REPORT and COMMENTARY
on
A SERIES OF CASES OF
BUCCAL CARCINOMA
Presented In Competition For The
PATTISON PRIZE IN CLINICAL SURGERY
JULY 1931
By
JAMES J. M. BROWN.
PREFACE.

In hospital practice epithelioma of the buccal region forms a considerable proportion of the cases of malignant disease. The increasing use of radium in the treatment of this class of case has prompted this study; for it seems that a full consideration of the problem is now necessary to enable us to estimate with what justification surgery has been superseded. The economic and the humane aspects of the problem are of distinct importance and every avenue that may lead to an advancement in our knowledge must be explored. By no fact is this more warranted than by the uncertainty that appears from the literature to attend the use of radiation therapy. From time immemorial fads have sprung up to hold the fashion for a brief space before being finally relegated to the limbo of the past, and in many instances these fads of fashion have served to hamper the field of progress. Radium treatment has been in use sufficiently long now for us to ask ourselves whether its use is justified by its results. If it has to its credit no better or more hopeful outlook
than Surgery, we will be justified in pressing for its abolition, lest its continued use should only raise false hopes or prevent fresh advances.

For these reasons I have chosen for discussion the following six cases of buccal carcinoma.
ACKNOWLEDGMENTS.

I am deeply indebted to PROFESSOR JOHN FRASER for his kindness in allowing me to make use of six of his Cases for the purpose of this Commentary.
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SIX CASES OF
BUCCAL CARCINOMA
TREATED IN SURGICAL WARD 7
OF THE ROYAL INFIRMARY.
CASE I.

T.M. Aged 65 years.
Occupation: A fisherman.
Admitted: 1st September, 1930.

Complaint: Growth on the lower lip of three years' duration.

History: Three years ago the patient developed a small sore on his lower lip. In association with this sore, there was an intermittent swelling of the lower lip; the sore was never more than slightly uncomfortable. When the swelling of the lip subsided he suffered no inconvenience, and on each occasion he thought he was cured, but the swelling invariably reappeared. This state of affairs went on until practically three months ago; since then, however, the swelling has remained constant.

From that time, i.e., June 1930, it has gradually increased in size, become uncomfortable and interfered with eating and speaking. Within the last month its increase in size has been much more rapid and the surface has become ulcerated. Within the last week or ten days, he has suffered severe paid, which has prevented sleep.
Case I.

Fig. 1. - Photograph taken before Operation.
Apart from this pain, he has no other symptoms and his general health has been very good for as long as he can remember.

**Previous Illnesses:** He has never been ill before.

**Family History:** No history of malignant disease in any other members of his family.

**Physical Examination:** He is a spare, brick-complexioned man who does not look his age.

**Local Examination:** Hanging from the lower lip there is a pedunculated tumour about the size of a small tomato. It is irregularly rounded in shape and is attached to the whole mucous surface of the lip. The tumour is brown in colour and is leathery in appearance.

The surface is irregular and shows numerous cracks and fissures from which there is a slight exudation of thin yellow discharge, occasionally blood stained. The adjoining mucous surface of the lip is covered over by a thin yellowish brown crust owing to the drying up of the discharge.

**Palpation:** The tumour is firm in consistence and firmly adherent to the lip. Pressure causes an increase of the discharge from the fissures, but
there is no tenderness. No other abnormality is present.

**Glandular Involvement:** There are no visibly enlarged cervical glands and no glandular involvement can be discovered on palpation.

**All other Systems:** Nothing abnormal could be detected.

**Wassermann Reaction:** Negative.

**Operation:** 2nd September, 1930.

**Anaesthetic:** Chloroform and Intra-pharyngeal ether.

A collar incision, with its mid point at the most prominent part of the thyroid cartilage, was made from one mandibular angle to the other. Another incision was extended downwards to meet the first incision from the lower border of the symphysis menti.

The triangular skin flaps thus outlined were dissected upwards and the platysma on both sides exposed. The platysma was then incised on both sides and reflected upwards along with the deep fascia.

The submaxillary salivary glands and the submaxillary lymphatic glands were identified.
The submaxillary salivary gland on the left side was larger and firmer than normal, but apart from that there was no maked eye evidence of glandular involvement.

The submaxillary, submental and upper anterior carotid glands were then dissected out, all bleeding was controlled, and the wound was closed, a rubber dam drain being left in situ.

With scissors the tumour and the unhealthy surrounding tissue were cut away, haemostasis was secured and the cut edges were sutured with inter rupted S.W.G. stitches.

Radium: Six 2 mgm. needles were inserted through the skin below the lower margin of the lip and arranged in a half circle around the area from which the tumour was removed.

Excision of cervical glands, removal of tumour and insertion of radium:

Interstitial Radiation: The six 2 mgm. needles inserted on the 2nd September were removed on 16th September, giving a total dosage of 2119 mgm. hours. The active length of the needles was 15 mm. and the radium was screened by .5 mm. of platinum.

The irradiation had produced an excellent reaction which was most marked on the lip but was
also considerable on the floor of the mouth. There was a dirty slough over the incision in the lip which, however, was healing up satisfactorily. The wound in the neck was soundly healed and he was discharged on 18th September, 1930.

Readmitted - 26th September, 1930: Three weeks after the operation he returned for further treatment and at this time the condition of the lip and neck was very satisfactory. The slough had separated from the lip wound and the scar was soundly healed.

Treatment: A Stent collar containing twenty 2 mgm. radium needles was applied intermittently from 27.9.1930 to 9.10.1930. He was very patient and was able to wear the collar for eleven hours on the first occasion. The total irradiation was 8,100 mgm. hours.

A marked erythema appeared soon after the application of the collar and he was discharged on the 10th October showing a generalised, well marked erythema. His general condition was eminently satisfactory.

10th November, 1930: Patient reported, and on examination there was no evidence of any local
Case I.

Fig. 2. - Photograph taken after Operation.
recurrence or of any glandular involvement. On this occasion a photograph (fig. 2) was taken, and affords an excellent contrast to fig. 1, which was taken when he was first admitted to hospital.
Fig. 3. - Primary Tumour x 140.
Morbid Histology of the Tumour:

Under the low power (fig. 3.) the tumour is seen to consist of large round or oval cells with poorly staining cytoplasm. The nuclei of these cells are for the most part eccentric in position, and take up the stain well therefore appearing black in the photograph. In some of the cells the very darkly stained nucleolus can be seen and these are the cells to which Broders has given the name - one-eyed cell.

The tumour is made up of irregular masses of cells, most of which are of the "one-eyed type". In the photograph there is no evidence of keratinization but a study of other areas of the section showed here and there traces of keratin, but no cell nests could be found.

A high power view (fig. 4.) shows the cells closely packed together with a very slight amount of stroma. Some of the cells are undergoing mitosis but this cannot be seen in the figure.

This tumour does not fall into any of the groups in Broder's classification because it
Case I.

Fig. 4. - Primary Growth x 300.
contains less and 25% of differentiated cells, i.e., Group 3, and less than 100% of undifferentiated cells, i.e. Group 4. It is therefore an undifferentiated squamous epithelioma intermediate between Groups 3. and 4. of Broder's classification.

None of the regional lymphatic glands examined showed metastases.
CASE II.

A.H.  Aged 64 years.
Occupation: Gardener.
Admitted: 10th October, 1930.

Complaint: Swelling on his lower lip for five months.

History: Five months before admission, patient noticed a small crack on his lower lip. In spite of local applications, the crack refused to heal and an ulcer formed. The ulcer had been gradually increasing in size, until the two weeks before he came to hospital, during which it had remained stationary. He had never felt any pain.

Previous History: Except for pneumonia forty years ago, there were no previous illnesses, and on this occasion he felt very well and would never have come for treatment if his doctor had not persuaded him.

Social History: He smoked fairly constantly at his work, but he thought the stem of his wooden pipe was preventing the ulcer from healing so he reduced his consumption of tobacco to three ounces per week.
Fig. 5. - Clinical Photograph before Treatment.
Wassermann Reaction: Negative.

Physical Examination: He was a well-built energetic old man whose bronzed skin showed his open air life. He looked well.

Lip: On his lower lip there was a raised area, about the size of a shilling, with irregular raised edges. The central portion was ulcerated, the base of the ulcer being shallow and irregular, and there was no discharge. The edges of the ulcer were very hard and were crusted over by a dry brown scab. The sore was situated to the left of the middle line of the lip (fig. 5). His teeth in the upper jaw were artificial but the lower teeth were very unhealthy.

Neck: There was a small enlarged gland in the submental region on the left side. No other glands were palpable.

Other Systems: Nothing abnormal was discovered.

Clinical Diagnosis: Squamous epithelioma of the lip.

Treatment: Under intra-tracheal ether anaesthesia the lip was prepared and a small incision was made through the skin at a point about an inch below
and one inch or more lateral to the ulcer. Special lip haemostatic clamps were then put on, one blade being inside the mouth and the other on the skin surface. By means of a similar clamp applied in the same manner on the opposite side of the tumour, the blood supply to the part was controlled. The tumour along with an area of skin corresponding to that marked out by the forceps applied to prevent haemorrhage was then removed. The mucous surface was stitched by means of cat gut sutures and the skin edges were approximated with interrupted silk worm gut stitches.

The wound healed up very quickly and little deformity resulted, although a fairly large area of tissue had been removed.

Eighteen days after the removal of the epithelioma, a block dissection of the left side of the neck was performed. Except for the small submental lymphatic gland mentioned previously, nothing abnormal was discovered.

The wound in his neck healed soundly in eight days and he felt very well indeed. Almost
a week later, it was decided to dissect the glands on the other side of the neck in view of the lymphatic drainage from the lip. As there was no swelling on that side of his neck and because he did not wish to submit to another operation, he refused operation and left hospital looking very well.

Result: I have not seen him since he left hospital but I wrote to him and received a reply at the end of May 1931. He is still very well, and his doctor writes "he is very fit and shows no sign of recurrence either locally, or in the glands on either side of the neck".
Fig. 6. - Primary Growth x 140.
Morbid Histology of the Tumour:

Under the low power (fig. 6.) the section shows large numbers of "cell nests" or "epithelial pearls". These cell nests are produced by the degeneration of the central cells just as these cells change in the normal keratinization of the skin. Possibly because of the cutting off of their blood supply, or because these tumours are not sufficiently malignant for the cells to have abandoned completely their normal function, granules of eleidin appear in the cytoplasm, and at a later stage the cells become a solid mass of keratin.

In some of the cell nests, the keratin is arranged in a series of concentric whorls, whereas in others, of longer duration, no structure can be observed. Outside the central core of keratin granule filled cells can be seen with the high power (fig. 7) and the periphery of the cell nest is made up of prickle cells.

The tumour is, therefore, a differentiated squamous epithelioma, which would fall into Group I. of Broder's classification (see Commentary). In no part of the tumour are there any of the typical
Case 2.

Fig. 7. — Primary Growth x 300.
"one-eyed" undifferentiated cells. This tumour forms an excellent contrast to the one in the previous case.

None of the glands examined showed metastasis, the palpable submental gland showing no abnormal features.
CASE III.

D.H. A man aged 83 years.

Occupation: A retired hotel-keeper.

Admitted: 15th December 1930.

Complaint: Swellings in the mouth of about four months' duration and a swelling under the jaw on the left side for about the same time.

History: Four or five years previously he had a cyst under the edge of his tongue on the left side. The cyst was painless and he treated it by means of mouth-washes, but it did not alter in size. Four months ago the cyst became sore to the lightest touch and he had great difficulty and pain when eating.

Shortly after this, the cyst began to increase in size and was followed by other swellings one at the root of the tongue and another just in front of the original one. He stated that those swellings changed their position from day to day.

