

# THE PATHOLOGY OF NASOPHARYNGEAL TUMOURS

By D. F. CAPPELL (Dundee)\*

THE pathology of nasopharyngeal tumours is too wide a subject to be dealt with adequately in a short paper, and I therefore propose to concern myself chiefly with the subject of lympho-epithelioma. Before doing so, however, I shall review briefly the tumour material submitted by my colleagues of the Dundee Royal Infirmary in so far as it concerns the subject of our discussion to-day. I have excluded from my analysis simple polypi and have included only lesions considered to be true neoplasms.

During the past eight years we have studied 122 new-growths from the nose and throat, the anatomical distribution of which is shown in the following Table.

Later I shall deal at length with the lympho-epithelioma group, but I wish in passing to draw attention to the relative frequency of parabuccal mixed tumours in the palate and faucial region, a point which does not appear to be sufficiently realized, judging by the frequency with which single cases are reported as rarities. Most of the conditions enumerated are too well known to merit special mention, but among the miscellaneous group is included one of the two cases of malignant rhabdomyoma of the palate reported by Montgomery and myself recently, the other falling outside the period of the present review. Since these growths present distinctive features, I wish first to draw attention to their main characteristics.

Tumours of striated muscle are relatively uncommon in any situation, and while a few examples have been reported in the nose (Reitter, 1921; Cooper, 1934) and in the epipharynx (Söderberg, 1932-33) only two examples have been recorded in the soft palate (Nicory, 1923-24; Martin and Alexander, 1924). These tumours are thus among the rarest with which the

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RHABDOMYOMA SARCOMATODES, CASE I.

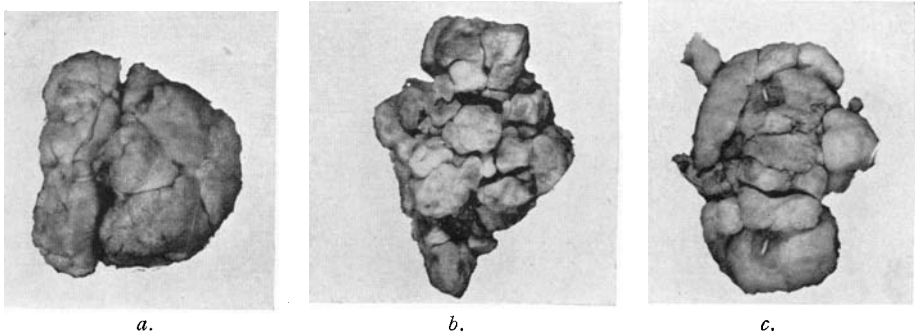


FIG. 1.

Rhabdomyoma sarcomatodes of soft palate: (a) original tumour; (b) first recurrence; (c) third recurrence. Natural size.

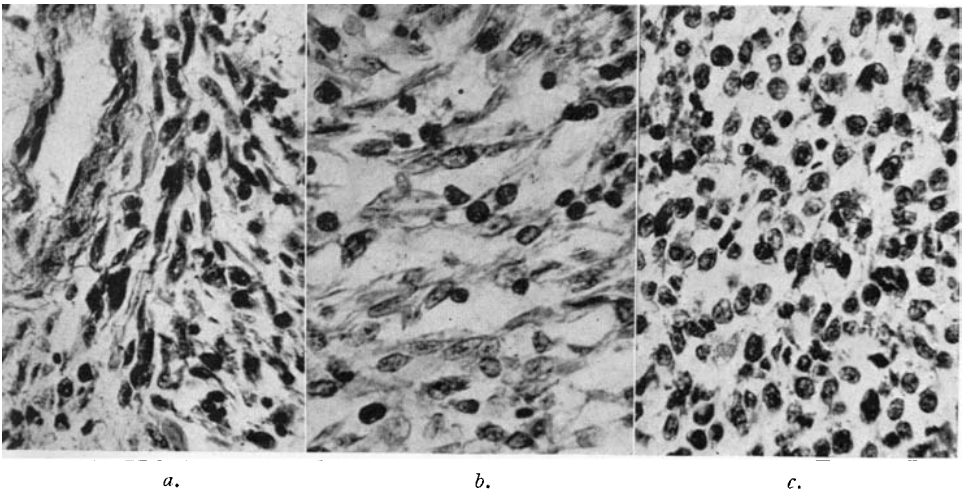


FIG. 2.

Original tumour: (a) small but well differentiated muscle fibres with pronounced cross striation; (b) spindle cells and less differentiated myoblasts devoid of cross striation; (c) "round-cell sarcoma" composed of very primitive, quite undifferentiated myoblasts (cf. Fig. 6). Masson's trichromic stain.  $\times 390$ .

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nasal surgeon has to deal, but it is not improbable that cases have gone unrecognized included within the general category of myxoma and sarcoma. While the diagnosis of rhabdomyoma will always rest upon microscopic examination, it is believed that the clinical and naked-eye appearances are so characteristic that it should be possible to recognize, or at least suspect the nature of such tumours in the consulting room, a point of much practical importance, as early recognition and radical operative removal at the outset appear to offer the only hope

	Naso-pharynx:	Nasal Sinuses.	Tonsils: Fauces.	Nasal Cavities.	Palate.	Total.
Squamous Epithelioma	31	13	22	3	9	78
Lympho-Epithelioma and Transitional Epithelioma .. ..	9		2		1	12
Mixed Salivary Tumour .. ..	1		1		8	10
Papilloma .. ..	1		1	3	3	8
Fibroma .. ..	2				2	4
Plasmacytoma ..		2				2
Angioma .. ..			1	1		2
Rhabdomyoma ..					1	1
Melanoma .. ..				1		1
Osteoclastoma ..		1				1
Sarcoma .. ..				1		1
Leukæmia .. ..				1		1
Total .. ..						121

of preventing a fatal outcome from local recurrence culminating in widespread dissemination.

Rhabdomyoma of the soft palate occurs chiefly in childhood or adolescence, and at first appears like a simple tumour, producing symptoms by local effects such as alteration of the voice, difficulty in speech or in swallowing or by causing discharge following ulceration of the surface. When first seen such growths are likely to present a nodular polypoid structure, of white or flesh colour, and, while they look soft, actually

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they are rather firm to the touch. The lobulated processes are often more translucent and tend to be broader at the free than at the attached end, thus presenting a clubbed appearance, very pronounced in both our cases. The growth may be sessile or the whole may be suspended from the mucosa by a thin pedicle. The polypoid form has long been recognized as characteristic of rhabdomyoma of the vagina and cervix uteri—the so-called sarcoma botryoides—and the assumption of a similar form in palatal cases is worthy of emphasis. Any tumour growing from a mucous surface which presents a lobulated polypoid form with translucent clubbed processes demands investigation to determine whether it is a rhabdomyoma, recognition of this being vitally important in prognosis and treatment. Following simple removal local recurrence is likely and, in spite of more radical operation subsequently, which may cure the local condition, dissemination by the lymphatics and later by the blood-stream appears to be inevitable. The only hope of cure lies in removal of the primary growth and the tissues from whence it springs much more radically than has yet been attempted in the initial stages. Recognition of the naked-eye appearances is thus of great importance.

