some Historical Developments of the Surgical Therapy of Tongue Cancer from the Seventeenth to the Nineteenth Century*, by K.B.Absolon et al, *Am. J. Surg.*, 104:686-691 (November) 1961.

resorting to an operation, and under the best aspect of treatment the operation can only be considered as a palliative measure." ⁷ Harris, 1720, realized the complications of a major procedure but philosophied that "if anyone is exceedingly wearied with such tumors (of the tongue), and especially dejected in mind, whilst he is prepared to bear equally whatever may happen, he should not be denied the trial of the operation of excision." ⁷ In the same frame of reference, Clarke (1873) stated that "although it may only be temporary, relief is given to both the mind and body of the sufferer." ⁷

Although the probability of a cure during these early years of experimentation was quite remote, the fortitude of the patients and surgeons resulted in the evolution of refined techniques until men like Kocher and Crile perfected the basic lingual cancer operation. During the early 1800's, the intraoral route for glossectomy was felt to be inadequate for complicated and extensive malignancies. Subsequently, attention was focused on devising new methods of exposing the tongue. (Fig.5). The suprahyoid entrance to the sublingual area was first used by Cloquet in 1827. Jaeger, 1831, was the first to divide the cheek for exposure and later Maisonneuve, 1859, split both cheeks. Then, in 1836, Roux followed by Syme and Billroth, split the lip in the midline and divided the mandible through the symphysis so both mandibular rami could

be retracted. Billroth later modified this procedure by separating the ramus of the mandible in two places; and after removal of the tongue, he utilized wire to suture the bone to its former position. One of the first en bloc procedures was described by Langenbeck, 1875, in which he divided the ramus opposite the first molar tooth, ligated the lingual artery, and excised the regional lymph nodes, primary tumor, and base of the mouth.^{8, 9}

By raising a musculocutaneous flap in the neck, Billroth sought another approach to the oral cavity. This method was later perfected by Kocher when he placed an incision parallel with the sternocleidomastoid muscle and another running from the symphysis of the mandible perpendicular to the original incision, thus forming a triangle. The next step was to raise the flap, incise the oral mucosa, pull the tongue through the submaxillary exposure, and excise the cancerous portion of the tongue by galvanocautery.^{8, 9}

As knowledge accumulated of the clinical characteristics of lingual cancer, a new emphasis was directed toward excision of the "metastatic glands." Because the exact nature of lymph nodes was still unknown, the exocrine glands of the head were routinely included for extirpation. Then, in 1890, Butlin and Wölfer developed concepts concerning lymph node metastases which are still of importance today. Because Butlin realized

the frequency with which successful cases of removal of a part or the whole tongue was spoiled by subsequent afflictions of the glands, he advised control of the primary tumor and then removal of the contents of the triangles of the neck.^{8,9}

Although Langenbeck was probably the first surgeon to develop an en bloc resection for oral cancer, George W. Crile, Sr., was the first to stress the necessity of this procedure for excision of regional metastases. Besides resecting neck lymph nodes, he advised the removal of the external jugular veins and submaxillary salivary glands because these structures are closely associated with the lymph nodes. Crile also stressed resection of the sternocleidomastoid muscle to permit better exposure of the nodes; and also, ligation of the external carotid artery to reduce hemorrhage.⁹

Due to the daring of these early pioneers, most of the basic procedures for excision of primary tumors and lymph nodes plus adequate hemostasis were devised before the turn of the twentieth century. Consequently, most surgical therapy today is the result of minor modifications of these developments. Even the present philosophy of lingual cancer therapy was stated more than two hundred years ago by Heister, when he advised the treatment of this disease should be as early and as radical as possible.

RADIUM AND EXTERNAL RADIATION THERAPY

Although surgical therapy for tongue cancer had made great strides since Marchetti's first operation in 1664, several surgeons in the latter part of the nineteenth century voiced doubts concerning future advances. In 1875, Sir John Ericksen declared that surgery had reached its furthest possible limits of development. Sir Morell Mackenzie, a British laryngologist, stated in 1880 that "the only possible termination of cancer is death;" and his assistant, J. Dolan Mackenzie declared "there was never any thought of cure." ¹⁰ Between 1901 and 1907, Butlin estimated that an average of 750 persons died of cancer of the tongue per year in Great Britain, and only fifty to seventy were treated successfully by operations. The stage was thus set for a new aspect of therapy.

Early Usage.

The discoveries of Wilhelm Conrad Röntgen in 1895 and the Curies in 1898 plus the subsequent development and application of the roentgen ray and radium in the treatment of cancer patients was enthusiastically received and extensively utilized for lingual cancer soon after the turn of the century. In some centers, radiation therapy for head and neck malignancies began to supercede surgery. During the

early 1900's, radium was used externally to treat cancer patients; but by 1920, radium was being used experimentally in the form of needles at the Curie Foundation in Paris and by Murdoch, Simon, and Stahel in Brussels. When the 200 k.v. roentgen ray machine was developed in the early 1920's, the therapeutic use of external radium gradually declined.¹⁰ Modern use of radiation has it usually combined with surgery, but the following paragraphs will illustrate its use as the sole form of therapy.

External Radiation.