About the time he began to experience pain he noticed a swelling in the left side of his neck. This swelling was not associated with any discomfort and was discovered first by his doctor. Since then the swelling in his neck has become
smaller without any treatment, but lately he has felt twinges of pain which pass upwards to his left ear.

For the last week or so he has found difficulty in speaking and his tongue feels stiff; he is now unable to protrude it.

He has felt perfectly well otherwise save for some nocturnal frequency of micturition.

Previous Illnesses: Appendix abscess and inguinal hernia.

Family History: He has three sons and two daughters alive. One son died aged 23 of tuberculosis of the larynx, one daughter aged 17 from phthisis, and another daughter aged 4 from diphtheria. He does not know what caused the death of his parents or of other members of his family, as he lost touch with them some time ago.

Habits: Alcohol: Drinks very little in spite of being a hotel-keeper.

Tobacco: About 2 ounces of black tobacco per week in a wooden pipe.

Examination: He looks very well for his age and, though heavily built, he is very active. His speech is difficult to make out. His right eye is absent having been removed after an accident 60 years ago.
Mouth: He has great difficulty in moving his tongue and can only protrude it far enough to show the tip. His teeth were all removed four years previously, and he has never been able to wear artificial teeth because of the cyst.

Extending from the frenum linguæ posteriorly to the alveolar margin anteriorly and on both sides of the middle line there is an ulcerated area covered by a yellowish foul discharge. The ulcerated area is situated more on the left than on the right of the middle line.

On palpation the ulcer is firm in consistence and has a fairly definite border. The alveoli were not involved.

Neck: On the left side of the neck there is a stony hard swelling about the size of a large walnut. The swelling is definitely glandular and is situated below and slightly posterior to the angle of the mandible and is an enlargement of the upper anterior group of the deep cervical glands.

The superficial structures are freely moveable over the swelling, but it is adherent to the deeper structures.

No other glands are palpable on either side of the neck.
All other systems: Nothing abnormal was discovered.
Wassermann Reaction: Negative.
Clinical Diagnosis: Epithelioma of floor of mouth.
20th December 1930: Diagnostic excision performed and a radium denture was inserted and kept in for twelve days. The dosage was 3600 mgm. hours. The tumour showed a well marked but not excessive reaction to the radium.

He was readmitted a month after the removal of the denture. The condition of the mouth was very satisfactory, but the cervical swelling was exactly the same as previously.

For the first 24 hours after his admission on this occasion he only passed six ounces of urine and the bladder was distended up to the umbilicus. Hot fomentations and morphine suppositories were of no avail, so a red rubber catheter was passed and 36 ounces of urine drawn off. He was thereafter able to pass water fairly well.

On questioning him, he admitted that he had had for the last year to get up two or three times at night to pass water and lately as often as six times. He had to strain to pass
water and the stream was smaller than it used to be and he never knew when he had finished.

The prostate as felt per rectum was enlarged uniformly and the surface was smooth and firm.

**Treatment:** Six 3 mgm. needles of radium were inserted round the swelling on the left side of the neck - three along the anterior border, and three along the anterior border of the sterno-mastoid muscle. The radium was removed eight days later after a dose of 6676 mgm. hours.

A week after the removal of the radium it was found necessary to perform suprapubic cystotomy and this was done under local anaesthesia. In view of his age and general condition, it was considered inadvisable to remove the prostate and he was fitted with a permanent bag.

When he was discharged one month later, the tumour in the neck had greatly decreased in size, and was not so hard as formerly.
Case 3.

Fig. 8. - Primary Tumour x 100.
Morbid Histology of the Tumour:

A low power view of the section (fig. 8.) shows the squamous epithelium of the floor of the mouth, and below it, the connective tissue of the deeper layer of the mucosa almost entirely replaced by densely stained cells. These cells are so closely packed together that it is impossible to make out any stroma between them.

The cells themselves, as seen under the high power (fig. 9.) vary in size and shape from small round cells to large spindle shaped cells. There is no attempt to form columns of cells, and no cell nests are present.

In this part of the section, the epithelium of the floor of the mouth is intact, but in other parts, ulceration had occurred. The epithelium of the surface does not show the normal, regular layers of cells, which are flat towards the surface, and gradually change to the polygonal prickle cells of the deeper layers. Here the cells, in the surface epithelium, are in some parts few and far between, while in other parts they are arranged in little clumps. In the deeper layer, from which the growth of the surface layers
Fig. 9. - Primary Growth x 300.
takes place, there are oval cells, some of which are darkly stained, whereas others can only be seen with difficulty, owing to their faint staining and the absence of nuclei.

The surface epithelium has, therefore, undergone some degenerative change, probably due to the impairment of its blood supply by the tumour lying deep to it, or to the pressure of the tumour upon it, or possible to the tumour cells elaborating some substance which is toxic to normal tissue cells.

On the free surface of the epithelium, there is a large amount of keratin, arranged in layers parallel to the surface, and formed by the degeneration of the cells as they get pushed upwards, by the division of the cells of the basal layer. In this section, the keratin is present in larger amount than usual, and this phenomenon will be discussed, in its relationship to malignant disease, in the Commentary.

The cells of the tumour vary and are round, oval polygonal and spindle shaped and all contain darkly stained nuclei. No mitosis could be seen.
The tumour is, therefore, an undifferentiated squamous epithelioma, and would fall into Group IV in Broder's classification.

No glands could be examined because the neck was treated by irradiation.
CASE IV.

D.McK.    Aged 65 years.
Occupation: Heating Engineer.
Admitted: 10th November 1930.

Complaint: Swelling on left side of neck for three months. Slight sore throat for three weeks.

History: About three months ago patient suddenly noticed a swelling on the left side of his neck. At that time the swelling was about the size of a hen's egg, but was painless. He consulted his doctor and was given iodex to rub into it. Under this treatment the swelling increased in size for a short time, but after that it got smaller and when I saw him first it was about the size of a pigeon's egg.

When he first noticed the swelling, it was soft in consistence and freely mobile, but since the application of the ointment it had become hard and stationery.

Three weeks previous to admission he constantly had to "clear his throat" because it felt exactly as if he had been smoking too much. This sensation only affected the left side of his
throat and it had been constantly present up to the day of admission.

Apart from these symptoms, he has been perfectly well and has lost no weight.

**Previous History:** Rheumatic fever, aged 40, and again aged 55. As far as he knows he did not have a cardiac lesion in either attack.

**Social History:**

**Alcohol:** Two bottles of beer per day and a little whisky occasionally.

**Smoking:** Previously he smoked about four ounces per week, but he cut it down to two ounces. He smokes constantly while at work.

**Wassermann Reaction:** Negative.

**Physical Examination:** He is a well-built, healthy looking man who looks at least ten years younger than he is.

**Local Examination:** Neck.

**Inspection:** There was a swelling about the size of a pigeon's egg on the left side below the angle of the mandible and anterior to the sterno-mastoid muscle.
Palpation: The swelling is stony hard and is not adherent to the skin or to the deeper structures. It is smooth in outline, involves the jugulo-digastric group of glands and no other glands could be palpated in the neck.

Mouth.

Inspection: There was a fungating, ulcerating growth on the anterior pillar of the fauces on the left side.

Palpation: The tumour was very hard in consistence and was found to be involving the left tonsil and the anterior pillar of the fauces on the left side.

There were very few teeth left, but they were quite healthy, and the tongue was moist and clean.

Circulatory System:

Pulse: Was regular in time and force, of moderate tension and the vessel wall was just palpable.

Heart: Was not enlarged. There were presystolic and systolic murmurs best heard over the apex beat. The second sound was short and
soft but pure. The mitral murmurs were conducted into the axilla and to a less extent to other areas.

Respiratory and other Systems: Nothing abnormal was detected.

Clinical Diagnosis: Epithelioma of left tonsil.

Treatment: Under intra-tracheal ether anaesthesia an incision was made from the left mastoid process to the left sterno-clavicular joint and another incision was carried down from the symphysis menti to join the first incision at right angles. The skin flaps thus marked out were dissected up and the platysma and the deep fascia were divided at the lower part of the wound and reflected upwards.

The external jugular vein was ligated and cut across and the upper part was dissected upwards. The sterno mastoid muscle was then divided about its middle and the divided portions were retracted backwards.

The internal jugular vein was exposed in the supra-clavicular region, ligated and cut
across. The upper portion was then dissected upwards along with the fascia and glands surrounding it. The digastric and jugular triangles were cleaned and the dissection carried up to the base of the skull where the internal jugular was ligatured and divided. A few small glands were removed from the supra-clavicular region.

The sterno-mastoid muscle was sutured with continuous cat gut sutures and the skin edges were approximated with interrupted silk worm gut sutures and Michel clips, a small rubber dam drain being inserted at the lower end of the wound.

A small piece of the primary tumour in the left tonsil was removed for examination and eight days later, a radium denture containing ten 2 mgm. needles of radium was inserted. This was in position intermittently for 12 days and a total dosage of 3800 mgm. hours was obtained. He was very comfortable while wearing the denture, and consequently he was able to wear it on the average for 16 hours out of the 24. He was discharged on the day following the removal of the denture, showed a very well marked reaction and
some reduction in the size of the growth.

I saw him again at intervals of fifteen days, two months and one month, and on each occasion there was no evidence of any recurrence in the tonsil or in the neck.

Recurrence: Five months after the initial treatment he returned to hospital to report and a small recurrence was found in the site of the original tumour. He was admitted for further treatment.

Treatment: Under intra-tracheal ether anaesthesia, a gag was inserted and the mouth was opened widely and ten 1 mgm. radium needles were inserted round the growth in the tonsil.

The needles came out at intervals, the total dosage being 1058 mgm. hours.

Progress: There was a very good reaction and some diminution in the size of the tumour, and he was discharged a fortnight later, his general health being very good.
Fig. 10. - Primary Tumour x 300.
Morbid Histology of the Tumour:

A high power view of a section of the tumour (fig. 10.) shows masses of cells which are to a certain extent arranged in columns separated by a small amount of stroma.

The cells are large, oval, round or polygonal in shape, and most of them stain darkly. In the photograph there are no cell nests, but a study of a complete section shows a few cell nests which are not so well marked as those in Case II.

The tumour is of the differentiated type of squamous epithelioma and falls into Group II. in Broder's classification.
Fig. 12. - Metastatic Deposit x 300.
Section of one of the Jugulo-digastric Group of Glands:

Low power and high power views (figs. 11 and 12) show metastatic deposits of carcinoma cells in the lymphatic gland.

The cells for the most part are grouped in solid clumps which at a rapid glance rather resemble acini in their formation.

The cells vary in shape just as in the previous section and stain very darkly. Surrounding the malignant cells are numerous small round well-stained cells, which however do not take up the stain as well as the malignant cells. These cells are small lymphocytes.

There is hardly any of the normal gland structure remaining, so completely is it filled with malignant cells.

Five other sections of the glands, including one of the supra-clavicular gland found at operation, were examined but showed no evidence of metastases.
Case V.

W.W. Aged 58 years.
Admitted: 19th October, 1930.

Complaint: (1) Swelling on the right side of the neck for four months.
(2) Breathlessness and difficulty in swallowing for one week.

History: Patient was always perfectly well until four months ago when he noticed a small swelling on the right side of his neck. The swelling slowly increased in size, but was associated with no symptoms until a week previous to his admission to hospital.

For the last week before admission to hospital he was unable to swallow solid food, but could swallow liquids without much trouble and he became breathless on the slightest exertion.

Previous History: No previous illnesses.

Physical Examination:

General: He was a very well-built man. His breathing was noisy and his voice was only a whisper, but the words could be made out quite
Case 5.

