removal plus radium for the remainder. Any node in which the disease has perforated the capsule is regarded as being inoperable even though it may be small and, from the standpoint of technique, removable in the gross together with the adjacent structures. All necks with bilateral metastatic nodes are regarded as being surgically inoperable, even though they may be quite readily removable technically. Once the disease has involved both sides of the neck it is considered as incurable by many means, except in very rare instances. For the very advanced metastatic nodes external irradiation only, as a palliative measure, is used.

Complete and permanent regression of fully differentiated squamous-cell carcinoma, secondary in the nodes, has not been observed from external irradiation alone. Metastatic nodes from anaplastic epidermoid carcinoma, even though coming within the definition of an operable node, are treated by radium alone. Usually, filtered radon tubes are implanted as well, just as in the treatment of the primary growth in this group, but the backbone of treatment in this type of lesion is external irradiation, and no resort is made to operative surgery for removal. The routine external irradiation of the neck is done within a period of a fortnight.

Unfortunately, from the standpoint of statistics, we continue to treat practically all cases applying at the clinic. There is no selection, except to decline acceptance of those equal to nursing care only. From a humane standpoint it has been necessary to do this, and, on the other hand, it has always been the feeling that observation of all stages of the disease is of value. Such a policy, however, precludes a satisfactory comparison of statistics with radiological clinics where selection is practised, or with surgical clinics where none but operative methods are employed.

Our reports on tongue cancer, made at the Second International Congress of Radiology in Stockholm in July, 1928, covered a group of 473 histologically verified and clinically unselected cases treated during the period from January 1st, 1917, to December 31st, 1927. The survivors in this group have been rechecked to December 31st, 1929.

The percentages of freedom from clinical evidence of disease are as follows:

	Cases.	Percentage.
Tip of tongue	6	40
Dorsum of tongue	10	17
Lateral border of tongue	54	19
Base of tongue	13	11
Recurrent... ..	4	17

Of the total group, 97, or 20 per cent., are alive and living active lives. Of these, 87, or 18 per cent., present no clinical evidence of disease.

The intervals of freedom from disease are as follows: 39 cases, five to twelve years; 24 cases, three to five years; 24 cases, two to three years.

Of the entire group, 69 per cent. are known to be dead. A number of these patients died of intercurrent disease, and while free from clinical evidence of cancer; 19 lived five years or over; 19 lived three to five years; 113 lived one to three years; while 179 died within one year.

In the group showing no evidence of metastatic involvement of nodes throughout—189 patients—66 have now no evidence of disease. The group of 161 patients with gross evidence of lymph node involvement on admission shows only 6 "no evidence of disease" now; and of the 103 developing nodes after admission, 12 only have now no evidence of disease.

It is true that all these patients did not die as a result of the metastatic involvement. Many were far advanced in the primary site. In many others the node involvement was hopelessly advanced. The group does not include an appreciable number of our gold tube radon implantation cases. The failure to control these cases with metastatic cervical nodes, however, leaves much to be desired in the treatment of the neck.

In the entire group of 473 cases, the percentages of surgical operability on admission were as follows:

	Percentage.
Tip of tongue	60
Dorsum of tongue	25
Lateral border of tongue... ..	46
Base of tongue	9

The percentage of freedom from clinical evidence of disease in the entire group of unselected cases—18 per cent.—is regarded as comparing favourably with the average of operative surgical statistics in the group of operable cases alone.

SUMMARY.

1. At the Memorial Hospital radium is the agent of choice for treatment of the primary growth in cancer of the tongue.

2. X-radiation is a necessary complement to the treatment of all cases of lingual cancer unless replaced by the use of very large amounts of radon for external application.

3. Radium must not be depended upon entirely, and in all cases, to the exclusion of other associated measures.

4. Operative surgery is indicated in the mouth for access, drainage, and in dealing with disease in bone.

5. Operative surgery is indicated in the neck in early definite involvement of adult epidermoid carcinoma, in addition to irradiation.

6. Surgical exposure in the neck, plus filtered radon implantation, is indicated in a variety of metastatic conditions other than the group operable by complete dissection.

7. The selection of technical methods and the guide to irradiation intensity is through an appraisal of the relative radio-sensitivity of the growth, as judged by the degree of cellular histological differentiation.

8. The irradiation must be directed with care and precision. The minimum intensity must conform to well-defined standards.

9. The best interests of the patient are served through close co-operation between pathologist, physicist, and clinician.

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RADIUM TREATMENT OF BUCCAL CARCINOMA.

