CANCER OF THE MOUTH.

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For all practical purposes cancer of the mouth is squamous-cell carcinoma (epithelioma). Other malignant growths occur, but since they are rarities this article will deal only with this one important type. In order to limit the field of discussion anatomically also, the mouth will be considered as including only the contents of the oral cavity proper, excluding lips, fauces, and the base of the tongue; the latter are really the borderline zone between the mouth and pharynx, and their treatment problems are rather those of the pharynx than of the mouth. In the mouth proper are included lesions of the anterior two-thirds of the tongue, the floor of the mouth, the palate, the upper alveolus, the lower alveolus, and the buccal surface of the cheek. Of these, lesions of the tongue itself constitute only one-third of the total malignant growths found (see Table 2), and the other areas are equally important. Nevertheless, in most surgical discussions of treatment of mouth cancer only lesions of the tongue are considered.

Cancer of the mouth represents some 10 per cent. of all deaths from cancer, and is one of the four main curable cancers. Its treatment is therefore of considerable importance. It is very much commoner in men and is quite distinctly a disease of the older decades of life (fifty to seventy) rather than of middle age. I have seen it at as low an age as eighteen years, however, so that age alone must not be held as a diagnostic contra-indication of its presence. It is more common in the poorer sections of the community, and it is possible that this incidence is related to a lower standard of oral and dental hygiene.

Clinical Features.

The clinical appearance of cancer in the mouth is so varied that no particular description covers the whole series of lesions. One constant characteristic, however, is a breach of the mucosa at the site of the lesion. Variation in appearance depends on the main direction of growth, whether outwards or whether penetrating into the underlying tissues and on the extent of infiltration. On this basis we can distinguish four main types of lesion, papillary or fungating, superficial, ulcerative, and indurated or scirrhus.

In general, painlessness is the rule even with quite large lesions. A painless ulcer in the mouth is always, therefore, a matter for grave suspicion and investigation. Exceptionally, however, quite a small lesion occasions acute pain so that painlessness must not be looked upon as an essential symptom.

The diagnostic criterion is biopsy and every doubtful lesion in the mouth should be sectioned. This procedure does *not* increase the likelihood of metastases.¹ A positive Wassermann does not exclude cancer since malignant disease is frequently incident on syphilitic endarteritis of the tongue.

A variety of factors may precede, complicate or accompany cancer in the mouth and it seems of interest to consider a number of the commoner conditions modifying either diagnosis or treatment.

Dental Sepsis. There has been much controversy regarding the advisability of complete edentulation when advanced dental sepsis complicates cancer of the mouth. If the teeth are left they make treatment more difficult, may increase pain, and certainly add to the liability to broncho-pneumonia during treatment. On the other hand, the removal of a number of septic teeth is not always a minor operation. Even under normal conditions healing takes some two weeks, already an undesirable delay, while if complications set in healing may be seriously delayed. Although arguments exist for and against pre-treatment edentulation, it is in general preferable to take the risks involved by retaining the teeth rather than those of delaying treatment, taking only such steps as may be speedily possible to clean up superficially.

Leukoplakia. The question as to whether treatment should be carried out for leukoplakia in the benign stage to prevent a later malignant change has not been satisfactorily answered as yet. Two forms of leukoplakia are seen, the single isolated patch, and multiple patches constituting generalised leukoplakia. Simple preventive treatment is not possible because

radiation at low dosage is useless, while both surgery and the full radiation dosage for squamous carcinoma which alone could be effective cannot really be considered practical politics. I believe that a watching policy should be adopted consisting in adequate arrangements for frequent examination. A biopsy should be taken at the first sign that a part of the lesion is becoming invasive—i.e., when any induration or thickening is felt below the white patches. When malignant change is found, the affected part is treated.

Syphilis. Syphilitic endarteritis of the tongue often underlies cancer and is a serious complication. The diagnosis of combined syphilis and cancer should be made on the typical appearance of the lesion—an indurated atrophy showing patchy glossitis, and not on the findings of a positive Wassermann in a patient who has an ordinary malignant ulcer in a mouth otherwise healthy. If the well-known local changes of syphilis are absent the cancer should have radiation treatment in the ordinary way, but if they are present the lesion will react unfavourably and surgical excision is to be preferred if it is practical. Extensive tumours of the syphilitic tongue do not benefit by radiation and should not be so treated.