¹⁰
According to MacComb, radiation therapy is the treatment of choice for most intraoral squamous cell cancers. Primary cancer of the tongue is said to respond well to low intensity, interstitial radium needles with necrosis being a rare complication. However, a major objection to radium needle or seed implantation concerns the trauma to the cancerous area during the implantation. Trauma is generally accepted as a significant objection if extreme care is not practiced in this area so rich in lymphatics and blood supply.

Cancer of the tongue is usually grouped with radio resistant tumors, and Richard's review of the literature in 1940 discovered most radiologists believed adequate external irradiation could not be achieved without damaging surrounding healthy tissue. Richards objected to this opinion and stated

adequate tumor doses could be achieved if one employed 400 k.v. roentgen rays or a four to five gram radium bomb and then delivered tumor doses in excess of 5,500 r to the entire tumor area. The object of this therapy is to achieve an intense reaction throughout the involved area, and treatment must be continued until this objective is attained.

Richards, 1942, reports his five year survivals for lingual cancer in which no lymph nodes were palpable to be forty-nine per cent and where lymph nodes were palpable to be twenty-seven and seven-tenths per cent. He further stated that whereas Butlin was a master of head and neck surgery, his five year survival was only twenty-seven and nine-tenths per cent for all stages of cancer, and the mutilation resulting from surgery is seldom seen after radio-therapy.⁵ Although Butlin was a "master surgeon", his work was performed long before the newer developments in anesthesia and blood replacement existing during the time of Richards' report, and thus tends to invalidate his argument.

Radium

Because of its location and late detection, most authors agree that cancer of the posterior one-third of the tongue is very difficult to treat. Martin and Martin attempted to treat forty such cases between 1936 and 1950 with low intensity radium needle implantation in the primary tumor. Lymph

node metastases were treated by interstitial radium implants plus heavily filtered radiation from conventional 220 k.v. equipment. The radium needles were four centimeters long, contained 2-4 milligrams of radium, and were implanted perpendicular to the tongue surface.

During the week of therapy, all patients were hospitalized and given supportive treatment as needed. All radium needles were sutured in place to prevent accidental displacement. If swallowing was obstructed by lingual edema, a nasogastric tube was passed.

None of the four patients with bilateral node involvement survived five years. (Table 1). While seventeen of the deaths were due to cancer, eight resulted from other causes before the end of the five year period. Radium needles were successful in producing healing of the primary lesion, usually within the first six to eight weeks, in over half of the patients treated. ¹¹ The author noted only one case of mandibular osteonecrosis and other than several instances of localized epithelial necrosis, there were no major complications. Advocates of radium needle implants stress the low incidence of irradiation sequelae, such as mouth dryness and teeth damage, as significant reasons for localized cancerocidal doses as compared to irradiation of larger volumes of tissue by external sources.

Complications of Therapy

Although some authors report minimal complications as a consequence of irradiation, Frazel and Lucas, 1962, studied a series of 683 patients receiving low voltage external and/or interstitial radon seed irradiation and found a significant number of major complications.¹ The total doses of irradiation varied from 5,000 to 12,000, with an average dose of 10,000 r. This was administered over an average of twenty-eight days. Complications were found to develop during treatment, immediately following treatment, or not for months, years, or decades later. Two-thirds of the complications resulted from radio necrosis of soft tissue and were usually accompanied by severe pain which necessitated nerve sections for forty-nine patients. Mandibular necrosis was present in twenty-eight patients and eighteen required resection. Ninety-one patients had severe hemorrhage at the site of radiation necrosis and ligation of the external carotid was required in forty-six of these patients. Ligation of the common or internal carotid was necessary in two patients. Mild symptoms of respiratory obstruction and aspiration pneumonia complicated the course in many patients, and a tracheostomy was subsequently necessary in nineteen of them. Secondary primary tumors were occasionally discovered at a distance from the original tumor and were often opposite to the port of irradiation. These tumors were suspected of being radiation induced.

Frazel and Lucas concluded that cancerocidal doses of irradiation given over large areas is equally as debilitating as major operative procedures. Despite the author's realization that prompt supportive measures and treatment of local infections is necessary in the post therapy period, forty-eight patients died during the treatment or immediately following.

Supervoltage roentgenotherapy, a relatively recent development, delivers a very high radiation dose while sparing the skin from complications. Because supervoltage therapy has usually been combined with radical neck dissections or composite operations, it will be discussed under combined therapy.

MODERN THERAPY BY OPERATION

As the result of marked improvements in anesthesia, such as, intratracheal intubation, intravenous sodium pentathol, plus the freer use of blood transfusions, World War II saw the development of a new era in surgery. ¹⁰ When the once hazardous combined procedure for removal of a primary oral cancer and regional metastases became feasible, a single operation offered distinct possibilities for improving end results. About this same time, some institutions began losing enthusiasm for radiation therapy because permanent sterilization of single or small groups of nodes was possible, but cancerocidal doses over an extensive area could not be tolerated by the patient. Surgical dissection, however, could remove all important nodes of the neck without great disfigurement or serious operative risk.

Consideration of Lymph Node Involvement

With the advent of renewed interest in head and neck surgery, one of the important questions was whether to perform conservative or radical procedures. Although conservative therapy is applicable in well localized tumors of the tongue without metastases, the radical neck or "commando" procedure, as advocated by Hayes Martin, became a popular operation when clinically palpable cervical metastases were present.