PRINCIPLES AND SOME RESULTS.*

BY

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REVOLUTIONS in medicine and surgery, as in anything that matters, are rarely successful, but it would appear that the treatment of carcinoma of the mouth and tongue is an exception to the general rule, and that it is extremely improbable that we shall ever revert to the older forms of treatment, at any rate for the primary growth. This surgical revolution, however, is more apparent than real, and takes no account of the painstaking work of the last two decades in radium therapy. It was Dominici—whose death was probably due to excessive exposure to the gamma ray—who drew attention to the importance of filtration in eliminating the direct action of the beta ray and so utilizing the selective action of the gamma ray. Later, Regaud showed that the prolonged action of the gamma rays in relatively weak intensities produced, in the squamous epitheliomata at any rate, a more favourable response than a high intensity for a short time.

During the war small unscreened glass emanation tubes, 5 to 10 millimetres in length and containing 1 to 2 milligrams of emanation, were used extensively in America for buccal carcinoma. These were buried and left permanently in the tissues. A very intense local reaction followed owing to the unrestricted action of the beta rays, but results were good in such patients as survived the ordeal with its distressing and painful complications. It is important to realize that this method embodied the principle of prolonged irradiation, of which Regaud is an advocate. Later, Failla, at the Memorial Hospital, New York, used gold seeds 0.3 mm. in wall thickness filled with emanation, which cut off about 50 per cent. of the beta rays; while,

* A communication to the Section of Surgery at the Annual Meeting of the British Medical Association, Winnipeg, 1930.

still later, Muir invented the removable platinum radon seed. We had used the unscreened seed in Manchester, and an analysis of our cases—when I took over the work from Dr. Arthur Burrows in 1925—revealed that 80 per cent. of our successes with the primary growth had followed this method of treatment. As a result, we began to employ the same method of treatment as Regaud for the primary growth, screening our source with a minimum of 0.5 mm. of platinum, and using as great an active length as possible.

Radium has improved out of all recognition the outlook in buccal carcinoma, and it has, I think, at the same time enriched our knowledge of the disease. The original surgical conception of the disease required the removal of the primary growth, the lymphatic tract to the lymph nodes, and the nodes themselves *en bloc*. The operation thus resembled in conception and execution the radical amputation of the breast as it is still performed, but involved a much higher mortality. It was realized, however, even before radium was seriously considered as a factor in treatment, that cases could be cured by the ablation on separate occasions of the primary growth and the lymph nodes, and radium treatment has conclusively proved that, in buccal carcinoma, metastasis to the lymphatic glands is by embolism.

But radium has done more than this, for the coincident investigations of the histological structure of buccal carcinoma in different parts of the mouth have shown that quite well-marked variations occur with corresponding variation in sensitivity. We know now that almost every carcinoma of the base of the tongue will be of an embryonic, undifferentiated, and radio-sensitive type; that consequently there is a good chance of local cure in almost every case, and that the danger lies in the rapid and widespread metastasis. The only cases I have seen of pulmonary metastases in buccal carcinoma have been of this type. We know that epithelioma of the cheek, lip, floor of the mouth, and anterior third of the tongue are almost invariably of a highly differentiated type, with abundant cell nests. They are radio-sensitive, but less markedly so than the preceding type. Our own observations indicate that practically every case in which the anterior third of the dorsum is affected the condition is superimposed upon a chronic glossitis of syphilitic origin. This interferes with the response to irradiation, and, occasionally, even small lesions do not respond. In such cases it is always advisable to point out that diathermy may have to be used later if radium is unsuccessful. Such cases strengthen the evidence that tissue reaction is an important factor in the effect produced by radium on malignant tumours.

In the middle third of the tongue, on the tonsil and fauces and soft palate, both histological types and also intermediate varieties are found.

It would seem from the above considerations that all squamous epitheliomata of the mouth and tongue are radio-sensitive, some more so than others, and that there is now unanimity of opinion that prolonged irradiation with gamma rays of low intensity yields the best results. The problem, then, should be mainly one of the insertion or application of the radium.

SEEDS OR NEEDLES.

It has always seemed to me that it is infinitely easier to insert a needle of active length, say, 30 mm., than six separate seeds of active length 5 mm., and it becomes the more evident the larger the growth. This is a general opinion in England, where we use needles of active length up to 50 mm. for the treatment of breast carcinoma. I would say unhesitatingly that needles are superior to seeds. There occur some occasional complications from radium treatment which certainly do not follow operative methods, involving necrosis of bone or of the soft tissues. If a lesion involves bone superficially, necrosis is almost inevitable if the disease is to be eradicated, and may be prolonged and distressing. If bone is extensively involved it is doubtful whether the disease will ever be eradicated by radium alone, and in such cases radium treatment of the soft parts combined with surgical excision of the affected bone, if possible, is the better procedure.