Fig. 13. - Clinical photograph on admission.
clearly. His face and head showed a cyanotic tint, and there was a large swelling on the right side of his neck and a slight fullness on the left side. (fig. 13).

**Mouth:** His tongue was furred but freely mobile and his teeth were healthy.

There was a large tumour about the size of a hen's egg involving the right tonsil and the hard palate and extending over towards the left side occupying practically the whole of the roof of the mouth. The tumour was red in colour, and had well defined irregular edges, and the surface was irregular but had not ulcerated.

On palpation the surface of the tumour was firm rather than hard in consistence.

**Neck:** There was a hard swelling on the right side of the neck involving the upper parts of both the anterior and posterior triangles. The swelling was fixed to the deeper structures and to the skin. The most prominent part of the tumour was soft and fluctuation could be elicited over it.
Several enlarged hard glands just below the jaw on the right side, and on the left side, the upper anterior and posterior deep cervical glands, were enlarged.

Other Systems: Nothing abnormal could be found.

Treatment: A tracheotomy was performed on the day of his admission to hospital and the trachea was found to be displaced considerably to the left side because of the large swelling on the right side of the neck.

Eight days later under intra-tracheal chloroform and ether anaesthesia, twelve 3 mgm. radium needles were inserted radially into the affected area on the right side of the neck, and were removed after seven days, the total dosage being 5688 mgm. hours.

After the radium insertion, he became restless and moisy and required morphine and hyoscine to keep him in bed.

His chest showed signs of congestion and he was given repeated injections of atropine sulphate and after four days, he made very good progress.
A denture containing ten 2 mgm. radium needles was then inserted, and as he was breathing through a tracheotomy tube he was able to wear it practically continuously for nine days, the complete dosage being 4320 mgm. hours. There was an excellent reaction from the denture and the tumour had almost entirely vanished in a week so the tracheotomy tube was removed and he was discharged a week later with his general and local conditions very satisfactory.

Almost exactly three months later, he returned to hospital because of a swelling in the left side of his neck which began six weeks after his discharge from the hospital. He looked very well and there was no evidence of any recurrence in the mouth and no swelling on the right side of the neck.

On the left side of the neck there was a hard fixed glandular mass about the middle of the sterno-mastoid lying mainly posterior of it. This mass was fixed to the skin and deeper tissues.
A diagnostic excision was performed and eighteen 3 mgm. and twelve 1 mgm. radium needles were inserted radially around the growth, the larger 3 mgm. needles passing deep to it. The needles were removed seven days later, the dosage being:

twelve 1 mgm needles, i.e.
  12 mgm. for 164 hours, i.e. 1968
eighteen 3 mgm needles, i.e.
  54 mgm. for 164 hours, i.e. 8856
  10824

i.e. a total dosage of 10824 mgm. hours.

There was a very well marked diminution in the size of the swelling and he was discharged feeling very well.

Result: After his discharge from the Infirmary in February, he returned home and was practically an invalid all the time until his death on 29th April 1931, i.e. six months after his first admission to hospital.

His doctor saw him two days before he died when he was suffering from marked dyspnoea and irregular heart action, due to metastases in the mediastinum. The dyspnoea became progressively worse, and he died two days later after a period
of unconsciousness, lasting twenty four hours.
There was no evidence of a recurrence of the
original tumour nor any enlargement of the cervical
glands.
Case 5.

Fig. 14. - Primary Tumour x 300.
Morbid Histology of the Tumour:

A small piece of the primary tumour was removed to determine the histological characters of the tumour. The piece on section showed for the most part the normal structure of the tonsil, but in one corner there was an area of tumour tissue. A section of this area (fig. 14.) shows a structure unlike that of any of the other tumours in this series of Cases, and I must confess a diagnosis was beyond my slight pathological knowledge until a portion was removed from one of the enlarged cervical glands. The section of the gland showed the typical structure of a Regaud's tumour which will be described and illustrated in the next Case.
51.

CASE VI.

S.F.L. Aged 30 years.

Occupation: Doctor.

Admitted: 9th September, 1930.

Complaint: Enlarged glands in the neck and swelling of the palate of two years' duration.

History: About the end of 1928 he became aware of a small swelling towards the back of the left side of his neck. The swelling was soft in consistence and was examined by a surgeon who diagnosed a branchial cyst. It was removed by operation in February 1929.

After this operation, the patient lost touch with the hospital and did not hear the result of the microscopic section until almost one year later when he reported at hospital with a recurrence of the swelling in the neck.

He was then told that the condition was malignant and was treated by means of radium. The swelling almost disappeared and he was discharged from hospital. He returned later for another application of radium, but on this occasion the results were not so satisfactory and he was
advised to leave Singapore and come to this country for treatment.

A few days before his admission to hospital on September 9th, 1930, he noticed for the first time that there was a swelling in the roof of his mouth.

He has had gradually increasing difficulty in breathing through his nose and has also complained of slight interference with his hearing on the left side.

He has been free from pain all along and has only experienced an indefinite, dull, uncomfortable feeling of stiffness in his neck. His general health has been very good and he was able to work until the day of his departure for Edinburgh.

**Previous Health and Family History:** Negative.

**Wassermann Reaction:** Negative.

**Physical Examination:** He is a well-nourished man who, apart from the swelling of his neck, looks well.

**Local Examination:**

**Neck:** There is a large swelling in the left side of the neck. It is irregular in
Case 5.

Fig. 15. - Clinical Photograph.
shape and extends from the parotid region and from the lower border of the external auditory meatus above, passing forwards over the sternomastoid muscle, and involving both the anterior and posterior triangles. (fig. 15).

The scar of the previous operation could be seen in the natural fold of the neck, passing directly over the swelling.

Palpation confirmed the situation of the tumour which was found to vary in consistency in different parts. Some parts were soft, but no fluctuation could be obtained and other parts were firm, but were not of the stony hard consistency met with in Cases III. and IV. (D.H. and D.McK.). The swelling was irregular in outline and was adherent to the underlying tissues. The skin, however, was freely moveable over the swelling.

The supra-clavicular glands were not palpable. No definite glandular enlargement could be made out on the right side of the neck.

**Mouth:**

**Inspection:** There was a bulging of the soft palate into the mouth. The swelling is
smooth and regular in outline.

**Palpation:** The tumour was soft in consistence.

**Abdomen:** No hepatic enlargement.

**X-Ray Examination:** Chest and mediastinum were free from metastases.

**All other Systems:** Negative.

**Treatment:** Under ether anaesthesia an incision about four inches long was made in the line of the fold of the neck over the growth in the posterior triangle. The incision was deepened and the surface of the tumour exposed. Two 3 mgm. needles of radium were then inserted into the growth and the wound was closed with interrupted silk worm gut sutures. Four 3 mgm. needles were then inserted into the growth over the angle of the mandible.

The mouth was widely opened and six 5 mgm. needles were inserted through the soft palate into the tumour and a small portion of the tissue of the tumour was removed, by means of a small scoop, for microscopic examination.

The total dosage of radium used was 5976 mgm. hours.
Progress: The tumour in the soft palate showed considerable reaction to the radium, the reaction affecting the tongue and cheeks and to a lesser extent the floor of the mouth. There was a slight but definite decrease in the size of the tumour.

The glandular metastases showed a marked response to the radium needles, particularly in the line of the skin incision.

He was discharged twelve days later with the tumour in the palate greatly decreased in size and no evidence of glandular enlargement in the neck. There was a small granulating area in the line of the skin incision which, however, was otherwise soundly healed.

He reported after a fortnight had elapsed and there was no palpable enlargement of the glands and the primary tumour had disappeared.

Recurrence: Exactly a month later he returned to hospital with two small swellings at the site of the original lesion in the neck. The condition of the mouth was very satisfactory.

Treatment: Four 3 mgm. and two 5 mgm. radium needles were inserted in the line of the original scar.
The radium was left in for ten days and a total exposure of 5280 mgm. hours was obtained.

**Progress:** There was only a slight local reaction to the radium, but there was a marked diminution in the size of the swelling.

He was discharged feeling very well and ten days later left for Singapore.
Fig. 16. - Primary Growth x 140.
Fig. 17. Primary Tumour x 300.
Morbid Histology of the Tumour:

Under the low power (fig. 16.) the whole field is composed of small cells, most of which are polyhedral, but some are rounded. The nuclei show up clearly as small dark hyper-
:chromatic spots in the scanty cytoplasm. The nuclei vary in position some being central and others eccentric. There is little or no inter-
:cellular substance.

The high power (fig. 17.) shows the structure of the tumour more satisfactorily. All the cells are small with scanty cytoplasm. The nuclei are hyperchromatic and in some cells mitotic figures are present, testifying to the extreme rapidity of the growth of the tumour. Some of the cells have two nuclei probably the re-
:sult of mitosis and prior to the division of the cytoplasm.

The high power photograph shows ex-
:cellently the structure of a Regaud’s lympho-
:carcinoma.

No glands could be examined because the enlarged cervical glands were treated by inter-
:stitial radiation.
COMMENTARY.
INTRODUCTION.

No problem looms more largely in the public mind at the present day than that of malignant disease. Both to the medical profession and to the man in the street it is a subject of absorbing interest and extreme importance.

The lay press is inundated with information as to its seriousness and with erroneous reports of its apparent cure so that it is difficult to estimate the value of such journalistic campaigns.

The discovery and application of radium in the treatment of cancer has inaugurated a wave of optimism even in the minds of a most conservative profession. While this hopefulness as yet may be said to have at best a very slender foundation in fact, there is no doubt that the increasing prominence which is being given to the facts of malignant disease will ultimately yield a fruitful return.

The urgency of the problem is borne witness to by two disconcerting facts:-

(1) that statistics - as Mr Sampson Handley informed us at a recent meeting of the Royal Medical
Society of Edinburgh — show that the death rate from cancer is increasing year by year.

(2) that, as indicated in the most recent Ministry of Health Memorandum on Cancer, patients with epithelioma of the lip and tongue are willing to suffer from this disease for a considerable length of time before seeking treatment.

The apparent increase may be due to the lengthening of the average span of human life, since Cancer is essentially a disease of the later decades, but nevertheless the bald statement, that one out of every seven persons will succumb to its ravages, is not only arresting, but sufficiently disquieting to command attention.

The education of the public mind must form an integral part of any reasoned or helpful cancer campaign; and it cannot be too strongly emphasised that nothing will more tend to defeat its object than vivid pictures of untreated carcinoma. Statements like that of Maclaurin — "No doctor who has seen an "old man with cancer of the tongue can refrain from "wishing that that man had died twenty years sooner,
"because however bad the fate in store for him it can hardly be worse than what he suffers here on "earth" - place in many cases an almost insuperable barrier in the way of early treatment for many people will suffer in silence the presence of a possible epithelioma rather than face a diagnosis that is equivalent to a death sentence.

Probably the dominant feature in the treatment of cancer is that cases treated sufficiently early have a good prospect of cure. That is the lesson it should be our duty to teach.

General Incidence of Malignant Disease of the Mouth.

Malignant disease of the mouth, like malignant disease in other parts of the body, is most common in the later years of adult life, the usual age period being between forty and sixty. The disease may of course begin earlier than this and Simmons quotes a case in which the patient was only eighteen years of age. The youngest case in this series was a man aged thirty and the oldest was a man of eighty-three.

The disease is commoner in males than in females; indeed it may be said to be almost limited
to the male sex. Simmons gives his figures as follows:— out of 387 cases 99.7% were males. Boyd on the other hand found that only 85% were males. All the cases in this series are males.

Site Incidence.