From the pathological point of view the extremely variegated structure of these tumours must be emphasized. The characteristic elements are the long tubular and strap-like cells with parallel sides and strongly acidophile cytoplasm in which both longitudinal and cross striation is usually demonstrable (Fig. 9). Owing to the plane of section, however, they may appear as merely protoplasmic fragments in which the myofibrils are seen as darkly staining acidophile dots. Such frankly striated elements are easily detected, but specific staining methods are desirable; of these Heidenhain's iron-hæmatoxylin is the most useful, but Mallory's phosphotungstic acid hæmatoxylin and anilin blue methods are excellent, and Masson's trichromic stains yield very beautiful results on suitably fixed material (Fig. 9). Cross striation is often best seen in the smaller fibres. Less highly differentiated cells are also present, and it is on these that the malignancy of the growth depends. In some parts large and small spindle cells may predominate (Figs. 2*a* and 2*b*) and careful staining by Heidenhain's method may reveal fine myofibrils in their tapering extremities, but in places the structure is that of

RHABDOMYOMA SARCOMATODES, CASE I.

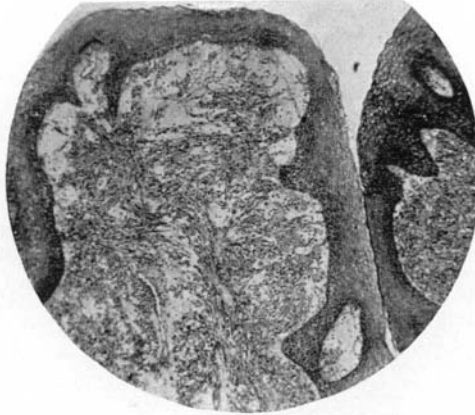


FIG. 3.

First recurrence. Beneath the squamous epithelium each polyp consists of a loose interlacing network of primitive muscle fibres. The tip of the process is œdematous. Masson's trichromic stain.  $\times 32$ .

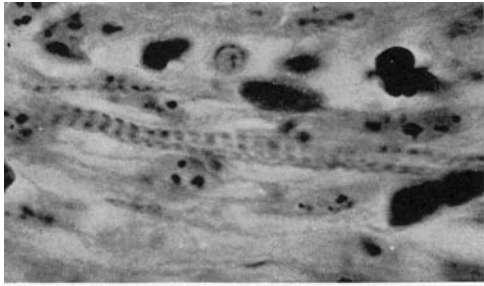


FIG. 4.

Second recurrence. Well marked transverse striation is seen in many of the finer fibres. Heidenhain's iron hæmatoxylin.  $\times 850$ .

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pleomorphic spindle-celled sarcoma (Fig. 7). In other parts œdema may produce a loose texture strongly resembling myxoma (Fig. 5), but the cells are not truly stellate and specific stains fail to reveal mucin in the interstitial substance. A constant feature is the occurrence of nests of round-cells with scanty cytoplasm which recalls the earliest stages in the embryonic development of the myotomes (Figs. 2*c*, 6). We believe that these primitive elements together with the small spindle cells are responsible for the malignancy of the tumours and that metastases arise by their dissemination, though in their new sites of implantation these cells may continue to grow and to differentiate so that in some cases immature fibres may appear in the secondary growths. In our own cases, however, differentiation was almost suppressed in the metastatic lesions and proper histological diagnosis from them alone would have been almost impossible.

In the development of metastases, rhabdomyomata differ from other sarcomata in the tendency to dissemination by the lymphatic pathway, and thus local recurrence in the palate is followed by enlargement of the deep cervical lymph nodes, which may be of hard rubbery consistency; in the larger metastases central necrosis and degeneration tend to occur. The cervical lymph nodes are replaced by extremely anaplastic round cells which expand the original reticular framework of the lymph-node and assume a frankly alveolar architecture (Fig. 8). This gives rise to appearances which call for much care in the interpretation of biopsy specimens owing to the close resemblance to anaplastic carcinoma. The strongly acidophilic cytoplasm may suggest the myogenic origin of the cells and, in the absence of elongated fibrils, cross striation may sometimes be detected in the larger round cells. Some of the latter elements may also be highly vacuolated—so-called spider cells, the vacuoles being filled with glycogen. These are not invariably present but they may give valuable evidence of the rhabdomyomatous origin of a tumour if detected in the absence of fully developed striation. In other cases, the cells after implantation undergo further differentiation and elongated, imperfectly formed, striated fibres may develop. In the later stages widespread dissemination by the bloodstream may also occur, but this is usually a terminal event and the lymphatic pathway is generally affected first.

I propose to devote my further remarks to the problem

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of lympho-epithelioma. The name lympho-epithelioma was applied by Regaud and Schmincke (1921) to certain highly radio-sensitive tumours of the nasopharynx and tonsillar regions which they thought possessed clinical and pathological features sufficiently distinctive to justify separation into a distinct class. There has never been unanimity of opinion as to the justification for this classification though it has been generally accepted on the Continent, and some American writers have continued to group such cases together with transitional-celled carcinoma, while others (Ewing, 1929) have accepted the distinction. Recently Harvey, Dawson and Innes (1937) have discussed the question and consider that there are no grounds for the use of the term "lympho-epithelioma", and that cases are either squamous carcinomata of anaplastic type or else reticulum-cell or lympho-sarcomata. In my opinion this assumption is quite unjustifiable, and while admitting the difficulty of accurate diagnosis, I believe that there is a distinct group of tumours, arising usually in the nasopharyngeal lymphoid tissues but occasionally elsewhere, which possess sufficiently distinctive features to warrant segregation into a special class. I propose first to show their microscopic appearances and then to indicate the general features. I shall then discuss the incidence of these tumours in my own pathological material and give the results of our experience in their treatment.