No matter how careful and experienced the operator may be, necrosis of the soft tissues sometimes follows. Over-treatment rather than under-treatment should always be our aim, since a second application does not meet with so active a response as the first, except after a long interval of time, when it is probably too late.

In the preceding remarks it has been assumed that the primary growth is treated first. The primary growth must be regarded as a source of embolic infection of the glands, and clinically we know that if the lymphatic flow is blocked by extirpation of the glands on one side of the neck, it is diverted to the opposite side. I have seen several cases which demonstrate this. Radium treatment is a conservative method which, if successful, restores function almost to normal; little need be said as to its advantages over surgery of the tongue. In the cheek, palate, and floor of the mouth little can be seen except slight scarring; in the tongue the same may be said, although slight deviation to the affected side with pointing of the tip to the opposite side is noted in lesions of the middle third. Speaking, eating, and drinking suffer no impairment. Local recurrence is rare after six months, and cases of so-called "recurrence" are those in which the growth has never really disappeared.

THE LYMPHATIC DRAINAGE AREA.

Although most workers are agreed as to the principles of treatment of the primary growth by radium, there is no method of using radium alone which has established itself as the method of choice in the treatment of the lymphatic drainage area. Even with a primary growth confined to one side of the mouth we have to consider the treatment of a wide area bounded in practice by the limits of the anterior and posterior triangles of the neck on the same side, although theoretically, and occasionally in practice, metastasis occurs in the opposite anterior triangle. Needling is a localized method of treatment, and if in the primary growth, which is relatively circumscribed, we are compelled to insert some fifteen needles, we ought to implant at least thirty to forty in the much wider secondary area. In the majority of cases of buccal carcinoma the upper deep cervical, and later the lower deep cervical, groups of glands are invaded, and some of these lie posteriorly to the internal jugular vein. These cannot possibly be dealt with adequately by the insertion of radium needles blindly through the skin, and a thorough exposure of the neck is necessary. Similarly, in order to deal effectively with the glands in the posterior triangle and supraclavicular fossa, the sterno-mastoid muscle should be divided and reflected upwards. I think, therefore, that if all this is necessary for adequate treatment by the implantation of needles, a block dissection might as well be done at the same time, in an operable case. With an experienced operator and a regular assistant the operation is not so formidable as it appears, and I am convinced that it is one of the best surgical operations in malignant disease. The tragedy is that so many block dissections are so only in name.

In an operable case the choice rests between the implantation of needles and some form of external irradiation. It is very doubtful if external irradiation, except in the case of the radio-sensitive types which are found at the base of the tongue, has ever cured a case with fixed secondary deposits in the neck. Our practice in Manchester is to reflect flaps, as in the case of a block dissection of the neck, and divide the sterno-mastoid. Needles are then inserted in the anterior and posterior triangles about 2 cm. apart. They vary according to circumstances in active length between 20 and 50 mm., and are left in position about eight days. Usually thirty to forty needles are required, and the wound has to be reopened under a general anaesthetic for their removal. One should never subordinate the position and direction of the needles to ease of removal.

There is justification, in my experience, for the adoption of a policy of observation if no glands are palpable, provided the patients are seen at least once a month. If means had permitted, these patients would have been subjected to external irradiation by about half a gram of radium at 4 to 7 cm. distance. At the Fondation Curie a routine block dissection is performed, followed by distance irradiation if microscopical deposits are found in the

glands removed. Our own position may be summarized as follows.

1. If no glands are palpable, observation at monthly intervals.

2. If glands are palpable and removable, block dissection, either combined with implantation of radium or followed by external distance irradiation.

3. If the glands are fixed, implantation of a large number of needles, thirty to forty, after thorough exposure of the neck.

THE RESULTS OF TREATMENT.

There are very few figures available for the results of treatment by radium alone.

Berven of Stockholm published in 1928 the results in 22 patients, of whom 13 were alive five years later (59 per cent.). These, however, were "operable" cases, and radium was not the only factor concerned. His practice is to use diathermy, either for excision or coagulation, and to supplement this with the implantation of radium for twenty-four hours. I do not think that these results should be included or compared with those obtained by radium alone. Any surgeon of experience will recognize that it is impossible to deal adequately by diathermy with any growth of the tongue which involves extensively the middle or posterior third. We all recognize that surgery can achieve good results with early growths of the anterior third of the tongue, but having seen what radium can accomplish at all stages of the disease by the technique first advocated by Regaud, with no mutilation and a complete restoration of function, we feel that it has established itself as the method of choice in the first instance.

Regaud's last published results were assessed in December, 1927, and I have abstracted and summarized them in the following table.