A study of cancer of the mouth reveals that the disease is almost entirely confined to certain definite areas and of these areas some are more commonly involved than others. Authorities differ slightly as to the relative frequency with which the various regions are attacked, but the following sequence may be taken as a fair average.

In the mouth itself the order of frequency is:—

1. The edge of the tongue in its anterior two-thirds.
2. In front of the palato-glossal fold.
3. On the floor of the mouth in relation to the frenum linguae and the ducts of the submaxillary gland.
4. Between the tongue and the jaw.
5. The soft palate.
6. The upper pole of the tonsil.

More common than in any of these situations however is disease at the junction of the mucous
membrane of the lower lip with the skin. According to Boyd, 2% of all cancer deaths are due to epithelioma of the lip.

In order to understand why the disease appears to have a selective affinity for these areas we must study the development, anatomy and histology of the region.

**DEVELOPMENT.**

About the middle of the first month of intra-uterine life, the prosencephalon bends acutely over the end of the notochord and sends out processes, which along with the mandibular arch, enclose a space known as the primitive mouth. The mandibular arch contains Mechel's cartilage and gives origin to the lower lip and the floor of the mouth.

One of the processes, known as the maxillary, is destined to form the soft palate, the lateral parts of the upper lip and part of the hard palate as well as some of the facial bones.

A small elevation, the tuberculum impar, appears in the floor of the primitive mouth and fuses with two lateral swellings, derived from the mandibular arches, to form the anterior two-thirds of the
From the groove behind the tuberculum impar, a bud grows downwards to form the thyroid gland. This bud retains for a time its connection with the buccal cavity by means of a stalk, known as the thyreo-glossal duct; the remains of this duct may persist even in the adult as thyreo-glossal cysts or fistulae and the site of its buccal extremity is seen in the foramen caecum of the tongue.

The ventral ends of the second pair of arches pass behind the tuberculum impar and fuse to form the posterior third of the tongue.

**ANATOMY.**

A study of the development shows that the tongue consists essentially of two parts, an anterior two-thirds and a posterior third and, in the adult, the dorsum of the tongue is divided into corresponding areas by the V-shaped sulcus terminalis at the apex of which the foramen caecum is situated. Further evidence of the difference in the development of the two areas is afforded by their nerve supply, for the anterior two-thirds is supplied by the lingual and chorda tympani nerves and the posterior third...
by the glosso-pharyngeal nerve.

The under surface of the tongue is connected to the floor of the mouth by a double fold of mucous membrane called the frenum linguæ, at the roots of which lie the openings of the ducts of the submaxillary salivary glands.

On the lateral border of the tongue just in front of the palato-glossal fold are several re-duplicated folds of mucous membrane with crypts between them. These are the lingulae.

**H I S T O L O G Y.**

In structure also the two areas of the tongue are different. The anterior two-thirds are covered by epithelium of the stratified squamous type, but this is only two layers thick. In this respect it resembles embryonic squamous epithelium rather than the thicker four-layered adult type. Below it is a layer of cells which are nearly columnar. This part of the tongue contains papillae but no glands.

The posterior third of the dorsum and the whole of the under surface of the tongue are covered by a thin epithelium, lacking a stratified surface layer, but containing numerous racemose mucous glands.
The tonsils are covered by stratified squamous epithelium, continuous with that of the pharynx. Under this there is a layer of fibrous tissue, and deep to it the lymphoid tissue which forms the bulk of the tonsil. The surface epithelium dips down into the lymphoid tissue to form the crypts.

The lip is covered on its inner surface by stratified squamous epithelium continuous with the lining of the mouth. Below this lies the submucous tissue containing a large number of racemose glands known as the labial glands. Deep to this layer lies the muscle tissue of the lip covered by the superficial facia and then the skin of the face.

The floor of the mouth, or more correctly, the sub-lingual region is covered by mucous membrane stretching from the inner aspect of the gum to the under surface of the tongue. When the tongue is raised, the mucous membrane forms, in the median plane, a prominent fold — the frenum linguæ which connects the inferior surface of the tongue to the floor of the mouth. The mucous membrane is of the stratified squamous type and rests on a layer of fibrous tissue which contains numerous glands most of which are mucus secreting.
C O N C L U S I O N S.

Certain features are now evident which might serve to explain the peculiar localization of carcinoma within the buccal cavity.

(1) There are a number of areas where two types of epithelium abut on each other, i.e.
   (a) the junction of the skin and the mucous membrane of the lip.
   (b) at the tongue edge where the thicker dorsal epithelium joins the thin epithelium of the under surface.
   (c) at the frenum, especially at the openings of Wharton's ducts where the epithelium lining the ducts meets that of the floor of the mouth.

(2) In front of the palato-glossal fold there are persistent embryonal remnants - the lingulae.

(3) The tonsillar crypts are apt to become sealed off by mucus and irritant secretions are then retained in their depths.

(4) In the anterior two-thirds of the tongue mucous glands are absent, whereas in the posterior third they are plentiful.

A consideration of the site incidence showed that the disease is much more common in the anterior two thirds of the tongue, the palato-glossal fold and, in relation to Wharton's ducts.
PREDISPOSING FACTORS.

While certain structural peculiarities are certainly present in the mouth, Boyd insists that carcinoma never occurs in a previously healthly tissue. He believes that some preceding lesion or disturbance of function in the tissue must have prepared the way for the malignant change. This theory is supported in malignant disease of the lip, by the fact that carcinoma is often found to occur at the site of a previous crack or fissure, or of an abrasion due to a jagged tooth. Boyd even maintains that the trauma associated with playing the bugle or the flute is sufficient to determine its onset. If this is so, one wonders why all flute and bugle players do not develop the condition, and why all those with chronic irritation of their lips do not develop malignant disease. Is it due to the fact that some people have a greater tendency to malignant disease than others? and, if they have, is this tendency inherited? Whether there is such a tendency or not is an extremely controversial point. Much has been written on the subject, but still there does not seem to be any unanimity in regard to it. If there is any such tendency, a survey of the literature seems to indicate that it is probably not
hereditary, but here again it is hard to be dogmatic, for Professor Fraser has treated epithelioma of the mouth in three brothers whose father died of the same condition.

Any lesion, therefore, which causes a solution in the continuity of the epithelium or continued irritation of the surface cells would seem to predispose to malignant disease. This is well illustrated by Cases 1 and 2 of this series, both of which gave a history of a previous crack or sore on the lip which was very troublesome and persistent.

Smoking as a predisposing cause has been widely discussed, and I think most people are agreed that it certainly predisposes to cancer of the lips and tongue. This is particularly so in those who smoke short clay pipes, the smoke from which is so hot that it often burns their lips and tongue. Broders, however, in analysing his cases found no difference in numbers between smokers and non-smokers. On the other hand, Simmons found that out of 387 cases of buccal cancer (excluding cancer of the lip) 310, or 80%, were smokers. A fact which greatly supports the contention that alcohol and smoking are predisposing factors is that of all cases 95-98% occur in males.
Cohnheim's theory that tumour formation is the result of the growth of misplaced groups of cells or foetal 'rests' is, to my mind, given support by the frequent occurrence of carcinoma anterior to the palato-glossal fold where, as previously mentioned, the developmental remnants, known as the lingulae, are situated.

While all the factors mentioned above may be said to predispose to cancer of the mouth, they are not nearly so potent in determining the onset of carcinoma as the condition which I have purposely left to the end - leucoplakia. Not only do I look upon this condition as of profound significance in the etiology, but I am inclined to believe that in the great majority of cases, it is actually the first stage in the pathology of cancer in this region.

The inter-relationship of syphilis and malignant disease and of syphilis and leucoplakia is also of considerable importance, and the whole question will be discussed when we come to consider the pathology of malignant disease in this region.
PATHOLOGICAL CONSIDERATIONS.

Naked Eye Appearances.

Lip: An epithelioma of the lip commonly occurs in two forms:—

(1) a proliferative,

(2) an infiltrating.

Usually either type commences as a flat nodule or an indurated crack at the junction of the skin and mucous membrane. In the proliferative type, the main growth is outwards and a fungating warty looking mass forms, the surface of which early becomes ulcerated. (Case I.).

In the infiltrating variety, a hard mass forms in the substance of the lip and the overlying mucous membrane only ulcerates at a late stage. (Case II.).

The ulcer, when it forms, presents the usual features of a carcinomatous ulcer—shallow irregular base, hard raised edges.

Tongue: The macroscopical appearances of lingual epithelioma vary widely; three groups are usually recognised.

(1) fissured,

(2) the solid plaque,

(3) the proliferative type.
The fissured or ulcerative type differs very slightly from the malignant ulcer occurring on the lip. It may form a deep irregular ulcer with raised nodular edges or a shallow regular one with marked induration of the edges and base.

The solid plaque: In this type there is a flat raised area on the dorsum of the tongue, its margins are sharply defined, and the appearance suggests that the plaque has been stuck on to the tongue.

The proliferative type varies from warty looking masses showing superficial ulceration to true pedunculated tumours.

Floor of the Mouth: The floor of the mouth may be the site of a primary epithelioma, or it may be involved by the spread of a lingual tumour. In both cases, the appearance is similar and such that no classification of type is possible.

A large deep ulcer forms; its base is covered with dirty sloughs and is very indurated and nodular. The edges of the ulcer lack the characteristic hardness of an epitheliomatous ulcer in other situations.
Tonsil: In the tonsils an epithelioma may arise as an irregular hard nodular growth, or as a fungating ulcerating mass. The tumour may attain a great size; in one of the cases in this series, for example, the tumour had practically filled up the buccal cavity before the patient sought advice. (Case V.).

HISTO-PATHOLOGY OF BUCCAL LESIONS.

A consideration of the histology of malignant epithelial tumours of the buccal region is not complete without some reference to the pathology of leukoplakia and chronic glossitis which so frequently precede the actual development of cancer.

Chronic glossitis occurs in two forms:—
(1) superficial
(2) deep.

The superficial form is usually referred to as leukoplakia. This was frequently believed to result only from syphilis. This, however, is not so for many patients with leukoplakia have not had syphilis and accordingly Mr Lees divides
leukoplakia into two large groups:—

(1) syphilitic
(2) non-syphilitic.

The non-syphilitic type results from any kind of chronic irritation, and Mr Lees believes that this type is more frequently followed by malignant disease than is the purely syphilitic type.

Syphilis, however, does play a part in predisposing to malignant disease in the mouth and many cases of buccal carcinoma have a definite strong positive Wassermann Reaction although to the naked eye they show no evidence of leukoplakia. In my series of cases, none showed positive Wassermann Reactions, but in Simmons series above quoted, 27% showed a positive result.

To the naked eye, leukoplakia presents a mozaic-like appearance of white milky patches which are raised above the surface but adherent to it. Painful cracks and fissures may appear, and form the starting point of an epithelioma. Mantilla has found that 32% of all cases of leukoplakia develop cancer.

The deep form of chronic glossitis is not so common as the superficial type, but in it
also malignancy is a common complication. It is almost invariably due to syphilis, and the tongue becomes nodular, fissured and contracted.

Syphilis and leukoplakia are of the utmost importance in the etiology of buccal carcinoma; indeed the successive histological stages between the two can be placed in various sections.

In the first stage, the squamous epithelium undergoes a series of remarkable changes. Normally the prickle cells are pushed up to the surface, where they lose their prickles and undergo keratinization, and are finally thrown off as dead epithelium. When leukoplakia is present, these cells reach the surface still equipped with active prickles; instead of being then cast off, they adhere to the surface by virtue of their prickles and a heaping up or thickening of the epithelium results.