Radical Neck Procedure

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As described by Martin, the operation extends from the lower edge of the mandible to the clavicle, and from the anterior edge of the trapezius to the midline. All tissues between the platysma and deep fascial layer are removed, with the exception of the common, the internal and the external carotid arteries, the vagus and phrenic nerves, and the trunks of the brachial plexus. The following structures are routinely removed: the sternomastoid muscle, omohyoid muscle, internal jugular vein, spinal accessory nerve, and submaxillary salivary gland. The following structures may be sacrificed if necessary; the external and sometimes even the internal carotid arteries, a lobe of the thyroid, the strap muscles, the tenth and twelfth nerves, and the lingual branch of the fifth nerve, as well as a portion or all of the mandible.

Although there is a variance of opinion as to when to utilize a radical neck dissection, Martin states the following prerequisites should be present:

1. Definite clinical evidence that cancer is present in cervical lymphatics.
2. The primary lesion should have been previously controlled or will be removed at the time the neck dissection is performed.
3. There is a reasonable chance of complete removal of the cervical metastasis.

4. There is no clinical roentgenographic evidence of distant metastasis.

5. Neck dissection offers a more certain cure than radiation therapy.

Arguments concerning Prophylactic Operations

According to Martin, the most significant criteria for performing radical neck dissections is the presence of clinically palpable cervical lymph nodes. Those advocates for radical surgery after the primary is controlled but before palpably enlarged nodes are present call this a "prophylactic" procedure. Martin, however, strongly disagrees with the wisdom of this operation and terms it unnecessary and illogical. Because Martin's series has contained contralateral metastases in ten per cent of the cases, he argues that a truly prophylactic procedure must be bilateral. Thus, two hospitalizations are required, an interval of two or three weeks between operations and a protracted hospital stay. "A rigid routine of prophylactic neck dissection is hardly practicable and is doubtful anyone can carry it out well enough to notice any significant increase in cure rate. At the Royal Cancer Hospital in London, the prophylactic neck dissection has been given up."⁹

On the other hand, surgeons at the Curie Foundation in France have advocated elective neck dissection for intra-oral cancer since 1939. In this country few men have sup-

ported such a stand. The validity of elective neck surgery in regard to clinical and experimental evidence was reviewed by Southwick,¹² in 1960. When the primary lesion is treated by surgery, "there is little doubt that lymphatic channels are opened that may lead to seeding of the operative wound." Smith examined the wound washings of 101 major cancer operations and noted a forty-seven per cent local recurrence rate when the washings were positive for tumor cells, but only twenty per cent when no tumor cells were discovered in the fluid. Thus, a considerable potential exists for local metastases.

Many people believe that lymph nodes containing tumor cells are relatively unimportant, except for local growth, as long as the primary is controlled. By his experiments with rabbits, Ziedman has shown that this is not necessarily the case. While the peripheral sinuses of a node become involved by afferent channels, the entire node does not have to be replaced before efferent embolization has occurred. The nodes acted as barriers to the carcinoma cells for only three weeks. Although Southwick does not attempt a direct application to man from these experiments, there is no guarantee that efferent embolization has not occurred before a node is enlarged enough to be palpable. He further noted a significant percentage of his patients, plus those of

other author's (Table II) had clinically negative but microscopically positive nodes when removed at the time of surgery. Because of this high percentage of microscopically positive regional lymph nodes, Southwick contends it is difficult to logically omit a radical neck dissection. Further support for prophylactic neck dissections is that an eminent pathologist reviewed the lymph nodes from neck dissections which he had called negative on frozen section, but later found thirty-three per cent of these to be positive. Thus, false security may result from frozen section diagnoses, and it is cited as further evidence for radical procedures.

According to Southwick, Martin's best argument for not performing a prophylactic neck dissection is that ten per cent of his cases had contralateral metastases and would thus have their operations on the wrong side. However, Beahrs found only two per cent of his patients had this phenomenon, and none were found in Southwick's series of 192 cases.

Kremen performed prophylactic dissections on twenty-three patients and had a five year survival of ninety-one per cent in those with microscopically negative nodes, and thirty-six per cent in those with positive nodes. The overall five year survival was sixty-five per cent and is "a¹² marked improvement over any other reported statistics."

Furthermore, argue the proponents of elective neck dis-

section, why should the principles of en bloc resection be applied to epithelial cancers in other regions of the body but not be applicable to carcinoma of the tongue in light of the previous evidence? Perhaps the most objective manner of deciding this controversy is to examine who is obtaining the best results. A review of the two largest series, Curie Foundation of Paris and Hayes Martin's of the Head and Neck Service of New York Memorial Hospital, revealed that both had over 1000 patients treated and that both had almost identical five year survivals of thirty-three per cent.¹²

En Bloc Resections

The en bloc resection of intraoral lesions was attempted during the late nineteenth century, but most attempts were thwarted by inadequate anesthesia and deficient knowledge of fluid and electrolyte balance plus post-operative infection. With great strides being made in solving these problems, new attention has been directed toward aggressive procedures which include sacrificing the mandible while removing the primary disease and regional lymph nodes. Although mandibulectomies do not cause momentous deformities, the cosmetic defect which does exist has prompted development of a procedure to remove primary disease, lymphatic channels and lymph node tissue without sacrificing the mandible.¹³ Slaughter and Southwick claim this procedure would be applicable to lesions involving the

tongue from the tip to the base, or to the floor of the mouth provided there was at least a centimeter of grossly normal tissue between disease and the margin of the gingiva.