Tuberculosis. Although less frequent than carcinoma, tuberculosis of the tongue is important from the standpoint of differential diagnosis. Biopsy in such cases shows chronic inflammatory changes and the absence of malignant cells. A radiograph of the chest always reveals advanced lung tuberculosis.

Anaemia. Microcytic anaemia is a frequent precursor of cancer of the mouth and throat in women and there is probably an aetiological relationship. The presence of anaemia of this or other type is a factor of importance in treatment, since anaemia renders the tissues less responsive to radiation. Active treatment of the anaemia should be undertaken even at the expense of some delay in commencing treatment.

Histological Type.

Histologically we are solely concerned with squamous-cell carcinoma. This type of carcinoma varies in form from anaplastic to high keratinizing, the degree of differentiation forming the basis of Broder's pathological "grading." This grading is important as an index of malignancy. It has also been considered as a guide to radiosensitivity on the basis that the less the degree of differentiation the greater the radiosensitivity. This is not the case, and it would seem that the dose necessary to produce permanent disappearance in the irradiated area is not related to the grade and is as high for grade 4 as for grade 1 tumours.

The name "lympho-epithelioma" is sometimes applied to tumours in this region. It is highly probable that lesions so diagnosed are either true lymphosarcoma and so highly radio-sensitive, or anaplastic squamous carcinoma, and therefore not specially sensitive.

Treatment.

The choice of treatment lies between radiation and surgery.

Radiation: Radium.

X-Ray.

Surgery: Systematic excision.

Diathermy coagulation.

It is the firm conviction of the writer of this article that with the exception of the use of surgery for lesions in a syphilitic tongue, radiation provides the best form of treatment for all malignant lesions of the mouth. As is also true in relation to the choice of therapy for squamous carcinoma in other accessible sites, this statement does not mean that surgery either by diathermy or excision is incapable of producing a certain percentage of cures, but merely that the probability of cure in any particular case is much greater if appropriate radium methods are employed as the *first* treatment, than if the most appropriate surgical measures be adopted. In practice, some 70 per cent. (see Table 4) of permanent resolution of the primary tumour should be achieved by radiation alone. Surgical excision does, however, provide a *second* line of attack, the value of which must not be under-estimated for radio-resistant lesions, or where failure results from errors in technique. A second radiation treatment of an already radiation-treated lesion is very rarely successful.

When we come to consider the various methods of radiation treatment we find that there are two main groups, intra-oral and external. These may conveniently be sub-divided as follows :—

Intra-oral.

- Radium - Needle Implantation.
Radon Seed Implantation.
Intra-oral applicator.
- X-Ray - " Low Voltage Short Distance " apparatus.
Deep therapy with special applicators.

External.

- Radium - Beam (Bomb) Therapy Unit.
- X-Ray - Deep Therapy.

Intra-oral Radium.

In general, present-day methods of employing radium intra-orally in mouth cancer are based on the principles of treatment evolved by Regaud at the Paris Fondation Curie between 1920 and 1930, and introduced to this country by various people, among the first being Birkett of Manchester in 1925. The underlying basis, which has not been changed, lies in the use of relatively small quantities of radium implanted for periods of from six to ten days continuously. Subsequent developments have perfected the actual technique and have contributed methods of dosage assessment. Up to some few years ago " dosage " was stated in terms of the amount of radium employed, the commonly used units being " milligramme hours," " millicurie hours," or " millicuries destroyed." Unfortunately this approach is only in the nature of an empirical guide and at that very undependable. It is essential for accurate work that dosage be determined and stated in respect of the amount of *radiation*, not the amount of *radium*. To this end a unit of radiation which is common to X and gamma radiation is now employed, viz., the international Roentgen (" r "), and methods of arriving at a statement of true dosage in radium therapy have been published.² Actual dosage to be employed varies to some extent, but over the accepted treatment period of eight days a tumour dose of between 5,500 and 7,000r is required to cause a permanent lethal change in the majority of squamous-cell carcinoma. The limiting factor is the tolerance of the normal tissue, the smaller the volume the greater being the tolerance and the higher the permissible implantation dosage. Using intra-oral radium applicators, the effect of which is highly superficial, surface doses of up to 8,000 to 10,000r are apparently tolerated without risk of permanent damage.