The retention of these dead surface cells is probably responsible for two further histological phenomena:

(1) The cells of the basal layer become activated, and nuclear mitosis and cell division are common appearances.
(2) A zone of lymphocytic infiltration occurs between the papillae of the epithelium and the sub-epithelial tissue. The function of the latter zone is probably protective - a response to the irritation produced by the dead surface cells.

The epithelial instability of the deeper layers is also probably to be attributed to the same irritation; indeed the hyperplasia may be designed to induce the shedding of the leukoplakic cells by means of a vis a tergo.

If the lymphocytic barrier remains unbroken, the pathology will remain that of leukoplakia; if it fails, however, the third stage supervenes. Here the prickle cells begin to grow downwards, and make their way through the zone of lymphocytes into the sub-epithelial tissue as advancing columns of cells. This is the stage of epithelioma.

Thereafter these columns may reproduce the various phases in the life cycle of squamous epithelium. Some of the cells are well differentiated resembling closely the normal squamous cell. Columns composed of this type show, sooner or later, towards the centre, the normal process of keratinization, and a "cell nest" or "Epithelial pearl"
Fig. 18. - Differentiated squamous epithelioma x 140.
Fig. 19. - Undifferentiated squamous epithelioma x 300.
develops. The central zone or core is composed of structureless keratin laid down in concentric lamellae; outside this are granule filled cells, and the periphery is composed of prickle cells. (fig. 18).

In other columns, the cells have large nuclei with darkly staining nucleoli - the "one-eyed cells" of Broders. These are undifferentiated cells unlike the normal squamous cell, and, in such columns no cornification or cell nest formation occurs. (fig. 19).

The degree of cell differentiation is of great importance for to a large extent it decided the prognosis, and to a lesser extent, the naked eye appearances of the tumour. From a consideration of this cell-differentiation, A.C. Broders has worked out a useful system of classification of epitheliomata. He divides the tumours into four groups:

- Group I. containing 75% differentiated cells.
- Group II. containing 50% differentiated cells.
- Group III. containing 25% differentiated cells.
- Group IV. containing 100% undifferentiated cells.
This classification is quite good as regards Groups I. and IV., but the decision as regards the intermediate classes is a matter for each individual pathologist, and opinion of necessity varies. According to Broders, the prognosis is good in Group I, gets progressively worse in Groups II. and III., and is hopeless in Group IV. However, since the advent of radium therapy the prognosis in regard to Group IV. has improved considerably, and I shall have more to say about this classification in discussing radium therapy.

The degree of differentiation of the cells also decides to some extent the naked eye characters of the growth. From the cases I have seen I am of the opinion that the undifferentiated type of cell more commonly forms a solid plaque-like tumour; the differentiated type commonly results in a fissured or ulcerated tumour while a mixture of differentiated and undifferentiated cells produces a tumour of the proliferative type.

Birkett working along these lines has been able to correlate these microscopical varieties with the different sites in the mouth. In brief, his correlation is as follows:—
(1) The highly differentiated type with cell nests and keratinization; of slow growth and late metastases, is found most commonly in:
   (a) the buccal surface of the cheeks.
   (b) the lips.
   (c) the floor of the mouth.
   (d) the inferior surface of the tongue.
   (e) the anterior third of the dorsum of the tongue.
   (f) the alveoli.

(2) The highly cellular undifferentiated type with no cell nests and early metastases is found at the base of the tongue.

(3) The intermediate type between Groups I. and II. are found in:
   (a) the middle third of the tongue.
   (b) the fauces.
   (c) the tonsils.
   (d) the uvula.
   (e) the soft palate.

Birkett's work was done with the idea that the knowledge of the site of the growth would indicate its histological characters, and appropriate
treatment. I hesitate to criticise the work of one who has done so much in the field of radium therapy in buccal carcinoma, but in my opinion, such a correlation, of sites with histological characters, is valueless. All his histological work was done only on metastatic deposits in the lymphatic glands since all cases were treated by irradiation of the primary growth, and Birkett does not believe in biopsy. Cell nests, as mentioned elsewhere, are as a rule not found in glandular metastases and the histological picture of the glandular tumour is seldom found even to have a close resemblance to that of the primary growth. For these reasons, I cannot accept this correlation. In addition, it does not apply to all cases for one of my cases (Case I.) had an undifferentiated squamous epithelioma of the lip - a site according to Birkett, immune from undifferentiation.
THE SPREAD OF THE DISEASE.

(1) The Direct Spread:

While undoubtedly squamous carcinoma spreads by local infiltration, this process is a relatively slow one save in the case of lympho-epithelioma (Regaud's tumour). (Case V.)

(2) Lymphatic Invasion:

Involvement of the regional lymphatic glands is an invariable sequel of squamous epithelioma. While it may occur early or late, it must be borne in mind that clinical enlargement of the glands is not of necessity evidence of the extension of the malignant process as there is often a glandular enlargement from mere septic absorption.

How do the malignant cells from the primary focus reach the glands? Theoretically cells may pass to the glands along the lymphatic vessels in two ways:-

(1) by embolism

(2) by permeation.

By embolism we mean that a cell or cells have been borne along by the lymphatic stream
to the regional gland. This is unlikely according to Sampson Handley, who believes that per-
meation is much more probable in the sluggish streams and stagnant pools of the lymphatic system. By this method which was first suggested by Handley, the malignant cells, having entered a lymphatic vessel, grow continuously along its lumen, thus forming a solid cord of cells. Fibrosis may occur and cut off the periphery of the cord from the primary tumour. This fibrous strangulation is prone to fail in certain areas and while the growing edge advances till the process reaches the gland, at the same time small islands of malignant cells, which have survived the fibrosis, are left behind.

Which is the usual method? Birkett states that in a large number of cases, cures have resulted from the operative treatment of the primary growth and of the glands as separate entities; he therefore concludes that permeation cannot have occurred because if it had, groups of malignant cells would have been left behind and the condition would have recurred.
also has been unable to secure any histological evidence of permeation, and while Handley's theory is attractive, the histological evidence, which he himself has advanced, has been relatively small. His theory was first worked out in connection with carcinoma of the breast, and it is significant that in a recent exhaustive histological study of breast tumours Fraser was unable to substantiate his claims. Further, it is a common-place of histology to find an isolated group of cancer cells in the corridor of a lymphatic gland at a point at some distance from the hilum, without any fibrosis or blocking of the lumen of the corridor between the metastasis and the hilum. Such a phenomenon has undoubtedly been the result of embolism, and it is now widely accepted that the latter is at least the more common method of glandular invasion.

(3) Blood Spread:

Haematogenous dissemination is rare in squamous epithelioma; but in Regaud's tumour it definitely occurs and metastases may be present in the bones, lungs, liver and mediastinum.
THE CHANGES IN THE GLANDS.

Commencing in the gland corridor the malignant cells infiltrate widely along the sinuses between the follicles and the septa. At first there is a small round celled infiltration, but this is usually an ineffective barrier and finally the cancer cells wipe away all trace of the normal gland architecture.

Eventually, the capsule becomes involved and the surrounding tissues invaded. Adjacent glands become matted together and form a large mass which may ultimately involve and destroy the overlying skin leading to a large fungating growth.

Four of the present series of cases were squamous epitheliomata, viz., an undifferentiated squamous epithelioma of the lip, a differentiated squamous epithelioma of the lip, an undifferentiated squamous epithelioma of the floor of the mouth, and an undifferentiated squamous epithelioma of the tonsil. The remaining two cases were of particular interest as both were lympho-carcinomas, one of the naso-pharynx, and the other involving the right tonsil, the hard palate and the roof of the mouth. Lympho-carcinoma is a special subvariety of epidermoid carcinoma, and I shall therefore discuss its pathology.
LYMPHO-CARCINOMA.
(Transitional cell epithelioma lymphoepithelioma, Regaud's tumour).

The tonsils, the naso-pharynx, the base of the tongue and the sinuses opening from the nasal passages are covered by a stratified epithelium made up of small delicate cells without spines or prickles. These cells do not produce keratin, and therefore do not undergo cornification. To this type of epithelium the name of lympho-epithelium has been given.

Tumours may arise from the epithelium in the above sites and their tendency is towards the formation of small infiltrating rather than of large bulky growths. The lymphatic glands are involved early in the disease and the spread extends beyond the regional glands to reach the liver, lungs, bones and mediastinum.

In 1923, Crowe and Baylor reported a series of cases of carcinoma in the upper air passages, in which they drew attention to the wide variations in the clinical course of tonsillar carcinomata. Some of the tumours grew slowly, remained localised for a long time and did not
metastasize until late; while others showed an almost fulminating course. Crowe and Baylor recognised that these were of a different type from the ordinary epithelioma and they pointed out the difficulty in differentiating them from the sarcomata.

Quick and Cutler described twenty cases of Regaud's tumour in 1927 under the name of Transitional cell epidermoid carcinomata. Let me quote from their work, - "within the group of epidermoid carcinomata, particularly of the tonsil, base of tongue and larynx, there occur cases which show a high degree of malignancy and run an unusually rapid course. Furthermore, in those cases which have shown this clinical picture the lesion has been associated with a specific histological structure. Histologically, these tumours have been recorded as atypical epidermoid carcinomata, anaplastic, or embryomal tumours".

The exact origin of these tumours is difficult to determine, but several possibilities suggest themselves.
(1) That they arise from lympho-epithelium.
(2) That they arise from squamous cells which in their growth fail to develop spines and become changed into rounded or polyhedral cells growing diffusely as an anaplastic tumour.
(3) That they arise from misplaced embryonic tissue rests.

I am inclined to favour the first theory for these tumours are only found in areas which contain lympho-epithelium.

Morbid Histology:

On section, these tumours show densely packed masses of cells with little intercellular substance. The cells are small with large hyperchromatic nuclei and scanty cytoplasm. In shape they are mostly polyhedral, but they may be round. They may be arranged in solid groups or in columns. This structure is very faithfully reproduced in cervical gland metastases and also, though to a lesser extent, in visceral metastases.
Though comparatively rare, I am sure that lympho-epithelioma is really more common than we believe and I think many cases of actively growing and rapidly fatal malignant tumours in the upper air passages are due to this tumour, which has been mistaken for a very anaplastic undifferentiated squamous epithelioma. Fortunately, this tumour is remarkably radio sensitive, and it is striking to see the miraculous way in which glandular metastases melt away after and even during irradiation.
CERTAIN CLINICAL CONSIDERATIONS.

Symptomatology:

In the majority of cases, there are no symptoms but when the disease spreads to the floor of the mouth, the tongue tends to become fixed, making deglutition and articulation difficult. This may even be the symptom which draws the patient's attention to the ulcer. It is more common, however, for the patient to complain of pain referred along the branches of the trigeminal nerve, especially towards the ear c.f. (Case III.)

In the lip there are often no symptoms, the usual complaint being of an ulcer or crack that refuses to heal despite antiseptic treatment.

In the tonsil and roof of the mouth, the tumour may grow to a large size before the patient is aware of anything wrong, and this is well shown by Case V. when breathing was seriously impeded by a large tumour.

Advice may be sought not because of the primary growth, but because of a swelling in the neck (Case IV.), and in many cases the patient
is astonished when the surgeon asks him to open his mouth.

**Examination:**

(1) **LOCAL:** In every case the primary tumour must be inspected and the edges, base and surroundings of the ulcer examined. The naked eye appearance of the tumours of the buccal cavity has already been described.

(2) **GLANDS:** Before a thorough examination of the cervical glands can be carried out, it is essential to know definitely the situations of the glands which drain the buccal cavity. I shall, therefore, discuss the lymphatic drainage of the buccal cavity before considering the methods of clinical examination.

**The lymphatic glands of the Neck:**

The glands of the neck may be divided into two large groups:-

(1) The circular chain.

(2) The vertical group.