	1922.	1923.	1924.	1925.	1926.
Total	33	54	55	60	54
Complete cure	6	10	11	17	21
Percentage	18.18	18.50	20.00	28.33	38.88

This table therefore gives results at one, two, three, four, and five years respectively. It will be observed that if a patient survives for three years he has an almost equal chance of living for two more years.

The methods we employ in Manchester, which are based on those of Regaud, were begun late in 1925, and so far the results have been reviewed only on a three-year basis. They are as follows.

	1926.	1927.	1928.
Total	80	74	113
Complete cure	18	25	51
Percentage	22.50	34.7	45.13

For the same periods of time they are approximately the same as Regaud's, but there are several points to which I should like to draw attention. It has been our custom at the Manchester and District Radium Institute to issue an annual report, and this is in effect an annual process of examination. Although we cannot claim as cures patients treated so recently as three months previously, yet by comparison with the same results year by year we discover whether our immediate results are on the up grade. For the primary site in buccal carcinoma our percentages of "apparent cures" for 1926, 1927, and 1928 were 38.7, 47.3, and 60 respectively, and, where the primary and secondary sites were considered, 27.5, 36, and 45 per cent. respectively. In other words, our immediate results improved each year. Naturally this percentage became lower when the results were reviewed at a later date, although we do not find that recurrences at the primary site are common. I think that this improvement is due chiefly to increased personal experience, and that it is an argument for the treatment of carcinoma of the buccal cavity at centres where special experience exists. Lane-Clayton (Reports on Public Health and Medical Subjects, No. 59) has reviewed the statistical

literature. She concludes: "It is probably fair to say that some 25 per cent. of patients operated upon will be alive and well three years after operation and 20 per cent. at five years."

Although the number of cases treated by radium is relatively small, the three- and five-year results are about the same as those obtained by surgery. But the likeness ends there, for the results by radium have been achieved not only in operable, but also in inoperable cases, and with no mutilation to the patient and no impairment of function. We all appreciate the art of surgery, but the selective action of the gamma ray in certain types of malignant disease and, in particular, epidermoid carcinoma of the mouth and tongue with complete restoration of function, must be placed on a higher plane, if degrees there be. The question naturally arises whether we can confidently look forward to improvement in results. I think we can if the following points are considered.

Early diagnosis is essential, the more so because involvement of lymphatic nodes is early and increases the gravity of the prognosis. With the education of the general public, particularly with regard to oral hygiene, I think that as the present generation reaches middle and old age the incidence of oral carcinoma will diminish, and that they will seek advice and treatment at an earlier stage when abnormalities exist. At the present time, in the hospital class of patient, one feels that if the patient will tolerate for many years, as he undoubtedly does, a mouth filled with carious teeth of all shapes and sizes, the presence of an early carcinoma is an unnoticed incident in his daily life. Commonly such a patient with an immobile tongue will give a three weeks' history only!

Secondly, I believe in the concentration of radium treatment at large centres. I know from my own personal experience that results with the same radiological technique improve with experience, and that only from the follow-up of large numbers of cases can faults be corrected. The same remarks, I think, apply equally to the performance of a block dissection, which at present is often an integral part of the treatment of a case of buccal carcinoma. Unless the surgeon has opportunities for the frequent performance of this operation I think the results will be poor. One must always remember that *Natura* does not help us a great deal, so far as we know, in malignant disease, whereas in the inflammatory diseases she plays a big part.

TREATMENT OF BLADDER TUMOURS BY RADON.*

BY

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ATTEMPTS to evaluate the application of radium to bladder tumours are beset with difficulty. For the purposes of this discussion I will limit myself to an analysis of the case records of thirty-two patients who consulted me for malignant bladder tumours from 1922 to 1930, who were treated by radon, and in whose records the complete results are shown. Diathermy was always employed as a preliminary to prepare the tumour for the seeds. Bare glass seeds were used from 1922 until July, 1926. Since July, 1926, glass seeds screened with 0.3 mm. of platinum were employed. For a knowledge of both these methods I am indebted to the Radium Corporation of New York, and to a study of the work of Keyes, Barringer, and Muir. All the tumours treated were clinically malignant, though the majority were small and of recent origin. Pathological evidence of malignancy continues to prove unsatisfactory. In a number of the cases described below the tumours removed were said by the pathologist to be innocent, yet the patients died of secondary deposits within a short time. The cases were selected for radon treatment mainly for four reasons.

1. Because the patient refused extensive operation, or would only consent to cystoscopic treatment.
2. Because the tumours were in a position badly situated for

* A communication to the Section of Surgery of the Annual Meeting of the British Medical Association, Winnipeg, 1930.