Various en bloc techniques have been described such as
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that by Kremen which involves sectioning the mandible at the symphysis after the neck dissection has been completed. The jaw is displaced laterally, and the intraoral disease is removed in continuity. The mandible is then replaced, wired in the midline, and the floor of the mouth is reconstructed by sutures. Grant Ward describes a somewhat cumbersome operation called a "pull through" in which he incises the floor of the mouth and pulls the neck dissection specimen intra-orally, removing it in continuity with the primary disease.

13
The procedure utilized by Slaughter and Southwick is to perform a routine radical neck dissection until one approaches the submaxillary triangle. An incision is then made along the external surface of the inferior border of the horizontal ramus of the mandible, and a subperiosteal dissection of the inner surface of the mandible is performed, entering the oral cavity at the apex of the alveolar ridge. The tongue is then pulled down into the neck field through the opening thus made, and both primary and metastatic disease are removed en bloc. Repair is accomplished by mobilizing the buccal mucosa and lateral gingiva and suturing this with interrupted 3-0 or 4-0 catgut suture to the cut margin of the intraoral tissue. Slaughter and Southwick's series consisted

of fourteen patients, but they had not been followed long enough to give five year survival rates.

From Lyon, France, an article was written by Marcel Dargent¹⁴ which prescribes suprahyoid total glossectomy and excision of the floor of the mouth for advanced tongue cancer. The author advises this procedure for tumors with massive local involvement of submucosal and deep musculature of the tongue in which radiation would result in massive necrosis. Contraindications are skin involvement in the submental region, the presence of clinically noted metastatic lymph nodes in the neck and involvement of the glosso-epiglottic fold.

The surgical technique consists of making a horizontal incision at the level of the hyoid bone and extending it to the angles of the mandible where short vertical incisions are made to facilitate raising the flap. The ramus marginalis branch of the seventh nerve is located and preserved. The facial vessels are encountered inferior to the posterior belly of the digastric muscle and are sacrificed along with the hypoglossal and lingual nerves and lingual vessels. After dividing the thyroglosso-epiglottic fold, the tongue musculature is detached from the mandible. The tongue is then removed en bloc with its suprahyoid musculature and hyoid bone. A free skin graft is then applied to the raw surface of the flap which was

previously raised, and a new floor of the mouth is formed. A tracheostomy and gastrostomy are always performed before the glossectomy is attempted. Post operatively deglutition is difficult and speech is unintelligible until the patient learns to use the lips and cheeks when speaking. Five cases are reported by Dargent, and all survived the operation but died within a year of either hemorrhage, pulmonary metastases or cachexia.

Extensive neck and intraoral dissections are advocated
15
by J. Barrett Brown. One illustration he cites is that of a sixty-four year old man who had a widespread squamous cell carcinoma over the entire lower molar region extending into the floor of the mouth, the side of the tongue, the ramus of the mandible, the tonsillar region and the lateral portion of the soft palate. At operation a complete resection of the neck nodes was done. The jaw was then sectioned in the canine region below the skin flaps; and the mass was removed by excision in the floor of the mouth, side of the tongue, tonsil and palate. The jaw, including the body and ascending ramus, neck, mouth, and palate tissues were then removed en bloc. The jaw was stabilized forward by a Kirschner wire driven across the

dissected area into a small piece of condyle left in for this purpose. The patient has been seen regularly since that time, and thirteen years later there is no evidence of recurrence. Thus, advocates of en bloc excision believe this is one of the most logical cancer operations because the local lesion and the metastatic regions are both included in one operation. If efforts for functional reconstruction are made, unnecessary disfigurement can be avoided.

COMBINED OPERATIVE AND RADIATION THERAPY

During the first fifty years of this century, the therapy of tongue cancer has seen the emphasis migrate from surgery to irradiation and then return to surgery. Finally, the two school visualized the inadequacies that each therapy entailed and strides were made toward uniting the advantages of both. Because numerous combinations of irradiation and surgery are utilized, the following paragraphs will attempt to relate an adequate cross section of the most popular programs.

M. D. Anderson Hospital

From the Head and Neck Service of M. D. Anderson Hospital comes the concept of planned combined and unplanned combined therapy. In planned combined therapy, the patients receive irradiation to the primary lesion; and four weeks later, a radical neck dissection is performed if cervical metastases are noted. Preoperative irradiation of regional metastases is frequently done by administering 4,000 to 4,500 r through a small field for five to seven days while the primary lesion is being irradiated. Such irradiation is believed to restrain the growth of neck metastases until the radical neck dissection can be performed four to six weeks later.

Another concept of planned combined therapy regards

the treatment of advanced intraoral tumors in which complete surgical extirpation would remove so much tissue that primary closure would be difficult and a functional result for the patient would be unsatisfactory. "By using radiation therapy before surgery, at times delivering slightly less than a full tumor dose, the amount of tissue to be excised from the primary site is decidedly less than would have been necessary with surgery alone." ¹⁰ Increased morbidity following this combination is said to be offset by better functional results obtained for the patient. Although delay in healing is sometimes noted, it usually does not occur if radiation to the operative field is not over 6,000 r tumor dose. Fatalities have resulted from necrosis of the common and internal carotid arteries and replacement of the arteries with prosthesis has not been feasible in an irradiated field.