The **circular chain** is made up of various groups of glands extending from the symphysis menti to the occiput and forming a chain of glands en-
circling the base of the skull. The groups of glands forming the circular chain are:

1. **Sub-mental glands** which lie on the mylo-hyoid muscle, and receive vessels from the tip of the tongue, the central portion of the lower lip and from the front of the floor of the mouth.

2. **Submaxillary glands** which lie in the submaxillary region below the lower margin of the masseter muscle and the mandible. They receive lymph from the upper and lower lips, from the anterior two-thirds of the tongue, the gums and the floor of the mouth.

3. The **preauricular, mastoid and occipital lymphatic glands** complete the chain, but as they are of no importance in connection with the mouth, I do not propose to consider them.

The **vertical group** of cervical glands or the deep cervical lymph glands are divided into two groups:

(a) The **anterior group** lie along the lateral surface of the internal jugular vein, external to the carotid sheath extending from the mastoid
Fig. 20. - Lymphatic Glands of the Neck.
process above to the root of the neck below.
They are divided into two groups by the omo-
hyoid muscle. —

(1) the **upper anterior deep-cervical glands**
above the omo-hyoid.

(2) the **lower anterior deep cervical glands**
below the omo-hyoid.

The gland of the upper anterior group
which lies in the triangle formed by the common
facial and internal jugular veins and the posterior
belly of the digastric muscle, receives lymph from
the tonsil, and so is known as the tonsillar or
the jugulo-digastric gland.

(b) The **posterior group** of cervical glands are
situated behind the internal jugular vein, and
are also divided into two sub-groups:—

(1) the **upper posterior cervical glands** which
lie in relation to the accessory
nerve and receive lymph from the
pharynx, the mastoid, occipital, and
upper anterior deep cervical glands.

(2) the **lower posterior deep cervical glands**
which lie in relation to the posterior belly of
the omo-hyoid muscle and receive lymph from the upper groups and from the lower anterior deep cervical glands.

The lymphatic drainage of the Buccal Cavity:

THE LIP: From the lateral part of the lower lip to the submaxillary glands and thence to the upper anterior deep cervical glands.

From the central part of the lower lip to the submental glands and from there to the upper anterior deep cervical glands.

FLOOR OF THE MOUTH: From the anterior part to the submental glands and from the remainder to the submaxillary glands and then as above to the upper anterior deep cervical glands.

From the alveoli the lymph passes to the submaxillary glands.

THE TONSIL: The lymph from the tonsil passes to the jugulo-digastric group of glands.

THE TONGUE: The lymphatic drainage of the tongue is more complicated. The lymphatics are divided into two groups:

(1) superficial
(2) deep.
The superficial lymphatics course all over the surface of the tongue and cross the middle line to join those of the other side.

The deep lymphatics on the other hand are distinct for each half of the tongue, and are separated by the median raphe of the tongue. Their drainage is as follows:

(a) from the apical area of the tongue to the submental glands and from there to the submaxillary glands.

(b) from the lateral areas of the tongue to the submaxillary glands and from there to the upper anterior deep cervical glands, and also unfortunately to the group of glands in relation to the posterior belly of the omo-hyoid.

(c) from the central area of the tongue the lymphatics pass to both sides of the neck to the upper anterior cervical glands and from there to the upper posterior cervical glands.

(d) from the base of the tongue the lymphatics pass to the upper anterior deep cervical glands under cover of the posterior belly of the digastric muscle. The vessels from this area communicate
freely with the corresponding vessels of the opposite side.

Clinical Examination of the Glands:

In the examination of a swelling in the neck, it is essential to find out -

(1) its position,
(2) its consistence,
(3) the degree of fixation to the deeper tissues,
(4) the amount of fixation to the skin.

The position of the swelling is important and its relationship to the sterno-mastoid muscle must be defined. We must then ask ourselves, is the tumour in the skin, the fascia or the muscles. Obviously, if it is entirely in the muscle, it cannot be a gland.

Malignant glands have a stony hard consistence, which is not found in any other condition.

I should just like to mention here again that clinical enlargement of the glands does not necessarily mean that they are the site of metastatic
deposits, - e.g., in Case II. there was a definitely enlarged submental gland which, however, showed no histological evidence of metastasis.

**Diagnosis:**

Presumptive evidence of malignant disease is afforded by the age of the patient, by the history, and by the presence of one or more predisposing factors.

The diagnosis is seldom in doubt clinically when there is a typical ulcer with raised margins and an indurated base, but it may be very hard to differentiate a malignant ulcer from a gummatous ulcer. Malignancy must always be suspected when an ulcer is slow in healing.

Perhaps the greatest difficulty in the diagnosis of Regaud's tumour lies in the fact that it very often occurs in young people in whom carcinoma is never even considered in a differential diagnosis.

**Differential Diagnosis:**

Buccal Carcinoma must be distinguished from,
(1) Primary Chancre: This usually occasions little or no difficulty, the clinical features of a syphilitic lesion being quite distinct. In addition, the Treponema Pallidum is present in the secretion. Primary Chancre is rare.

(2) A Gummatous Ulcer does not show much induration, is serpigenous in outline, tends to heal at one part while spreading at another, and shows no lymphatic enlargement. Biopsy must always be performed in doubtful cases. It occurs chiefly on the dorsum of the tongue.

(3) A chronic inflammatory ulcer may be mistaken for a malignant one, and biopsy may be required in doubtful cases. Tuberculous ulcer is very rare indeed and as it is always secondary to disease of the lungs, it need not be seriously considered.
Introduction:

How much nearer has 1930 brought us to a solution of the problems of the treatment of cancer? It may well be that many who ask this question would derive but small satisfaction from the correct answer - even if it were possible to find one. Anxiety breeds impatience, and to impatient people a year is a long time.

In cancer research and treatment a year's progress may vary, for time may gallop, or it may be like the schoolboy, "with his satchel and shining morning face, creeping like snail unwillingly to school". In the past year the advance in treatment has resembled not the lithe grace and speed of the thoroughbred, but the steady plodding of the cart horse. No great discoveries have set the pulses of the nation racing, confident once more that at last a cure for cancer has been discovered. No, 1930 has done more than that, it has led to a reconsideration of all our methods of treatment and to the assigning of each to its proper place in our armamentarium against malignant disease.
Surgeons now have a more reasoned view of the possibilities of radium treatment and it is used in intelligent association and co-operation with surgery in most cases. Great changes have taken place in our methods of treatment! What a marvellous change from the disabling radical operations for the removal of the tongue, to the wearing of a radium denture. It is not to be wondered at that patients are becoming more optimistic, but do our results justify this hopefulness? Although it is too early yet to be absolutely certain, evidence goes to show that they do.

One day in December an emergency case was brought to hospital by her husband. After attending to the case, the surgeon asked the man the reason for the large scar on his neck. He had had an epithelioma of the tongue eleven years previously. On examining the neck, nothing abnormal could be found except that the sterno-mastoid muscle had been removed. The tongue had been operated on by Whitehead's method and here he was cured eleven years afterwards.

While this paper was being prepared, I saw an old gentleman, aged seventy, who reported
at hospital with an epithelioma of the lower lip. Nine years ago a similar epithelioma in the same situation had been excised with complete success.

W. B. Coley of New York also quotes a case alive twenty seven years after the removal of a tumour of the floor of the mouth and tongue, the pathology of the tumour being confirmed by Ewing.

On the other hand, the tragedy of radical surgery is well shown by a case I saw, with no evidence of any recurrence, after a complete removal of the tongue, (radium having failed). Although he was cured, for some time at least, he was so miserable that he went about with the thought of suicide ever uppermost in his mind. He not only suffered severe pain, but the thought of his uselessness without his tongue made him believe he would be better dead than a constant burden to his relatives.

Radium therapy has not been in existence long enough to have any successes such as those above quoted, yet no one will deny that it has inaugurated a new and more hopeful era in the treatment
of buccal carcinoma, and it is indeed a fact that in most surgical schools, it has almost entirely superseded surgery in the treatment of the primary lesion. The treatment of malignant disease, however, is more than the treatment of the initial lesion, and we must ask ourselves just to what place in our armamentarium we can definitely assign radium therapy.

In attacking carcinoma many problems have to be considered; indeed we may say that the problem is a three-fold one.

1. the attack on the primary tumour.
2. the extirpation of the regional glands.
3. the treatment of distant metastases if they are amenable to treatment.

Foremost among many debatable questions is that of whether attention should be first directed towards the primary site of the disease, or to its regional lymphatic distribution.

Should the Primary Growth or the Glands be treated first.

This is a difficult matter to decide and surgeons are almost equally divided in their opinions. All are agreed, however, that as regards the mouth,
it is inadvisable to treat both in one operation since this would involve too great a risk to the patient. The mouth is a septic cavity and infection would readily extend to the neck wound. That this is not an invariable sequel is shown by Case I. in whom the primary growth and glands were removed at one operation with excellent results.

Reasons in favour of Gland Dissection first.

(1) It is a clean operation, and the removal of the glands is relatively easy compared with their removal after an operation on the mouth, which is followed by adenitis and even cellulitis of the neck.

(2) The lingual, facial or external carotid arteries may be ligated to lessen haemorrhage at the second operation which, however, must then be done before the collateral circulation develops.

(3) The patient may refuse further operation if the primary growth is removed first. cf. A.H. (Case II.)

(4) Carcinoma cells which are deposited in the glandular area between the two operations are stranded by the fibrosis which is occurring in the recent wound.
The reasons for treating the primary growth first are summarised by Birkett as follows:—

(1) The lymphatic glands are the natural means of defence against the spread of disease. It is therefore reasonable to remove the primary growth first and so eradicate a source of sepsis and malignant embolism.

(2) If a unilateral Crile's dissection is done first, the lymphatic flow will be directed to the other side of the neck and the glands there will become involved.

(3) The block dissection interferes with the blood and lymphatic supply of the affected side and if radium is to be used in the treatment of the primary growth, it makes radio-necrosis more likely.

On considering the reasons for and against the removal of the glands first, it seems to me that there is more to be said for the removal or radiation of the primary growth first. In the first place, there is no definite evidence to prove that carcinoma cells deposited in the glandular area subsequent to treatment of the
primary are strangled by fibrosis; secondly, the difficulty of removing the glands, after treatment of the primary growth, is not sufficiently increased to make primary gland dissection essential. Again, it is very often quite unnecessary to ligature the external carotid or lingual arteries, and if the patient is told beforehand that if the condition is to be cured, it will be essential to remove the glands subsequently, then I am sure there will be no difficulty in securing his consent to a second operation.

Sometimes, however, it is difficult to obtain the patient's consent, and this was well shown by one of the series of Cases (Case II. A.H. - 64 years), who had a local excision of an epithelioma of the lower lip on 24th October 1930, and a dissection of the glands of the left side of his neck on 15th November 1930. After that he refused point blank to have the right side done and left hospital as soon as the wound on the left side was soundly healed.

I do not approve, however, of using the disease, and the name of cancer as a means of terrorising the patient to obtain his consent for
the second operation. The curability of the disease rather than its dangers should be the means of persuasion, if any is required.

The question of obtaining the patient's consent and of telling him that a later dissection of the glands will be required, raises that ever present and difficult problem of whether the patient should be told the exact nature of his illness. I well remember while still at school enjoying a lively debate on this subject, but since that time I am afraid my opinion is the exact opposite to what it was then. The name of cancer is regarded by the man in the street with such fear and horror that it seems unwise to tell and I believe it would be better to tell only if the patient asks definitely whether it is cancer or not. Even then there are cases where the truth is better disguised for there are patients who, not so stable mentally as others, lack the courage to face their troubles, lose the desire to live and go steadily downhill on that account.