In my original account published in 1934, I reported twelve cases of which ten were considered to be typical lympho-epitheliomata, the remaining two cases, lacking the very intimate admixture of lymphocytes, possibly to be classified as transitional-celled carcinoma. Since then, I have encountered six new cases and, on reviewing our material for the past eight years, have found three additional examples two of which, previously classified as transitional-celled carcinoma, should probably be included here. There are thus twenty-one cases in all. Of the twenty-one cases, nine were clearly nasopharyngeal and one other in the palate was probably of nasopharyngeal origin; five of these ten were histologically of the Regaud type, three of the Schmincke type, and two transitional-celled carcinoma. In seven cases the primary growth was in the tonsil, three being bilateral and all were of the Schmincke type. In three the primary site was in the hypopharynx, two being of Regaud type and one possibly to

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be separated as transitional-celled carcinoma. The remaining case came to Hospital with bilateral enlargement of the cervical glands, but the primary focus was not detected.

In the histological classification of lympho-epitheliomata the appearances described and illustrated by Regaud and Schmincke were not identical, and in my previous paper I referred to cases as belonging to the Regaud type (3/12) or the Schmincke type (7/12) while at the same time I gave reasons for believing that all degrees of transition could be found between the appearances characteristic of each type. Further experience has strengthened this opinion, and while certain broad distinctions might be drawn between the two types, there is no clear-cut separation, and cases presenting intermediate histological character are not uncommon. Similarly I am of the opinion that transitional-celled carcinoma and lympho-epithelioma are closely related and from the clinical and therapeutical point of view are not to be distinguished.

On histological grounds the cases may thus be separated into three main groups, (a) lympho-epithelioma of frankly carcinomatous type corresponding to the description of Regaud and Jovin (1926); (b) lympho-epithelioma as described by Schmincke (1921), of less obviously epithelial origin and bearing a strong resemblance to what has formerly been called large round-celled sarcoma of the tonsil; (c) transitional-celled carcinoma which differs from the first two groups chiefly in the less intimate association of lymphocytes and malignant epithelial cells. It must be emphasized that many cases present intermediate characters rendering it difficult to fit them exactly into one or other group.

Tumours of the first group (Regaud type) are composed of strands of epithelial cells with large pale-staining vesicular nuclei and poorly delimited cytoplasm, embedded in a stroma more or less rich in lymphocytes (Fig. 10). The nuclei are usually round or oval, rather poor in chromatin and containing one or two prominent nucleoli. The outlines of the individual epithelial cells are very indistinct and no intercellular bridges can be demonstrated; in many places the appearance is that of a protoplasmic syncytium (Fig. 15). Throughout the epithelial columns there are many small round darkly-staining nuclei apparently belonging to lymphocytes which have infiltrated between the epithelial groups. In places the epithelial cells appear as broad sheets lying in a well-formed



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fibrous stroma (Fig. 12) ; in other parts they are seen as thin strands penetrating deeply into the tissues of the palate and nasopharynx (Fig. 11). The individual cells may be closely packed together (Fig. 14) or may form in each mass a rather loose reticulum heavily infiltrated by lymphocytes. Where the stroma shows very massive lymphocytic infiltration, the columns of epithelial cells appear to disintegrate, liberating individual epithelial elements among the small, darkly-staining lymphocytes. Such areas present appearances resembling those seen in the second group and form an important link in the evidence for including both types within one main class of neoplastic disease.

In two cases the formation of an epithelial syncytium is especially striking and the bloated character of the nuclei and the basophilia of the cytoplasm are more pronounced than in the others (Fig. 13) ; the degree of eosinophile infiltration of both stroma and epithelial columns is also unusual.

The second group is more difficult to define but the histological appearances correspond closely to those described by Schmincke. The epithelial elements consist of irregular anastomosing trabeculae of ill-defined cells with large vesicular nuclei (Fig. 17). In many places the appearance of epithelial columns is lost and the cells become dissociated from one another giving rise to a loosely packed mass of round, oval or polygonal cells. In some parts these elements form the bulk of the tissue (Fig. 16, 20), but in other parts they are separated by a dense lymphocytic infiltration which tends to isolate them from one another and renders recognition of individual cells difficult (Fig. 21). The structure of such tumours thus varies in different areas, but from the examination of many sections, it is clear that all stages of transition can be traced between the epithelial cells in trabeculae and the loosely packed "sarcomatous" cells. Further, silver impregnation of the reticulum reveals a sharply alveolar architecture in each of these tumours, clearly defined where the epithelial elements are in the majority but somewhat broken up where lymphocytic infiltration is pronounced. The process of migration of cells from the epithelial network and their transformation into free round cells which give rise to the sarcoma-like structure can be clearly followed in some cases which thus forms an important link between the two groups. A similar occurrence was noted in the first group and it seems

RHABDOMYOMA SARCOMATODES.

second recurrence, to show the variation in structure in closely adjacent fields in the same section.

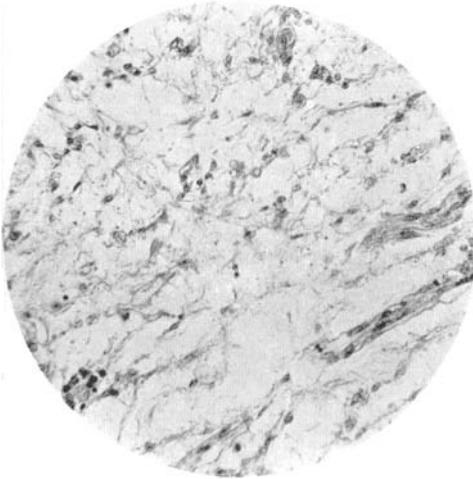


FIG. 5.

pseudo-myxomatous tissue. The fibres are the very long, fine processes of primitive muscle cells and the intercellular matrix does not stain like mucin.  $\times 150$ .



FIG. 6.

Closely packed round cells with scanty cytoplasm form a solid nodule amongst the looser tissue.  $\times 150$ .

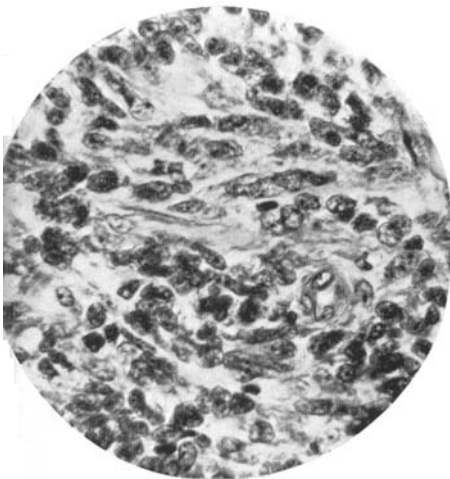


FIG. 7.

Pleomorphic spindle-cell sarcoma.  $\times 400$ .