The best arrangement of radium for any particular lesion depends on the therapist's judgment as to how he can best produce a homogeneous or nearly homogeneous radiation field throughout the " treated zone." This conception of a " treated zone " is important. Such a zone must include the whole of the tumour if cure is to be expected, yet at the same time the minimum volume of tissue which will so include the whole tumour must be irradiated. In surgical removal, as is so well illustrated in breast cancer, wide excision is the rule if tissue can be spared. Similarly, in radiotherapy, at first sight it would seem that the safest scheme of treatment would be to include in the treated zone such a volume wide of the tumour as to make certain that it easily contains the true tumour bearing area with tissue to spare. Unfortunately, the analogy with surgery does not hold, because the response of the tumour to radiation and the tolerance of tissue to radiation decrease appreciably with increase in irradiated volume. In practical therapy, therefore, a compromise is always being made between the need to cover the whole tumour bearing area completely and the desire to keep down radiated volume to the minimum. This is obviously purely a matter of experience and individual judgment.

Needle Implantation.

In general, a satisfactory implantation of radium calls for an arrangement of radium sources in some definite geometric form. Such arrangements are known as planar implants, two plane implants, volume or cylindrical implants, and so on. The modern implant not only needs careful previous planning and physical pre-calculation, but subsequent check by radiographic examination to determine that arrangements are satisfactory and to measure areas and volumes for calculation of the exact treatment time.

Figures 1 and 2 show radiograms of two fairly typical implants, the first a planar and the second a volume implant. These show that a remarkably good approximation of the ideal layout is quite possible, given experience plus a certain stereognostic sense on the part of the operator. Planar implants are of use for the side or dorsum of the tongue, and for the cheek. Volume implants are used for the more bulky lesions of the tongue and for lesions of the floor which extend into the tongue rather than over the alveolus.

Gold Seed Implants.

An alternative method of treatment by implantation is provided by the use of gold radon seeds permanently implanted. Although perhaps liable to be a little less accurate than needle implant methods, these have also distinct advantages in certain circumstances. They undoubtedly provide the best approach to superficial lesions on curved surfaces—the tip or sides of the tongue anteriorly, the dorsum of the tongue, and the soft palate. They require a shorter period of hospitalisation and can therefore be particularly advantageous for old people. In my own practice I have kept seeds for relatively minor lesions, but in the Memorial Hospital in New York they are used with great success as the main intra-oral implant medium for both flat and bulky tumours.³

Intra-oral Applicators.

The alternative intra-oral method to implantation is provided by the use of specially constructed dental applicators bearing radium. Intra-oral applicators are moulded on dental plaster models of the relevant parts of the interior of the patient's mouth. They can be made in vulcanite as in ordinary dental practice, but in view of their temporary life they can equally well be fashioned in one of the various dental compositions. Where the situation permits, treatment by mould is superior to treatment by implant, because of the avoidance of trauma and of anæsthetic risks, and because of the more accurate distribution of the radiation foci. Moulds can be used for lesions of the alveoli, the anterior half of the palate, the buccal surface of the cheek, and the alveolar half of the floor of the mouth. Not infrequently it is advisable to "sandwich" the tumour bearing area between two moulds, one external and one intra-oral. Treatment of a lesion of the lower alveolus and the floor of the mouth by such a double mould is illustrated in Figure 3.

Intra-oral X-Ray Therapy.

The use of intra-oral radium probably provides the most successful approach to treatment of mouth cancer. Nevertheless, X-rays must also be considered, as of recent years various methods have been evolved of employing *intra-oral* X-ray therapy. This is achieved either by fitting ordinary X-ray therapy plant with special buccal applicators, or more usually, and with greater applicability, by the use of the newer "low voltage short distance" plants (Chaoul or Philips). The number of cases so treated is still inadequate to allow final assessment of the value of these methods. They are undoubtedly promising if their use be carefully restricted to accessible lesions where the whole tumour with adequate margin can be maintained in the treatment field. In Manchester, using the Chaoul type of apparatus, we have found that it is worth while to give an anæsthetic and to set up with meticulous care in a manner quite impossible with a conscious patient—indeed, to make almost a major procedure of the treatment.

Radium Beam Therapy.