The surgeon therefore must be something of a psychologist - sizing up each patient and,
if necessary, looking him in the face and telling him what he knows to be untrue. This problem has recently become more complex because radium has been the subject of so many articles in the popular press that patients are almost sure to realise the nature of their complaint as soon as they know that radium is being used; it may therefore be advisable to tell the patient at once rather than let him find out suddenly in this way.

After this somewhat lengthy digression on the subject of medical ethics, let us return once more to consider whether or not the primary growth should be treated first. The reasons for treating the primary growth first are in my opinion so sound that I think this should be done in most cases. As time goes on, radium is being used more and more in the treatment of malignant disease inside the mouth, and as a previous glandular dissection renders radio-necrosis more likely or as some authorities maintain, inevitable, it now becomes essential to deal with the primary growth first if radium is going to be employed.
METHODS OF TREATMENT.

Glandular Metastases:

Although I believe that the primary growth should receive the first consideration in treatment, I propose to discuss the methods of attacking the glandular metastases first, because most surgeons are agreed that a block dissection of the glands of the neck is the method of choice. I do not propose to discuss this operation here, since the details can be found in all text books of operative surgery and the actual operations and the pathological findings at operations have already been described under each case of this series.

Are there any contra-indications to this method of dealing with the glands? Although this is a severe operation and sepsis is a possible complication owing to the opening up of the tissue planes in the neck, most patients recover very quickly and in no one of these three cases was there any great delay in healing.

In cases of lympho-epithelioma or Regaud's tumour, I believe that the glands are
better treated by radium for even the most radical surgery is almost inevitably followed by a recurrence of this rapidly growing tumour. As the tumour also responds to irradiation in a most amazing manner, I think that radium is undoubtedly the method of choice. Good results followed the use of radium in my two Cases, V. and VI., both of which were examples of lympho-epithelioma.

The patient's general health is another important consideration because there can be no doubt that the shock following surgical interference is greater than the effects of radium therapy. In very old patients and in those who are debilitated or cachectic, radium is very much safer than surgery. (c.f. D.H. - Case III.).

The block dissection required in most cases is unilateral, but there are certain tumour sites where the lymphatic drainage necessitates a bilateral dissection. If the primary growth is situated in

(1) the tip or midline of the tongue,
(2) the floor of the mouth,
(3) the posterior third of the tongue,
(4) the lip,
the operation should be performed on both sides of the neck.

The post-operative application of a collar containing radium and the methods of treating the glands will be described later in the discussion on radium treatment.

TREATMENT OF THE PRIMARY GROWTH.

Pre-operative Treatment:

Before radium or surgical measures can be instituted in the treatment of neoplasms inside the mouth, it is imperative to attend to the hygiene of the mouth.

The patient should have his teeth thoroughly overhauled, carious teeth being removed, cavities stopped and pyorrhoea eliminated. An antiseptic mouth-wash should be used for some days before operation. If the tumour is lying in close proximity to the alveolus, it is probably wiser not to extract teeth in the immediate neighbourhood, but to be content with cleaning them up as well as possible.

In growths involving the palato-glossal fold and tonsil, particularly when they are bulky,
respiration and swallowing may be so impeded that it becomes necessary to perform a tracheotomy and in some cases even a gastrostomy.

Tracheotomy is rarely, if ever, required as an emergency operation, since the symptoms are not acute but slowly progressive, and due to the gradual growth of the tumour.

Obstructive dyspnoea is not the only indication for a pre-operative tracheotomy. Indeed the situation of the neoplasm is more important because treatment by the surface application of radium involves the wearing of a denture, which in these sites may seriously impede respiration. Tracheotomy was performed in one of my Cases, W.W., in whom the tumour occupied the right tonsil and had spread fairly widely in the roof of the mouth, and had caused marked dyspnoea for a week prior to his admission to hospital.

**Radium or Surgery?**

Here we encounter a great problem - has it to be radium or radical excision?

Radium has been coming into the limelight recently and although it may be said that it is scarcely out of the experimental stage, some
very striking results have been obtained from its use. It becomes necessary at this stage, therefore, to survey briefly the position of radium in the treatment of malignant disease.

It has been known for many years that the use of surface applications of radium have curative effects on superficial epitheliomata, and during the last few years the technique of radium therapy has advanced considerably with the introduction of the radium needle. The tongue and the buccal cavity are, on the whole, very satisfactory areas for radium therapy for the effects of the radium can be seen and judged, and in most situations, the tumour is fairly accessible.

In the primary growth is operable and a sufficiently large area can be removed and yet yield a good cosmetic result, I consider it advisable that excision should be practised because as yet it is not really known whether the changes produced by radium are permanent or not. On the other hand, if radium cannot cure the early primary lesion more certainly than the knife, at least it does so without mutilation, and in addition "inoperability" is a term without meaning so far as radium is concerned.
In my opinion, therefore, only the small localised neoplasm which can be dealt with by a limited excision should be treated surgically; and radium should be used for all other cases, because of the conservative nature of the treatment, and when patients realise that mutilation is not now part and parcel of the surgery of buccal cancer, they will come much earlier for advice.

Let me quote from the Ministry of Health Memorandum on Cancer of the lip, tongue, and skin (1931). The report refers to the difficulties of early treatment in the following words, -

"The rapid spread of the disease to the neighbouring lymph glands militates against successful operative treatment, only 20% of all cases surviving after three years. One of the chief factors in this low survival rate appears to be the length of time patients are willing to suffer from this disease before seeking treatment. Although experience of treatment by radiation is less extensive, and sufficient time has not elapsed since its inception, it is justifiably assumed that the results are equal to, and possible even better than, the results of surgical operation."
Some will say that these opinions consider too much the patient's feelings rather than his disease, but it assuredly is our duty to try and place ourselves in the patient's shoes and decide what methods of treatment we should ourselves prefer if we were the sufferers.

Turning aside from its undoubted aesthetic advantage, however, reasoned opinion seems to indicate that it cures - at least temporarily - the malignant process. And so it may be said to fulfil all the necessary requirements.

Let us therefore summarise the advantages of radium therapy over surgery.

(1) It ensures the disappearance of the primary growth.

(2) There is no extensive mutilating operation.

(3) There is little or no discomfort while the radium is in situ in contrast to the discomfort which follows radical excision.

(4) The patient is more likely to seek treatment at an earlier date.

The difficulties of radium therapy:

Professor Gask of London in an address on radium therapy of the buccal region said, "the attack on the primary growth is in a sense
The treatment of the primary growth may be the easiest part of the task, but if all these essentials are going to be carried out, radium therapy must be under the charge of a skilled worker. These then are the difficulties of radium therapy.

What are the disadvantages of Radium Therapy:

(1) A portion of the tumour may remain non-irradiated, but this disadvantage can be overcome by proper technique.

(2) The difficulty of giving the right dose and exposure in radium therapy. The dose may be too small when the tumour of course will not disappear completely; on the other hand, the dose may be too large, and result in burning or sloughing of the tissues with the formation of obstinate slow healing ulcers.

(3) The detrimental effect of radium on
the health of those who are constantly using it for the treatment of others. This is not a very serious disadvantage, but to safeguard himself, the radiologist or surgeon who uses radium often should have a white blood count performed at regular intervals. Radium produces a leucopenia, and a recent report would seem to indicate that it may inaugurate a leukaemia.

None of these disadvantages is so great that it cannot be overcome by proper technique and adequate precautions, and I think the only disadvantage of radium therapy of the mouth, is its liability to produce radionecrosis of the bone when it is used for tumours at the alveolar margin. It is impossible to screen the jaw effectively even by the use of lead.

In my opinion, therefore, it is unwise to be dogmatic as regards the choice of treatment; it is better to consider each case on its merits, and elaborate the treatment accordingly - whether radium alone, surgery alone, or a combination of the two. At the same time, I think it is advisable to place oneself in the patient’s position and consider which method is going to produce
the least disfigurement; if that method is as good, or nearly as good, as the other as regards its curative effect, then I think for the patient's sake it should be employed.

The Selection of Cases for Radium Therapy.

The suitability of a case for radium therapy is judged on four factors, -

(1) The anatomical position of the tumour.
(2) The degree of extension of the lesion.
(3) The condition of the surrounding tissues.
(4) The type of tumour.

These four factors must now be considered in greater detail.

The Anatomical position of the Tumour:

By this I mean the accessibility of the growth. Tumours involving the tip, lateral border and dorsal aspect of the tongue are readily accessible, but tumours on the inferior surface are less so, and radium treatment is almost certain to cause necrosis of the jaw particularly if the floor of the mouth is also involved. Surgery, however, is out of the question in these cases and
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radium is the only possible method of treatment for tumours of any size in the floor of the mouth.

Epithelioma of the postero-lateral part of the tongue, close to the pillars of the fauces is very difficult to treat because of its in-accessibility and its proximity to the angle of the jaw and to the palate. The difficulty can be overcome, however, by means of ingenious dentures and plates.

The degree of extension of the lesion:

The degree of extension does not mean the presence or absence of glandular metastases, for though affecting the prognosis very materially they do not affect the treatment of the primary growth per se. The factor under consideration therefore is the degree of local extension of the growth, and it may be said quite definitely that the smaller the growth the easier the treatment will be since less radium is required and radio-necrosis therefore is more improbable.

The Condition of the Tissue surrounding the Tumour:

This is the most important factor in the treatment of the primary growth by means of radium. Evans and Cade have said "whatever the karyokinetic
"activity of the malignant cells may be, they respond to irradiation; but if the stroma be oedematous, it is not sufficiently resistant to irradiation however well screened the radium may be; its blood supply is interfered with and radionecrosis is very probable."

Any oedema of the surrounding tissue is therefore a contra-indication to the use of radium.

The Type of Tumour:

Generally speaking, the undifferentiated epitheliomata react much more rapidly and effectively to radium therapy than do the differentiated types. Perhaps the most radio-sensitive tumour of all is the transitional cell epithelioma or lympho-epithelioma (Regaud), and this is well shown by two of my Cases (V. and VI.) Although these tumours are extremely radio-sensitive, they appear to be more malignant and more liable to recurrence.

Radium and Radium Treatment:

It may be out of place to mention some of the facts regarding the action of radium in a paper of this kind, but unless one has some idea of the action of radium, it is impossible to assess its dangers, and take adequate precautions, such as
screenage of the radium. I shall therefore discuss this matter very briefly.

When we speak of radium treatment we do not mean treatment by radium metal. The actual element is not used because it becomes converted into the hydroxide. One or other of the salts of radium - the chloride, bromide, or sulphate - is used. The sulphate of radium is very convenient because it is insoluble and its radium content is as high as 70%.

**Physics of Radium:**

Radium and its salts give off three types of rays - alpha, beta, and gamma; in addition, by their disintegration, they produce a radioactive gas, known as radon which also gives off the same three varieties of rays.

The *alpha rays* are positively charged helium atoms and, having poor powers of penetration, are therapeutically useless or nearly so.

The *beta rays* are negatively charged electrons with considerable powers of penetration and are divided according to their powers of penetration into "soft", "medium", and "hard".

The *gamma rays* are similar to X-rays, but are of shorter wave-length. They have great powers...
of penetration and can be detected after passing through 190 mm. of lead, whereas X-rays can scarcely penetrate 3 mm. of lead.

The rays of low penetration are absorbed by the skin and subcutaneous tissues and as they produce burns and telangiectases they must be filtered out. The alpha rays can be excluded by means of a sheet of paper, but the beta rays are harder to stop. 99% of the beta rays are filtered out by .6 mm. of platinum, and as .5 mm. of platinum only filter, 6% of the gamma rays which are the rays required for irradiation, platinum is very useful for screenage. In all my cases the screenage employed was .5 mm. platinum.