Unplanned combined therapy is reserved for the recurrent cancers of the intraoral cavity managed originally by radiation therapy. Further irradiation may cause necrosis; and for this same reason, second intraoral primary lesions are treated by surgery if the first was irradiated. Surgery is also utilized to remove areas of necrosis which have resulted from irradiation. Refer to Table 3 for survival statistics.

Stanford University Hospital

At the Stanford Tumor Clinic and X-ray Department a system of staging tongue cancers has been developed to facilitate analysis of cases and be a guide for programming therapy. The headings used are:

Stage I: Confined to organ of origin

Stage II: Adjacent tissues invaded but lymph nodes not involved.

Stage III: Lymph nodes involved

a. Adjacent tissue not invaded

b. Adjacent tissue invaded

Stage IV: Remote metastases present.

Treatment of stage I cancer is usually with 6000 - 7000 r and spread over four to six weeks. Surgical excision is sometimes utilized for tumors of the anterior two-thirds of the tongue if at least a 1.5 cm margin of uninvolved tissue remains around the lesion. If recurrences appear after heavy irradiation, the tumors are treated by surgery. When the local recurrence is extensive, yet resectable, a hemiglossectomy is performed in continuity with a hemimandibulectomy and radical neck dissection.

Treatment of stage 2 lesions is individualized. Radiation treatment as outlined for stage 1 is employed if the soft tissue spread is not extensive. However, a composite operation is often used as a primary procedure in this stage;

and if the mandible is involved, radical surgery is the only treatment.

Because only ten to fifteen per cent of the patients survive for five years when a primary tumor is treated by irradiation and metastatic nodes are removed surgically, a composite dissection is utilized for stage 3 tumors as initial treatment. Contraindications for the composite operation are contralateral or bilateral nodes believed to contain metastases. If the primary tumor is controlled by irradiation or surgery, unilateral or bilateral radical neck dissection will subsequently be performed. Because distant metastases are present in stage 4, the only therapy is palliation of the primary lesion and regional nodes. Refer to Table 4 for the survival statistics.

University of Pennsylvania Hospital

From the departments of Radiology and Surgery at the University of Pennsylvania, a recent report analyzes their patients with lingual cancer treated between 1925 and 1955. The treatment techniques utilized varied considerably during this time. For instance, between 1925 and 1946, operations were always conservative in that local excisions, occasional hemiglossectomies, infrequent partial neck dissections composed the main surgical attack. Since 1946, surgery has been radical in that en bloc and prophylactic neck dissection have been commonly employed. Irradiation tech-

nique between 1925-1935 consisted of the surface application of radium plus small doses of external irradiation. Then, in 1935-1945, interstitial radium or radon was combined with Xray. Between 1945 and 1955, they employed radioactive irridium in nylon tubing instead of radium needles. This supposedly is more comfortable for patients and decreases the radiation exposure to the operation. ¹⁹

The tables for analysis of this report are based on staging groups as follows:

Stage I. Early, primary lesion limited to one-half of the tongue, less than 3.0 cm. in diameter, no lymph node involvement.

Stage II. Moderately advanced primary lesion 3 cm. in diameter or greater with infiltration of the tissues of one half of the tongue and/or discrete, unilateral lymph node involvement.

Stage III. Far advanced, primary lesion far advanced with infiltration of tissues of both halves of the tongue and/or massive unilateral lymph node involvement and/or minor bony involvement and/or involvement of adjacent structures.

Stage IV. Very far advanced - primary far advanced with massive bilateral lymph node involvement and/or intensive bony involvement.

Stage V. Unknown.

Table 5 presents the results of lingual cancer therapy at the University of Pennsylvania. One disadvantage of this report is that it did not analyze the survival data in regard to specific changes in therapy technique during the years 1925 to 1955. The authors concluded that greater emphasis should be placed on use of radical surgery especially in Stage III lesions.

Barnes Hospital

From the Department of Surgery at Washington University a recent article emphasizes the "cure" of carcinoma of the tongue by combined radon seed or resection and neck dissection. Therapy is begun as soon as the diagnosis is established because even debilitated patients tolerate radon seed implantation without serious consequences. The amount of irradiation is based on the finding that one cubic centimeter of carcinoma may be destroyed by one millicurie of radon, which delivers 133 millicurie hours of radiation. The total mouth dosages rarely exceeded 4,000 mc. h. The total amount of irradiation is essentially expended after one month, so further irradiation to the patient is inconsequential. Introduction of the gold seeds is usually performed under direct vision or by palpation in regions difficult to expose.

Cervical lymph nodes are always regarded by the author as part of the tumor field; and although the decision for

radical neck dissection depends on clinical experience, the procedure is always considered for even the smallest lingual cancers. Regional node resection is never attempted before there is reasonable assurance the primary tumor is controlled. Postoperatively the patients are followed at least three times a year, and scrupulous mouth hygiene is stressed. Two cases are given as examples, but no survival statistics are reported.

CHEMOTHERAPY

Regional cancer chemotherapy has recently been stimulated by several factors: (1) Systemic administration of the presently available agents in patients with far advanced cancer has proved impractical. (2) Although many cancers remain localized, they produce symptoms, death, and may be too advanced for conventional therapy. Consequently, in patients whose tumors are advanced yet within the distribution of accessible arteries, regional chemotherapy is an attempt to deliver cancerocidal drug doses but prevent systemic reactions.