In the field of radium therapy the main alternative to intra-oral radium is radium beam therapy. This employs massive amounts of radium, 3, 5, or even 10 grams in one unit, mounted in special apparatus now known as the radium beam unit, but formerly more graphically, though scarcely as accurately, known as the radium bomb. The radium beam unit is used to deliver radiation to the tumour from outside, using multiple portals of entry in a manner exactly homologous to the use of "crossed fire" in X-ray therapy. Radium beam methods were first practised with success on a large scale in the Radiumhemmet in Stockholm. A full description of the major piece of experimental work in this country with this type of therapy is given in a Medical Research Council Report.⁴ It is still too early to arrive at a final assessment of the relative value of intra-oral and beam methods of radium therapy. At the present stage of development it seems as if the advantage lies with intra-oral methods, and it is certainly

of interest to note that many cases treated by beam therapy require subsequent minor implantations. It may be that a combination of extra-oral radiation with intra-oral radium will ultimately provide the optimum method.

X-Ray Therapy.

Apart from intra-oral use, X-ray therapy used alone is of no value in curative therapy for mouth lesions. It is useful in combination with radium and it has an important place in regard to palliative therapy of advanced cases with large primary lesions and fixed lymph nodes.

Secondary Involvement of Neck Lymph Nodes.

As will be seen from the tables which follow, the treatment of the primary tumour is only half the battle, and ultimate success is as dependent on the treatment of the secondary lymph node involvement as of the primary. Where the nodes are operable there is no doubt that surgical removal is vastly superior to any radiation method. Such surgery must, however, be the full radical block dissection of the neck described by Crile, which later became almost a "standard" operation both in the U.S.A. and Paris. Recently it has been developed technically to a high degree of perfection by W. R. Douglas of Manchester, with results shown in Table 3. The removal of the lymph node area must be radical, sweeping the whole of the fascial layer of the neck upwards in one piece, including the sterno-mastoid muscle and the jugular vein.

Where nodes are inoperable, or age precludes operation, treatment may be carried out by either radium or X-ray, but the ultimate results are disappointing.

Where no nodes are present before treatment, and still absent on completion of the primary treatment, the question of "prophylactic" block arises. Having regard to the large numbers of cases in which nodes are absent, there is little doubt that the use of prophylactic block as a general routine procedure is not justified. This does not mean, however, that the probability of secondary neck invasion can be forgotten, and it is essential to adopt what may be called a "watch" policy. Under this scheme a patient is examined regularly at short intervals for a long period, and it is impressed upon him that these periodic visits are an *essential part of treatment* and not a matter of casual interest. For the first year intervals longer than one month are without doubt dangerous. My own practice is monthly attendance for the first year, two-monthly for the second, three-monthly for the third, and so on up to at least five years. I have seen nodes become first involved in the third and fourth years not infrequently. If palpable nodes are found, the radical block dissection is carried out. Dissection of the second side later if that too becomes involved is not impossible, and can be successful.

End—Results.

In conclusion, it is of interest to briefly examine the results of the methods of treatment which have been described. In the Tables which follow there are given various analyses of the results of treatment of mouth cancer at the Radium Institute in Manchester over the period 1932 to 1935 inclusive. The figures given are in terms of net survival rate at five years—that is, deducting from the whole sample as non-statistical, cases either not traced (of which there are very few indeed), and those died of intercurrent disease with at death an apparently healed cancer. The figures shown include *all* cases treated by radium, whether early or late. The great majority of them are proved by section and subsidiary analyses⁵ showed that the results in the total group are certainly not higher than those of a section proved group taken alone. In all cases intra-oral methods of treatment, implantation or dental applicator, were used. The cases are divided into four stages according to the degree of advancement of the disease, and details of the staging are published elsewhere.⁵ Briefly, Stages 1 and 2 are small and large lesions with no nodes when first seen, Stage 3 similar cases with operable nodes, and Stage 4 comprises the advanced cases.

Table 1 gives the details of the results of the whole group by stages showing the enormous difference in results for early and late cases. In the final column attention is drawn to the

difference between the cases with nodes affected when first seen and those node-free when first seen. Many of the latter will have subsequently developed nodes and been dealt with either by block dissection or other means.

TABLE I.—Cancer of Mouth (Lip, Fauces and Base of Tongue excluded).

FIVE-YEAR SURVIVAL OF CASES TREATED RADIUM 1932-3-4-5.