As radon seeds were employed in none of my cases, I do not propose to discuss them here.

Radium Needles:

Radium is used in the form of one of its salts, and we have already seen that the alpha and beta rays require to be filtered and this is brought about by platinum. The radium needle has made the introduction and removal of radium an easy matter, and also provides the right amount of screenage for the radium. The needles are
made of platinum and have a hollow cylindrical shaft to contain the radium element. At one end of the needle, there is an eyelet and at the other end a trocar point which is hardened with iridium. The thickness of the wall of the needle is .5 mm. giving the right amount of screenage.

Needles are for the most part constructed with a definite amount of radium per centimetre of their active length but, unfortunately, no absolute standard has yet been arrived at. The needles are rarely more than 1.5 mm. in diameter, and therefore they can be introduced through a very small puncture, and their removal is almost invariably an easy matter if proper care is exercised.

**Dosage of Radium:**

If radium treatment is to be on a scientific basis, a rapid method of calculating the amount of irradiation employed is essential, since there are distinct dangers of both under and over dosage.

The dosage is calculated by multiplying the amount of radium element by the number of hours for which it was employed, and the result is
expressed as mgm. hours, e.g. Case I. - T.M.
A "radium collar" containing twenty 2 mgm. needles was applied for 202 \( \frac{1}{2} \) hours and so the total dose was \( 20 \times 2 \times 202 \frac{1}{2} \) - 8,100 mgm. hours. The dose in millicuries may be found by dividing the dose in mgm. hours by 133.3, but this method of expressing the dose is usually employed only when radon is used.

**Cost of Radium:**

Radium element costs about £12 per mgm. but to this must be added the cost of the platinum needles which is about £3 for .6 mgm. needles and £7:10/- for 10 mgm. needles, and the charge made by the Brussels University for estimating the amount of radium - about £1 per 5 mgm. A radium needle containing 10 mgm. therefore costs £120 for radium, £7:10/- for the platinum tube, and £2 for estimating the amount of radium, i.e. £129:10/-. On this account when radium is being used, it is essential to make sure that no needles get caught in dressings and that when not in use, the radium shall be kept in a lead casket securely locked up.

**Methods of Employing Radium:**

There are three main methods of applying
radium element to the treatment of malignant disease of the mouth. -

(1) Distant radium therapy.
(2) Surface Applications.
(3) Interstitial radiation.

**Distance Radiation** entails the use of a very large amount of radium element in a radium bomb, and can only be used in hospitals where there is a large amount of radium and special apparatus.

**Surface Applications** were those employed first of all in the treatment of cancer and at that time large amounts were employed for a short period. The effect of radium rays varies inversely as the square of the distance so this method is only suitable for superficial growths. To increase the effect the intensity at the surface was increased and as filtration was then unknown the beta rays were given full play and necrosis or burning of the surface resulted.

Dominici introduced the method of filtration by which the harmful beta rays were excluded while the penetrating gamma rays were scarcely affected. The surface then remained intact.
The tendency now more and more is to use a smaller amount of radium over a longer period of time, and the results have improved greatly with this change in technique.

Having decided to use a surface application of radium for malignant disease in the mouth, how is it possible to keep the radium in position, to make sure that other parts are adequately screened and to give the patient as little trouble as possible? It is here that the surgeon has to rely on some other member of his team for there must be very few surgeons who are also highly skilled and ingenious dental mechanics. The best method is to have a denture made to hold the radium, and it is remarkable how beautifully these dentures can be fitted and surprising to find them causing so little discomfort. The patient soon becomes accustomed to the wearing of the denture, at first only wearing it as long as he can, but later on he will be able to wear it for long periods without distress. In this way doses up to 10,000 mgm. hours can be used.

In my series of Cases, three were treated by means of dentures containing radium.
Case III. (D.H.) was treated entirely by radium in view of his age. The primary growth, an undifferentiated squamous epithelioma of the floor of the mouth, was treated by the application of a denture for 3,600 mgm. hours and the neck was attacked by interstitial irradiation.

Case IV. (D.McK.) was treated by means of a denture containing ten 2 mgm. needles and a total exposure of 3800 mgm. hours was given to the primary growth, which was situated in the left tonsil.

Case V. (W.W.) - A lympho-epithelioma of the left tonsil was treated by means of a denture containing ten 2 mgm. needles applied for 216 hours, i.e. 4320 milligramme hours.

Surface applications of radium were also used after the block dissection of the cervical glands in the hope that this method of irradiation would be sufficient to destroy any malignant cells which had escaped destruction at the operation. I must confess I am rather sceptical of the efficiency of this procedure, but as its value cannot be estimated in any way, it is better to
employ it in case any treatment which might be advantageous to the patient should be withheld from him.

The neck is irradiated by means of a "radium collar". The collar is made of either:

(1) columbia paste which consists of 100 gm.
    beeswax, 100 gm. paraffin which melts at 62°C. and 20 gms. fine sawdust to diminish the weight, or

(2) Stent wax.

Both materials are easily moulded when heated, but it has been proved at the Radium Institute in Paris that Columbia paste produces a homogeneous irradiation and a diffuse superficial distribution of the rays. The radium needles are embedded in the collar and usually 40 mgm. of radium are used. The dosage varies, for if the collar is being used as described above, as an extra precautionary measure, then 5-10 thousand mgm. hours will suffice, but if the collar is intended for treatment instead of operation or interstitial radiation up to 25 thousand mgm. hours will be required.
In the series of cases reviewed here, Case I. - T.M., was treated by means of a Stent collar containing 40 mgm. of radium and a dose of 8100 mgm. hours was used. The collar was applied shortly after the wound in the neck had healed.

**Interstitial Radiation:**

Stevenson and Joly in Dublin were the first to implant radium in and around malignant tumours, but they used a fairly intense unfiltered source, and it is largely through the work of Regaud who employed filtration and smaller amounts of radium with a longer exposure, that interstitial radiation has assumed such a prominent place in the treatment of malignant disease all over the body.

Instead of the intense pain, sloughing, sepsis and exhaustion occurring in the methods of Stevenson and Joly, there is now very little discomfort, and what is of very much greater value, there is a uniform result.

The needles are implanted at equal distances round the tumour, and a dosage of 2000 mgm. hours is aimed at.
In my Case (Case I. T.M.) the primary growth was removed at operation and interstitial radiation 2119 mgm. hours was employed in case the whole tumour had not been removed.

In Case VI. (S.F.L.) both the glands and the primary growth were treated by interstitial irradiation.

The glands were treated by interstitial radiation in Cases III. and V. because of the age of the patient in Case III. and because of the diagnosis of lympho-epithelioma in Case V.

**Clinical Appearance of the Primary Growth after Radium Therapy:**

The changes taking place can be divided into two:-

1. the normal reaction,
2. the abnormal reaction.

**The normal reaction:** By the tenth day, there is as a rule an appreciable change. The lesion, if of the raised variety, has become more flattened, and for a variable area around the mucous membrane is covered by an adherent greenish yellow fibrinous deposit and rather resembles an infarct so sharply is it defined from the normal mucous membrane.
This later becomes more marked, and the induration becomes progressively less and in about four weeks it has disappeared, although the treated area may feel slightly firmer than the healthy tissue.

In about six weeks to two months, there should be little or no trace of the lesion.

In the ulcerated type of lesion, epithelialization takes place from the periphery, leaving hardly any scarring. The mobility of the tongue returns to normal.

Abnormal Reaction: This reaction may be divided into two classes:

(1) due to under exposure.

(2) due to over exposure.

In under exposure, although the ulceration may have disappeared and everything may appear normal, persistent induration should make one suspect too small a dosage and the necessity for further applications.

Over exposure varies in degree from slight cases which are shown by the persistence of the fibrinous deposit to extreme cases in which owing to pain sloughing and inability to sleep or
feed, death may supervene. Cases between these two extremes show a well defined central ulcer surrounded by oedematous and indurated tissues. The base of the ulcer is covered by a tough adherent green slough. The ulcers are very painful and require 8-12 months to heal. They leave a depressed scar, and the tongue does not regain its mobility properly.

We must therefore err rather on the side of safety in dosage, for it is easier to give another exposure than to cure an abnormal reaction.
Fig. B.—Semi-diagrammatic figure showing on the left the normal epidermis (Ep) of the lip, on the right cancer cells damaged by interstitial irradiation (Case 1). C₁, C₂, C₃—cancer cells; ch—chromatin, and n—nucleolus of cancer cells; F—fibroblasts, L—lymphocytes; Py—pyknotic nuclei; P—polymorphonuclear leucocytes.

Fig. 21. — Diagram of lip cancer after irradiation (Cheatle).
Fig. 22. - Diagram of the various cellular and nuclear changes after irradiation (Cheatle).
THE ACTION OF RADIUM ON THE MALIGNANT CELL.

The actual effect of radium on the life history of the cell is as yet obscure; certain facts, however, are known. These have recently been summarised by Ludford and Cheatle who found that -

(1) Radium has a specific effect, in therapeutic doses, on the cells of malignant tumours.

(2) This change consists of coagulative necrosis with final disintegration of the protoplasm.

(3) The nucleus undergoes a series of changes which particularly affect its chromation content and which ultimately lead to its destruction. (Fig. 21, 22).
CONCLUSIONS.

(1) That malignant disease in the mouth usually takes the form of an epidermoid carcinoma, but that other more malignant and much more rapidly growing tumours - the lymphoepitheliomata - are occasionally met with.

(2) That the malignancy of the epidermoid carcinoma varies with the degree of differentiation of its cells.

(3) That in the epidermoid carcinoma distant metastases are rare.

(4) That the disease is predisposed to by a variety of factors which may be summed up under the heading of chronic irritation.

(5) That leucoplakia is definitely a pre-cancerous condition.

(6) That radium combined with surgery is the method of choice in the treatment of the disease when it is situated inside the mouth.
No one can be satisfied with the treatment of malignant disease at the present time. The only region in which results are consistently good is the breast and, in my opinion at least, this success is due to the method of removing the primary growth, the lymphatics and the lymphatic glands in one block. The Monobloc method is of course inapplicable to malignant disease of the mouth.

I am dissatisfied, however, with our methods of treatment, although they are the best available at the present time, because I believe we are going about it in the wrong way. All we can do is to wait until cancer has developed and then we do our best to deal with the final stages of the disease. A large amount of work has been done on the etiology of cancer and we are no further forward. Are we going on the right lines in our research work? I must say I do not think we are going to find the cause in infection or any such theory. Surely when such a vast number of factors have been found to predispose to the occurrence of malignant disease, they cannot be the cause of it. To my mind, the cause is an instability of the tissues. This would explain why so many
people who have chronic irritation in their mouths do not develop cancer.

Let us study the laws of cell growth. The cell must grow, reach maturity, fulfil some function, degenerate and then die. What factors control the growth of the cell? We know that the absence of thyroid secretion in early life results in the small, square headed, dry skinned, unintelligent human animal, we call a cretin. If this cretin were fed on thyroid substance in the early years of his life, he would grow both physically and mentally. The thyroid, therefore, is one factor in cell growth. The body normally grows to a certain size and then stops growing except for the replacement of cells which are lost in the wear and tear of life. Growth in the normal individual is a perfectly balanced and controlled process. What is the controlling factor? Supposing it to be of endocrine origin — and surely this is not unlikely when we consider the effects of deficiency and excess of other hormones — if we were able to isolate it and use it, I do not see why it should not have the desired effect of controlling the unrestrained growth of
the malignant cell.

Such a theory would of course mean that the affected person had some deficiency of endocrine secretion by reason of which the growth of the tumour became possible.
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