A typical method for regional perfusion is to administer an antimetabolite such as methotrexate in supralethal doses through a catheter in a vessel supplying the tumor area, and then prevent systemic toxicity by supplying specific antidotes such as citrovorum factor by intramuscular injection. Because this is a relatively new and hazardous technique, the medical literature has few specific references to its use in lingual cancer. The following case report by Sullivan and McPeck, 1962, will illustrate this form of therapy.

A fifty six year old man was seen in May, 1960, with epidermoid tongue cancer as diagnosed by biopsy. The lesion was on the right side between the middle and posterior portions, and there was no local fixation or neck metastases. Radiation therapy was administered, using a cobalt-60 unit, and a total dose

of 4,000 r was delivered. The tumor, however, continued to grow; and by September, 1960, it involved the entire right side of the mouth. The only palpable node was in the right submaxillary area.

On September 9, 1960, a polyethylene catheter was inserted into the right, external carotid artery proximal to the superior thyroid artery. For five and one-half days, a continuous infusion of methotrexate, 50 mgm. per 24 hours, was given concurrently with the antidote, citrovorum factor, 6 mgm., every six hours. Thirteen days after the therapy started the tumor had completely disappeared, and six weeks later a biopsy failed to reveal any tumor. On February 14, 1961, a 0.5 cm area of ulceration was noted at the site of the previous tumor; and a biopsy revealed it to be epidermoid carcinoma.

Two separate courses of arterial infusion chemotherapy were given over a period of one month. Moderate unilateral mucositis and hematologic depression occurred with each course of therapy. No tumor was evident ten months after the original administration of chemotherapy infusion.

The complete remission following the second course of therapy would suggest that drug resistance does not readily develop. Because the tumor recurred once in the original site, surgical excision might have been a beneficial combination for removing the partially arrested cells and possibly achieving a complete cure.

EXPERIENCE AT THE UNIVERSITY OF NEBRASKA HOSPITAL

The following statistics are primarily based on information gathered from the tumor files, and represent sixty-four patients with lingual tumor seen at the University of Nebraska Hospital between 1931 and 1957.

Age, Sex and Race Incidence

The age range was from thirty-three to eighty-seven years with an average age of sixty-three and one-half years. This is only one and one-half years older than the average reported by most authors of larger series.

Of the total sixty-four patients, one was an American Indian, two were Negroes, and sixty-one were Caucasians. This is a rough approximation of the population distribution in Nebraska and would seem to indicate there is no racial predominance of the disease.

The sex distribution, however, seems to be significant because only fifteen (twenty-three per cent) of the sixty-four patients are females. This would agree with Hayes Martin's finding that lingual cancer is five times more prevalent in males than females, but is below the frequency of eight to ten times usually reported. This variation is difficult to explain because the urban population of Martin's report, the mostly rural society of this series, plus the varied economic backgrounds from both situations contribute a broad cross

section for the two reports which make other statements questionable.

Histological Classification

All but two patients or ninety-six and eight-tenths per cent had squamous cell carcinoma as compared to ninety-seven per cent of the cases in the series of 1,554 patients treated at New York Memorial Hospital. There was one case of adenocarcinoma, the second most frequently encountered tumor; but there was one reticulum cell sarcoma, a rare finding according to Hayes Martin.

Metastases

Table 6 reveals that at least forty-seven per cent and possibly ninety-two per cent of the patients had metastases when the tumor was first discovered. This correlates with similar studies and likely emphasizes the necessity for improved education regarding this disease.

Survival Time

The information in Tables 7 and 8 supports the common finding that the percentage of patients surviving for five years is markedly effected by the development of the neoplasm before therapy is initiated. Only thirteen patients or twenty per cent survived for at least five years. This is a low percentage as compared to other reports and may represent numerous factors, such as, more advanced malignancies or improper or insufficient therapy.

Although one might attribute the low survival rate resulting from Xray therapy to its use as palliation, it was actually utilized only three times for this purpose. A review of numerous hospital charts revealed a majority of the total tumor doses were below the 6,000 r level currently recommended. Consequently, the amount of radiation delivered may not have been cancerocidal.

Although the survival rates for surgery and radium therapy are quite good, they represent an insufficient sample for proper analysis. The combination of surgery, radium and Xray at this University appears to be promising; but future experience should not neglect combinations of surgery and radium (J. Barrett Brown- Washington University) or surgery and Xray (Stanford University, University of Pennsylvania, and M. D. Anderson Hospital).

Symptoms and Survival Time

Forty-two per cent of the patients (Table 11) sought medical advice at least four months after the onset of symptoms. The reason for deferred consultation is not determinable but may stem from minimal symptoms, lack of visualization, slow tumor development, or ignorance of lingual cancer.

Although fifty-two per cent of the diagnoses (Table 12) were made within fourteen days following medical consultation, fourteen per cent of the tumors were not properly evaluated

for more than 120 days. The latter probably reflects cursory history and physical examinations and deficient knowledge of the disease.