Group.	Treated.	Alive.	Died of Cancer.	Died of intercurrent disease. Cancer well.	Not Traced.	Net % Alive.	Effect of Nodes.
Stage I	162	86	52	23	1	62%	} 46% alive of cases "node-free" when first seen.
Stage II	187	56	117	11	3	32%	
Stage III	167	32	128	7	—	20%	} 14% alive of cases with nodes when first seen.
Stage IV	86	4	82	—	—	5%	
TOTAL	602	178	379	41	4	32%	

In Table 2 the same group of cases is analysed by site and the interesting fact becomes apparent that although there seems to be quite a variation of results stage by stage, the total results for each site are remarkably similar (variation of 30 per cent. to 36 per cent.), a fact also borne out by the analysis in Table 4.

TABLE II.—Cancer of mouth (Lip, Fauces and Base of Tongue excluded).

FIVE-YEAR SURVIVAL BY SITE OF CASES TREATED RADIUM 1932-3-4-5.

SITE.	Stage I.		Stage II.		Stage III.		Stage IV.		Total.	
	“ Node-Free.”				Nodes Present.					
	Treated.	Net % Alive.	Treated.	Net % Alive.	Treated.	Net % Alive.	Treated.	Net % Alive.	Treated.	Net % Alive.
Tongue Anterior 2/3rds	80	57%	57	25%	55	13%	22	0%	214	30%
Floor	31	73%	52	24%	52	30%	31	10%	166	31%
Cheek	18	63%	27	46%	25	18%	13	0%	83	33%
Palate	20	58%	28	38%	16	7%	6	17%	70	35%
Alveolus	13	80%	23	48%	19	26%	14	0%	69	36%
TOTAL	162	62%	187	32%	167	20%	86	5%	602	32%

Table 3 is an indication of the value of block dissection. The 178 cases were those in which block was carried out during the years 1932 to 1935 inclusive on cases of mouth cancer (fauces and base of tongue included). The results were assessed at five years from the date of the operation, not of the mouth treatment. As it is urged that the good results could be due to cases in which the palpable nodes were not in fact malignant, a subsidiary analysis of the cases in which the excised tissue was examined and found positive is also given. This would seem to show that the total results are in fact significant.

TABLE III.—FIVE-YEAR RESULTS OF BLOCK DISSECTION, 1932-3-4-5.

	Whole Group.	No. with section proven nodes.
No. of Treated Mouth Cases (including Fauces and Base of Tongue) on which Block Dissection carried out in the presence of palpable nodes—(i.e., excluding prophylactic block)	178	62
Deduct from sample :	.	.
(i) No. of cases in which death due to recurrent primary lesion ; nodes apparently well	26	11
(ii) No. of cases not traced	2	1
(iii) No. of cases in which death due to unrelated intercurrent disease ; nodes and mouth apparently well	8 36	3 15
No. of Cases for Analysis	142	47
No. of Cases dying within one month of Block (index of operative mortality)	13	5
No. of Cases alive at five years from date of Block Dissection	49	17
Results—Net percentage alive at five years ..	35%	36%

There is another question to which it is of value to seek statistical answer—that is, the effectiveness of the local primary treatment considered alone. This information was arrived at by special analysis of a small group of cases (1932-1933), initially node-free and remaining node-free for five years or dying as a result of failure of the primary treatment. The analysis of these cases is given in Table 4. This shows that cancer within the mouth is essentially a curable disease (70 per cent.), a fact also borne out by the results of treatment in the early stages as shown in Table I.

TABLE IV.—Cancer of Mouth.

ANALYSIS BY SITE OF CASES IN WHICH ISSUE AFFECTED BY RESULTS OF PRIMARY TREATMENT ONLY (1932, 1933 cases only).

SITE.	Number remaining "node-free."	Net Five-Year Survival.
Tongue ..	47	70%
Floor ..	23	61%
Palate ..	15	74%
Cheek ..	15	67%
Alveolus ..	18	67%
TOTAL ..	118	68%

Cure, however, is dependent on early diagnosis, which means prompt taking of a section, and on *immediate* radical therapy, however small the lesion.

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PLATE 1.

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FIG. 1.—Radiograph of a
“Planar” implant.

FIG. 2.—Radiograph of a
“Volume” implant.

FIG. 3.—Radiograph of a
“Double Mould.”