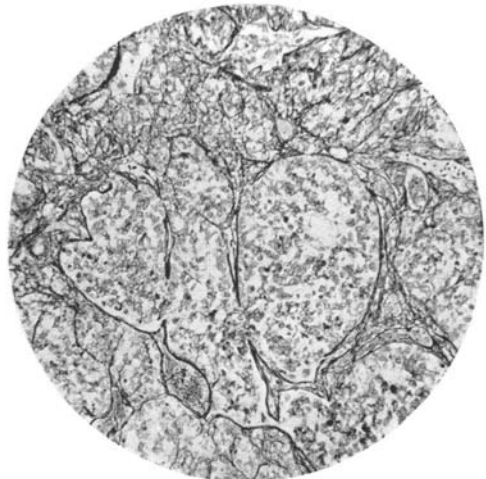


FIG. 8.

Lymph-node metastasis. The round cells are arranged in an alveolar architecture, emphasized by silver impregnation of the reticulum. Foot's method (modified).  $\times 185$ .

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clear that the two classical types are not sharply separated but merge gradually into one another. The difference is quantitative rather than qualitative and the appearances seem to depend upon the degree to which the cells remain in syncytial strands or become detached in the form of free elements.

Aberrant cell types and giant cells with convoluted nuclei occur in both groups but are usually inconspicuous. Imperfect keratinization in some of the deeply penetrating epithelial trabeculae was observed in one case but not in any of the others.

In spite of the great cellularity of these tumours and the delicacy of their stroma, the histological resemblance to lympho-sarcoma is not very close. The arrangement of cells to stroma is not nearly so intimate, and lympho-epitheliomata lack the fine intercellular reticulum stainable by Mallory's method and by silver impregnation which is seen in true lympho-sarcomata. In general, lympho-epitheliomata are not very highly vascular, and it is remarkable that necrosis and degenerative changes are not in evidence in any of the cases; possibly this is correlated with not very rapid growth.

The third group, so-called transitional-celled carcinoma, is distinguished from the other two groups by two features. In the first place, the origin from surface epithelium is much more obvious than in the other types, and the tumour cells form broad alveoli in which central necrosis and degeneration are more common than in the Regaud type. There is usually no trace of keratinization and the cells in general are devoid of the intercellular bridges (prickle cells) which often reveal the squamous nature of anaplastic non-keratinizing tumours; a few small groups of prickle cells may be present, but this feature is not general throughout the growth. The epithelial cells may be embedded in a fibrous stroma or in a stroma rich in lymphocytes but there is an absence of the intimate admixture of lymphocytes throughout the epithelial alveoli as in the Regaud and Schmincke types. Ewing states that such tumours often grow diffusely and that the epithelial characters of the cells are inconspicuous; he states further that lymphatic metastases tend to occur somewhat later in this group, the chief clinical features being ulceration and bleeding. The points of difference are, however, only general tendencies which, when maximal, may give the impression of a separate class of tumour; but, in my experience, the differences are more often much less clear cut and I cannot make an absolute distinction

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between lympho-epithelioma and transitional-cell or Schneiderian carcinoma. Lacassagne includes all such neoplasms under the general heading of lympho-epithelioma, and Ewing (1929) admits that separation is often difficult and the distinction a matter of opinion on which different observers fail to agree. Salinger and Pearlman (1936) submitted twenty-four nasopharyngeal tumours to three pathologists of repute and the chief difference of opinion was whether cases should be called transitional-cell carcinoma or lympho-epithelioma. On the other hand, these authorities did not make any marked distinction between transitional-celled carcinoma and anaplastic squamous epithelioma. I consider that cases showing a general tendency to keratinization or with widespread formation of prickle cells should be excluded from the transitional-celled carcinoma group and classified as anaplastic squamous epithelioma. When this separation is made, transitional-celled carcinoma falls naturally into place as a sub-group of lympho-epithelioma, which may thus be said to have three broad sub-divisions, united by intermediate appearances, *viz.* the Regaud, Schmincke and transitional-celled types. Both Ewing (1929) and Cutler (1929) and also Salinger and Pearlman (1936) state that transitional-celled carcinoma is much more common than is lympho-epithelioma, but this has not been our experience, if we exclude cases which are obviously anaplastic squamous epithelioma. It is clear from a survey of the literature dealing with primary naso-pharyngeal carcinoma that there is great diversity of opinion in the classification of such tumours and, whereas the clinical features are similar, the numerical incidence of the different types varies enormously. It is improbable that such differences have any real basis in fact and it seems likely that they are attributable to the varying interpretation of different observers. This is well brought out in the review of Salinger and Pearlman (1936). It is thus difficult to compare one set of statistics with another and to feel certain as to exactly what type of growth is under discussion in many of the published papers. My experience agrees with that of Salinger and Pearlman that the vast majority of malignant nasopharyngeal growths are carcinomatous and that the frequent diagnoses of endothelioma or lymphosarcoma are usually due to faulty interpretation.

Concerning the histogenesis of these nasopharyngeal

RHABDOMYOMA.

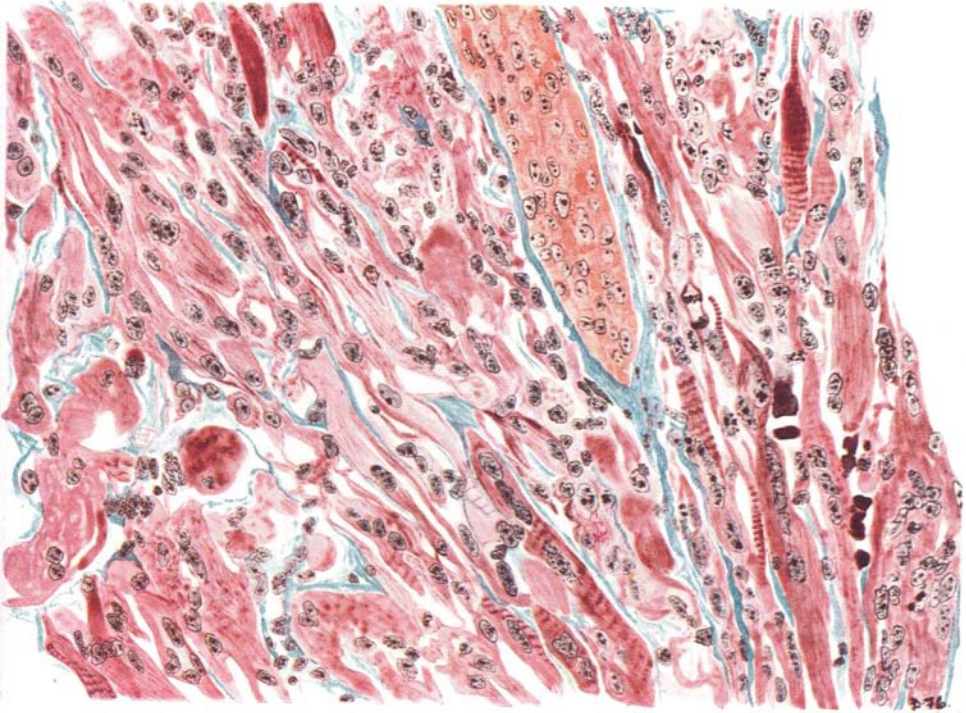


FIG. 9.