Four patients were treated within one month of their original symptoms (Table 13), yet only one person survived five years. Twelve people, however, did not receive therapy for over one year from the occurrence of the first symptoms, yet thirty-three per cent of them lived for more than five years. These statistics could be markedly affected by the subjective sensation thresholds of the patients or by peculiar growth rates of the tumors in different individuals.

Miscellaneous Facts

Twelve of the patients had a positive family history of cancer in other tissues, and one patient had a near relative with lingual cancer.

An old scar or burn area was the neoplastic site in three patients and twelve persons developed the disease in an area of chronic irritation. The former etiology is probably from smoking or drinking hot beverages and the latter from loose dentures or irregular teeth.

Fifty-eight patients of this series have died and forty-five of them died of causes directly related to lingual cancer. Thirteen patients lived for five or more years, and their present status is as follows:

- 1) Two died of tongue cancer
- 2) One died of cancer other than tongue cancer
- 3) Three died of causes other than cancer
- 4) One died of unknown causes
- 5) Six are still alive.

S U M M A R Y

During 1963, approximately sixteen hundred, or six-tenths of one per cent of all cancer deaths resulted from neoplasms of the tongue. The apparent quiescence and occasional inconspicuousness of the tumors frequently results in prolonged self-therapy and medical mismanagement. When hospitalized at the University of Nebraska, forty-seven per cent of the patients had definite, distant metastases. Squamous cell carcinoma was present in about ninety-seven per cent of the cases. Possible etiologic factors include poor oral hygiene, syphilitic glossitis, pernicious anemia, and Plummer-Vinson Syndrome. Rarely is the disease present before the third decade, with the average age being in the mid-sixties. The incidence is five to ten times more in males than females, but no racial selectivity apparently exists.

Although Alexander Reade, 1638, was the first to explicitly mention lingual cancer, occasional references are present in ancient works such as the Ebers Papyrus, B.C. 1500. Hippocrates undoubtedly recognized the disease when he warned that chronic ulcers often developed when jagged teeth created lingual irritation. Because religious superstitions regarded tongue disease as divine punishment, therapy stagnated until Marchetti's bold lingual excision by hot iron cautery in

1664. The succeeding centuries witness ^{ed} numerous innovations including strangulating ecraseurs, vessel ligations, techniques of exposure, and theories of metastases. However, three conspicuous obstacles; hemorrhage, infection, and anesthesia, hindered surgical therapy until the early 1940's. Lingual cancer was enthusiastically treated by radium and Xray until failures and complications resulted in refined techniques and case selectivity. The advantages of surgery and radiotherapy have recently been merged to yield the best survival statistics yet available.

For the past twenty-five years, "porphylactic" neck dissections have provided a debatable and interesting question. The opposition argues that bilateral metastases and protracted hospitalization create an impracticable situation obviated by scrutiny for clinically palpable regional lymph nodes after resection of the primary lesion. Proponents defend the procedure by stating that bilateral metastases are statistically insignificant, that forty per cent of non-palpable regional nodes contain neoplastic cells, and that tumor cells are not restrained until a lymph node is palpable. If the primary tumor can be contained, the latter arguments are more convincing. Although an en bloc resection is the most logical operation, the invariable deformity and high morbidity markedly limit its present popularity.

As compared to larger series, the sixty-four patients with lingual cancer seen at the University of Nebraska, represent a typical cross section. A disappointing comparison is the total five year survival of twenty per cent. Although the survival rates for surgery, thirty-three and three-tenths per cent, radium sixty-six and six-tenths per cent; and combined surgery, radium and Xray, fifty per cent; represent only fifteen patients, these statistics are among the best currently reported. Only nine per cent of the forty-nine patients treated solely by Xray lived for at least five years, and an incomplete chart review indicated the therapy had been insufficient by current standards.

C O N C L U S I O N S

Lingual cancer is an uncommon but disasterous disease deserving educational emphasis. Physicians are cognizant of numerous rarer entities and frquently seach for their existence, yet they remain ignorant of the characteristics of a disease which is readily detectable. Symptomatic treatment without exploration and delayed patient-doctor consultation are areas of needed correction which would markedly improve life expectancy. Too much dependence has rested on the great therapeutic evolution of the past to resolve the problem of lingual cancer, but today an educated profession and enlightened public could substantially reduce the mortality from this disease.

Because hesitation invariably results in greater deformity and eventual demise, prompt and frequently extensive procedures must not be compromised by reluctance to alter facial features. Although the mode of treatment remains debatable, the thoroughness advised by Louis in 1774, "il n'est pas exerce pas des ⁷ hommes timides", will remain a credo for future therapy of lingual cancer.