RHABDOMYOMA OF SOFT PALATE.

Rhabdomyoma sarcomatodes of soft palate, first recurrence. Myoblasts of various types, some fully striated, some showing longitudinal and marginal striation, others with marked granularity or vacuolation of the cytoplasm. Note the characters of the nuclei.  $\times 275$ .

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tumours very little that is certain can be advanced. It is assumed chiefly on the evidence of the close association of epithelium and lymphocytes that the lympho-epithelial growths arise from the lympho-epithelial organs of the nasopharyngeal region, and Cutler (1929) had emphasized that they often appear to take origin in the deeper tissues, causing fixation of the intact mucosa over a deeply-placed mass before invasion of the surface with subsequent ulceration occurs. Transitional-cell carcinoma on the other hand, betrays more clearly its origin from surface epithelium which is here of transitional type and with which it can usually be seen to be connected. Salinger and Pearlman (1936) suggest that the degree of lymphocytic participation in such tumours is determined by the lymphatic constitution of the individual; and may be abundant or scanty, depending on whether the lymphoid tissue at the site of origin are well preserved or atrophied. Mathies (1934-35) has pointed out that the development and subsequent involution of Waldeyer's nasopharyngeal lymphoid ring varies greatly in different individuals and that usually the more cranially situated deposits develop and involute before those lying more caudally. While individual variations in the local supply of lymphocytes may be a factor in determining the type of tumour that arises, such a view is purely hypothetical and does not take into account that the characteristics of the primary growth are usually maintained in the metastases in the cervical lymph nodes where lymphocytes are abundant. The point, however, does not seem to be one of great practical significance, since the clinical syndrome and therapeutic response is similar in both types.

### General Features

From a survey of the clinical histories of my cases, it is found that their features are in accordance with the classical description given by Trotter (1911) and amplified by Jovin (1926), Ewing (1929) and others.

Lympho-epithelial tumours are met with most frequently in the nasopharynx and tonsils, less often in the hypopharynx. The nasopharyngeal growths give rise to slowly growing tumours of moderately firm consistency in the lateral wall; the commonest site being close to the mouth of the Eustachian tube so that unilateral deafness is often present and may be the first symptom. The primary growth is usually small when

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first seen, with a finely nodular surface, often superficially ulcerated, which bleeds easily on being touched. For a time the tumour grows expansively and pushes aside neighbouring structures, but, later, infiltration of the surrounding tissues becomes pronounced, and owing to the anatomical site, involvement of the levator palati muscle and of the inferior maxillary nerve easily occurs, with consequent palatal asymmetry and often severe pain in the side of the face and jaw. Invasion of the internal pterygoid muscle leads to difficulty in opening the mouth. In the late stages, especially after surgical intervention and insufficient treatment, the primary growth may attain a large size and give rise to nasal obstruction and difficulty in swallowing and in speaking. There is a great tendency to invasion of the skull-base, especially at the foramina for the cranial nerves, so that nerve palsies are common. This feature was emphasized by Trotter (1911) and by Ch'eng (1935); it has also been observed in the present series.

In tonsillar cases there is usually a history of repeated attacks of tonsillitis and sore throat over a period of years but the ætiological significance of this is uncertain. Subsequently one or both tonsils are found to be enlarged, firm, and of fiery red colour, but pain and difficulty in swallowing are not always present and the contrast between the naked-eye appearance and the relative freedom from symptoms may be striking. In many cases the condition of the throat is thought to be merely persistence of an attack of tonsillitis until progressive enlargement of the cervical lymph nodes causes the patient to seek advice.

In pharyngeal cases the local symptoms of pain and difficulty in swallowing are likely to attract attention first, but sometimes the spitting or coughing up of blood may be the first sign to which the patient pays attention.

In all cases early enlargement of the cervical lymph nodes is likely to be a striking feature and often they attain a large size. The lymph nodes on the side of the lesion are, as a rule, involved first, but bilateral enlargement is usually early and the enlarged glands usually remain discrete and not adherent to the skin. The diagnosis of Hodgkin's disease or lymphosarcoma may thus be made on clinical grounds and the primary growth in the nasopharynx or tonsils may be overlooked. Jovin (1926) and Ewing (1929) emphasize this feature and the

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latter states that many cases formerly regarded as primary endotheliomata of the cervical lymph nodes are lympho-epitheliomata in which the primary growth has escaped detection. Of the present series of twenty-one cases, five presented themselves for examination on account of cervical glandular enlargement; of these, the primary was nasopharyngeal in two, pharyngeal in one, tonsillar in one, and in the remaining case the primary site was not detected; the last case had, however, been treated with radium before being examined by the throat specialist and owing to the extreme radio-sensitivity of such tumours the primary might by then have become unrecognizable by clinical examination.

At a later period, widespread metastases in internal organs may develop and secondary growths in the vertebral column are characteristic. The opportunity for examining such a case post mortem has not occurred in the present series and in the literature complete autopsies are rare. Derigs (1923) and Cutler (1929) noted that metastases in internal organs maintained the structure of the primary tumour and showed the same curious and intimate association of lymphocytes and malignant epithelial cells.

Lympho-epithelial tumours occur at all ages from childhood to old age. Through the kindness of Dr. Miller of Edinburgh, I have had the opportunity of studying sections from children of 8 years and 12 years, with nasopharyngeal and cervical lymph node growths respectively. These cases in young children were of typical histological structure, and there is in my opinion no justification for assigning them, merely on account of their age, to the category of lymphosarcoma, which they in no way resemble. At the other end of the scale, I have observed the disease at 70 and at 82 years of age. Most of the cases, however, are seen in the adult period of life, with a tendency for the Regaud type of nasopharyngeal growth to occur in young subjects.

Attention was first called to these tumours by their special radio-sensitivity, the primary growth in Regaud's original case having disappeared in a remarkable fashion following radiation therapy but death ultimately occurred from spinal metastases. In my own series this extreme radio-sensitivity has been apparent, the four cases surviving in 1934 being still well after five years, eight years, eight years, and five and a half years respectively. In four



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other cases the local response to radium treatment was remarkable, the growth disappearing in a few weeks ; no local recurrence took place, but death occurred about two years later from metastases. Good immediate response to radiation therapy was obtained in two other cases but death from intercurrent disease took place before the ultimate value of the treatment could be assessed. In the earlier cases in this series the importance of treatment by radiation was not appreciated, and in several instances death followed attempted surgical removal of the growth. It is clear that surgical excision except for biopsy is contra-indicated and treatment by radiation is the method of choice.

From our twenty-one cases we have thus five still alive, one being just recent and still under treatment by radium, so that it is too early to know the ultimate result. The other four have all survived over five years and have remained well. All were female subjects. Two cases were nasopharyngeal and two were tonsillar in origin ; all four were of the Schmincke type. Three were treated by radium and one by deep X-rays. One of the patients has since re-married and has recently undergone a successful operation for removal of gall-stones. I have scrutinized the histological appearances to see if there is anything which might enable us to distinguish such favourable cases, but I am unable to detect any significant difference from those which did not react so well. In all cases the initial response to radiation therapy may be expected to be good but the danger lies in metastatic involvement of distant organs, especially the liver and vertebral column. In all four surviving cases, the diagnosis was reached by microscopical examination of tissue removed surgically and open biopsy for histological examination does not seem to exercise any harmful influence, but treatment by irradiation should be begun immediately after biopsy is performed without waiting for the pathological report.

### Summary

The classification and anatomical distribution of 122 new growths from the nasopharynx, tonsils and pharynx are presented. Sixty-four per cent. of the tumours were classified as squamous epithelioma, 10 per cent. as lympho-epithelioma and transitional-celled carcinoma, 8 per cent. were parabuccal mixed tumours. Among 4.5 per cent. of miscellaneous

Lympho-epithelioma.

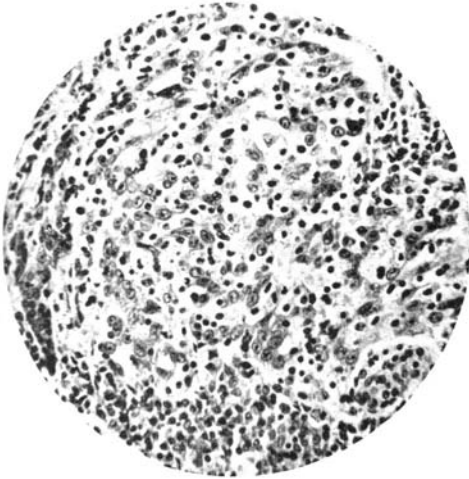


FIG. 10.

Case I. A group of tumour cells in trabecular arrangement, showing rich lymphocytic infiltration between the epithelial cells.  $\times 190$ .

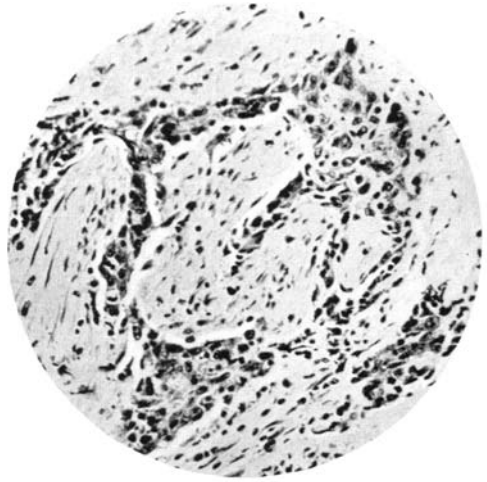


FIG. 11.

Case I. Delicate anastomosing cords of invading epithelium in a fairly dense fibrous stroma, from the deeper part of the growth.  $\times 190$ .

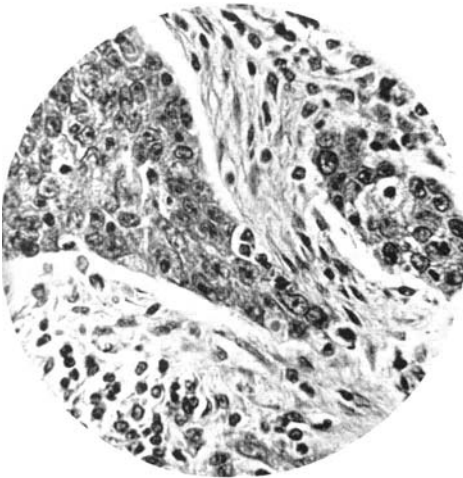


FIG. 12.

Case I. Invading epithelial cells showing actively slight lymphocytic infiltration; note resemblance to transitional-cell carcinoma (cf. Fig. 23).  $\times 380$ .

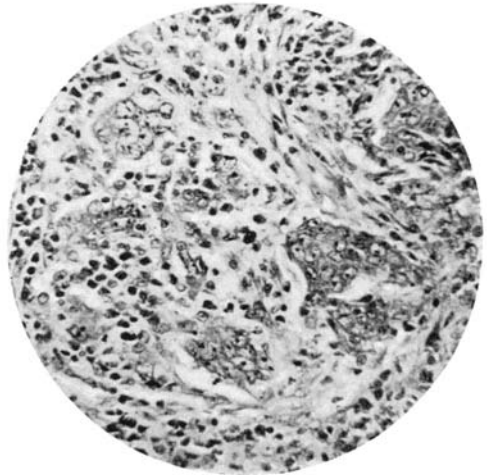


FIG. 13.

Case II. Epithelial syncytia, eosinophils and lymphocytes in fibrous stroma.  $\times 190$ .

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neoplasms, an example of malignant rhabdomyoma occurred, and the clinical and pathological features of such tumours are briefly indicated.

Attention is directed chiefly to the neoplasms classified as lympho-epithelioma and their clinical and pathological features are discussed.

Twenty-one cases have been observed, of which four have survived over five years following radiation therapy, three being treated by radium and one by deep X-rays. One other recent case is still under treatment. Good local response to radiation was obtained in six additional cases but death took place from intercurrent disease or from metastases, the site of the local lesion remaining free from recurrence.

Emphasis is laid on the absence of harmful results following open biopsy but further surgical measures are unnecessary and treatment by radiation is the method of choice.