A P P E N D I X

TABLE 1

CARCINOMA OF THE POSTERIOR TONGUE:
FIVE YEAR SURVIVALS

	<u>Total Cases</u>	<u>Five year survivals</u>
Patients without palpable nodes	18	10 (56%)
Patients with palpable nodes on admission	14	3 (23%)
" " " " later	8	2
Totals	<u>40</u>	<u>15 (38%)</u>

TABLE 2

INCIDENCE OF CLINICALLY NEGATIVE BUT
MICROSCOPICALLY POSITIVE NODES

Kremen, 1956;	43.0 %
Beahrs, Define, and Hensen, 1959;	25.3 %
Southwick, 1959;	39.9 %

TABLE 3

SURVIVAL RATE OF PATIENTS TREATED ONLY AT
M. D. ANDERSON HOSPITAL

<u>Site</u>	<u>No. of Cases</u>	<u>Years of Survival</u>	<u>Percentage</u>
Oral Cavity	130	1	83.5
		2	64.2
		3	55.5
		4	49.0
		5	49.0

TABLE 4

RESULTS OF TREATMENT OF 50 PATIENTS AT THE
STANFORD TUMOR CLINIC

<u>Stage</u>	<u>No. of Cases</u>	<u>Five Year Survivals</u>	<u>Percentage</u>
I	21	12	57
II	6	1	17
III	23	1	4

TABLE 5

RESULTS OF TREATMENT OF STAGED PRIMARY LESIONS
FIVE YEAR SURVIVALS

<u>Stage</u>	<u>Treatment</u>	<u>Alive</u>	<u>Dead</u>	<u>Totals</u>	<u>Percentage</u>
I	None	1		1	100
	Surgery	11	7	18	61
	Irradiation	3	5	8	37
	Surgery and irradiation	5	4	9	55
II	Surgery	3	7	10	30
	Irradiation	4	15	19	21
	Surgery and irradiation	3	6	9	33
III	Surgery	5	6	11	45
	Irradiation	2	34	36	6
	Surgery and irradiation	0	7	7	0
IV	None		1	1	0
	Irradiation		5	5	0
V	None		5	5	0
	Surgery		3	3	0
	Irradiation		2	2	0
	Surgery and irradiation		1	1	0

(The crude five year survival is 24 per cent)

TABLE 6

STAGE OF NEOPLASM AT TIME OF DIAGNOSIS

	<u>Patients</u>	<u>Percentage</u>
Stage I Local only, under 2 cm.	5	8
Stage II Invasion into surrounding tissue, possible metastasis	29	45
Stage III Definite metastases to regional lymph nodes	28	44
Stage IV Distant metastases	2	3

TABLE 7

STAGE OF NEOPASM WHEN DIAGNOSED AS CORRELATED WITH SURVIVAL TIME FROM DIAGNOSIS TO THE PRESENT STATUS

	<u>1-6 mo.</u>	<u>6 mo.- yr</u>	<u>1-3 yr.</u>	<u>3-5 yr.</u>	<u>Beyond 5 yr.</u>
Stage I	0	0	3	0	2
Stage II	2	5	8	5	9
Stage III	14	9	3	0	2
Stage IV	<u>2</u>	<u>0</u>	<u>0</u>	<u>0</u>	<u>0</u>
Total	18	14	14	5	13

TABLE 8

FIVE YEAR SURVIVAL RATES CORRELATED WITH
NEOPLASTIC DEVELOPMENT AT THE TIME OF DIAGNOSIS

	<u>Patients</u>	<u>Five year survivals</u>	<u>Percentage</u>
Stage I	5	2	40
Stage II	29	9	31
Stage III	28	2	7
Stage IV	2	0	0

TABLE 9

SURVIVAL TIME CORRELATED WITH THERAPY

<u>Type of Therapy</u>	<u>0-1 yr.</u>	<u>1-3 yr.</u>	<u>3-5 yr.</u>	<u>Beyond 5 yr.</u>
1.) Surgery	3	1	0	2
2.) Radium	1	0	0	2
3.) Xray	23	6	0	3
4.) Combination of 1 and 2	0	0	0	0
Combination of 1 and 3	0	0	0	0
Comb. 1,2 & 3	2	0	1	3
Comb. 2 & 3	2	6	3	3

TABLE 10

FIVE YEAR SURVIVALS CORRELATED WITH THERAPY

<u>Type of Therapy</u>	<u>No. of Patients</u>	<u>Five Year Survivals</u>
1.) Surgery	6	33.3 %
2.) Radium	3	66.6 %
3.) Xray	32	9 %
4.) Combination 1 & 2	0	0
Combination 1 & 3	0	0
Combination 2 & 3	14	21 %
Combination 1, 2 & 3	6	50 %

TABLE 11

TIME FROM FIRST SYMPTOMS TO
CONSULTATION

	<u>1-14 days</u>	<u>15-30 days</u>	<u>31-60 days</u>	<u>61-90 days</u>	<u>91-120 days</u>	<u>Beyond 120 days</u>
Number of Patients	9	9	3	8	4	27

TABLE 12

TIME ELAPSED FROM CONSULTATION TO DIAGNOSIS

	<u>TIME</u>					
	<u>1-14</u> <u>days</u>	<u>15-30</u> <u>days</u>	<u>31-60</u> <u>days</u>	<u>61-90</u> <u>days</u>	<u>90-120</u> <u>days</u>	<u>Beyond 120</u> <u>days</u>
Patients	32	15	3	1	1	9

TABLE 13

TIME ELAPSED FROM FIRST SYMPTOMS TO THERAPY
AS CORRELATED TO SURVIVAL TIME

<u>Symptoms to</u> <u>Treatment</u>	<u>TIME</u>			
	<u>0-1</u> <u>year</u>	<u>1-3</u> <u>year</u>	<u>3-5</u> <u>year</u>	<u>Beyond 5</u> <u>years</u>
1-30 days	1	1	1	1
30 - 90 days	7	2	0	4
91-180 days	8	3	1	2
181-365 days	9	3	3	2
Beyond 365 days	5	2	1	4

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