## CASE HISTORIES

### **Malignant Rhabdomyoma (Rhabdomyoma Sarcomatodes) of the Soft Palate**

*Clinical History.*—W.S., a schoolgirl, aged 10 years, was admitted to Arbroath Infirmary in 1928 with a nodular fleshy tumour, almost the size of a walnut, suspended by a short stalk from the soft palate in the mid-line just anterior to the uvula. The cervical glands were not enlarged. The tumour was removed with a snare. In October, 1931, the patient was admitted to Dundee Royal Infirmary complaining of thickness of speech. Examination revealed a firm, painless, nodular tumour of pink colour attached by a narrow base to the mid-line of the soft palate; on the left side it covered the anterior pillar of the fauces. There was no palpable glandular enlargement. Removal by the snare was again performed. A second recurrence appeared about nine months later, producing thickness of speech, and on examination in October, 1932, an extensive cauliflower growth was seen, involving the soft palate covering the left tonsil and attached to the left posterior pillar of the fauces. On this occasion the tumour was removed by diathermy and radium was applied to the wound by means of needles and a dental applicator, the total exposure being 600 mg. hours. Two months later the patient came back looking much better; the palatal condition was limited to scarring and no neoplastic tissue was observed. Despite intermittent exposure to radium throughout the next year a third recurrence was observed nine months later (July, 1933) and grew rapidly. The patient was re-admitted in

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December complaining of pain in the palatal region. On examination the tumour resembled very closely the previous recurrence except that it was not so widely attached to the palate and could be pushed aside to reveal the posterior edge of the soft palate, which was not involved. The cervical glands were not palpable on either side. Removal was again performed by diathermy and the left tonsil with a portion of the posterior faucial pillar was resected. The patient was dismissed on January 26th, 1934, with the pharynx and palate clear.

She reported for treatment with radium and no further palatal recurrence took place. Fourteen months later, however, she was re-admitted to Arbroath Infirmary with a flaccid paralysis of the lower limbs and signs of compression of the spinal cord. Enlargement of the cervical glands and irregular pulmonary consolidation were then noted and the patient died of exhaustion seven years after the first appearance of the palatal tumour.

### *Pathological Examination.*

*The Palatal Tumours.*—The original tumour is roughly ovoid and measures  $2.5 \times 2.7 \times 1.5$  cm. It was of a pink, fleshy colour when fresh, but after fixation is white and non-translucent, and although it looks soft, it is surprisingly firm to the touch. It is a lobulated, slightly nodular tumour, but the nodules do not project much above the general surface of the growth (Fig. 1*a*). The recurrent tumours were of similar appearance and present the characteristic lobulated appearance with blunt, clubbed processes, some of which are superficially ulcerated. Their naked-eye characteristics are shown in Figs. 1*b* and 1*c*.

Microscopic examination of the original tumour shows a varying histological picture (Figs. 2*a*, 2*b*, 2*c*), the structure in places showing well-formed small fibres with transverse striation, areas of spindle cells and also highly anaplastic round cells. In the recurrent tumours similar histological appearances were maintained, but with increasing areas of anaplasia (Figs. 5, 6, 7), and in the metastases in glands and lungs the structure resembled a large round-celled sarcoma with practically no differentiation (Fig. 8). The histological appearances are described fully in the paper by Cappell and Montgomery (1937) and representative illustrations are shown.

### **Lympho-Epithelioma of Nasopharynx and Tonsils**

CASE I.—J.W., male, æt. 21, ploughman, was admitted to the Dundee Royal Infirmary complaining of swelling of the roof of the mouth on the left side, painful to the touch and on swallowing. The mass had increased gradually during the preceding six months with increasing difficulty in opening the mouth. Recently the left

LYMPHO-EPITHELIOMA.

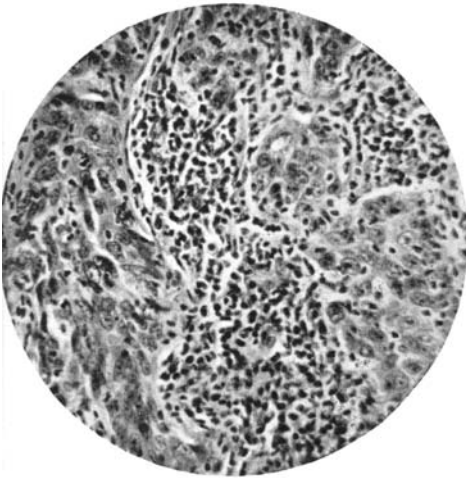


FIG. 14.

Case III. The epithelial columns are clearly emarcated; lymphocytic infiltration of both epithelium and stroma is very marked.  $\times 190$ .

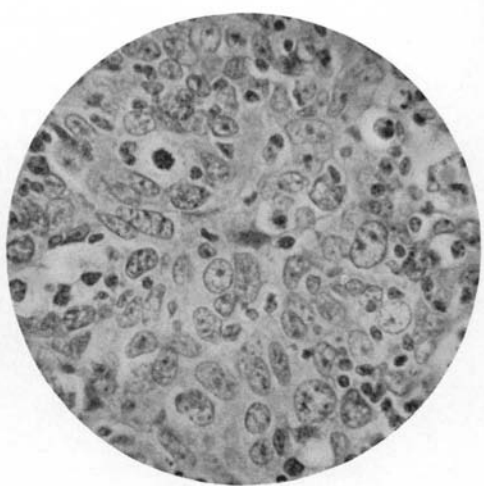


FIG. 15.

Case III. The syncytial character of the epithelial strands is shown; the large vesicular nuclei lie in a protoplasmic network in which cell boundaries cannot be clearly distinguished.  $\times 380$ .

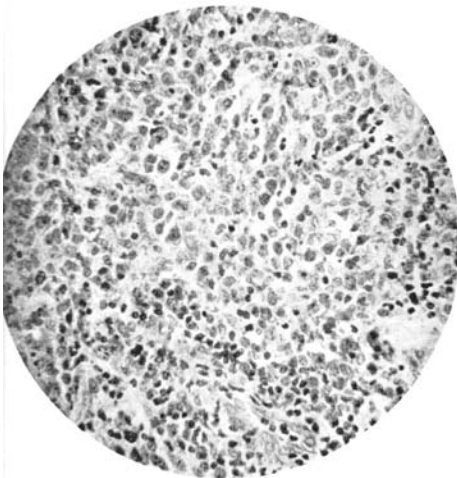


FIG. 16.

Case IV. Large pale-staining epithelial cells in only defined trabeculae with scattered lymphocytic infiltration.  $\times 190$ .

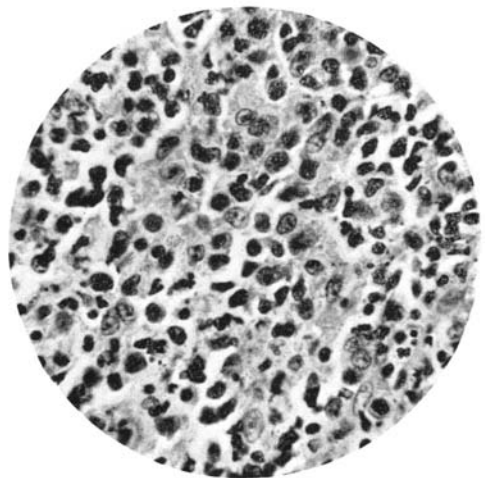


FIG. 17.

Case V. Sarcoma-like structure showing permeation by strands of larger pale-staining cells.  $\times 380$ .

## The Pathology of Nasopharyngeal Tumours

nostril became obstructed and there had been three attacks of epistaxis. He now complained of difficulty in swallowing and of deafness in the left ear with some tinnitus. The general health was good.

On examination marked trismus was found, the teeth separating only half an inch in front. The left cheek was swollen and there was tenderness and swelling over the left half of the soft and hard palates extending down to the fauces. The swelling was firm and non-fluctuant and there was a hard, tender, non-fluctuant swelling about the size of a walnut below the angle of the jaw on the left side, not fixed to the skin but adherent to the deep structures. Under an anæsthetic a large firm tumour was found in the nasopharynx invading the upper part of the pillars of the fauces on the left side. A portion was removed for pathological examination and was reported as lympho-epithelioma.

*Treatment.*—A few days later radium was inserted into the nasopharynx and left maxillary antrum and an external radium collar was applied. A total dosage of 2,983 milligram hours was given internally and 11,880 milligram hours externally.

*Subsequent History.*—After six weeks the local condition was greatly improved, the tumour in the palate and nasopharynx had disappeared entirely with only slight scarring, but a sinus led from the nasopharynx into the maxillary antrum. The patient remained well for about twelve months with no sign of local recurrence. Paresis of the right leg and arm then appeared, followed very soon by paresis of the left arm and leg so that within a few weeks the patient became totally incapacitated with spastic paralysis of all four limbs. Lipiodol injection showed obstruction in the spinal canal at the level of the IVth and Vth cervical vertebrae due to pressure from metastases in the vertebral bodies. The patient returned home at his own request and died from respiratory complications about nine months later. It is noteworthy that there was no local recurrence of the tumour in the palate, nasopharynx or glands of the neck.

*Pathological Specimen.*—Several small pieces of whitish tumour growth were obtained by curetting from the nasopharynx. Microscopic examination reveals the characteristic structure of lympho-epithelioma of Regaud. The tumour is composed of strands and anastomosing trabeculae of epithelial cells with large rather vesicular nuclei and poorly defined cytoplasm. There is no trace of intercellular bridges and the epithelial elements cannot be sharply distinguished from one another. In places broad sheets of tumour cells are seen lying in a stroma very richly infiltrated with lymphocytes (Fig. 10). In other parts the epithelial cells form small strands which penetrate deeply into the underlying tissues (Fig. 11). The surface is in places ulcerated but elsewhere the covering epithelium

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is intact and in a few situations the tumour cells appear to be continuous with the surface epithelium. In a few situations the invading columns of epithelial cells have partially disintegrated with the formation of mucin, pointing to the origin of the epithelial cells from the Schneiderian membrane.

A striking feature is the almost uniform permeation of the epithelial groups with small darkly-staining cells resembling lymphocytes (Figs. 10 and 11). This feature is present not only in the epithelial strands which lie in the stroma rich in lymphocytes but also in the most deeply penetrating epithelial columns which are embedded in fairly dense fibrous tissue and among the muscle bundles of the soft palate (Fig. 11). In places the epithelial columns become broken up and disintegrate among the masses of lymphocytes, liberating the individual cells as larger pale-staining units; among these occasional multi-nucleated giant cells and large cells with convoluted nuclei occur.

CASE II.—K.McL., female, æt. 23. The patient was previously operated upon for septal deflection and double antral disease. Some months later she complained of pain in the left upper jaw and had several teeth removed without benefit. Soon after this a swelling appeared in the palate. This was lanced twice but pus was not obtained. On admission to the Western Infirmary, Glasgow, under the care of the late Dr. Syme, there was found a hard tumour arising in the nasopharynx and displacing the soft palate and pillars of the fauces downwards. A portion was removed for pathological examination and was at that time reported as a malignant epithelial tumour of unusual type.

*Subsequent History.*—The patient's condition gradually deteriorated during the following two months, signs and symptoms of pulmonary disease appeared with consolidation at the apices and a suspicion of cavity formations in the left lung. Tubercle bacilli could not be demonstrated in the sputum. The patient died suddenly about two months after operation. Post mortem examination was not obtained.

*Pathological Specimen.*—A portion of tumour about the size of a hazelnut was received. It was of a firm consistency and dull, whitish colour. Microscopically, the specimen consisted of columns of peculiar epithelial cells with very large globular nuclei and scanty basophilic cytoplasm. The cytoplasm is very poorly defined and seems in most places to form a syncytium (Fig. 13). In places the epithelial cells occur in broad sheets, in other parts they form small deeply penetrating groups from which individual cells appear to wander off into the stroma. They then appear as oval cells with deeply basophilic cytoplasm forming a mere rind around the large vesicular nuclei. The stroma shows general infiltration with

# The Pathology of Nasopharyngeal Tumours

lymphocytes and there are also very many eosinophils. These occur in clusters and in some places are intimately mingled with the epithelial cells.

CASE III.—H. McC., male, æt. 25. The patient was admitted to the Western Infirmary, Glasgow, complaining of swelling in the back of the throat and difficulty in breathing of some months' duration. On examination the soft palate was seen to be pushed downwards and invaded by a tumour arising in the nasopharynx. The glands below the angle of the jaw were enlarged and hard. A portion of the growth was removed under chloroform anæsthesia but the patient collapsed and died under the anæsthetic. Post mortem examination was not performed.

*Pathological Specimen.*—A mass of growth about the size of a walnut was received for examination and it seems clear that the tumour must have been of considerable size as the portion submitted was not complete. Microscopically the structure is practically identical with that in Case I, being composed of syncytial strands of large pale-staining epithelial cells with large vesicular nuclei (Fig. 15) in a stroma richly infiltrated with lymphocytes (Fig. 14). In places the epithelial columns become broken up and the individual cells appear to wander off among the lymphocytes. Both large and small epithelial masses show pronounced lymphocytic infiltration and mitotic figures are numerous.

CASE IV.—H.S., female, æt. 51. Since March, 1930, the patient had experienced a sensation as if the nose were blocked. Shortly after she noticed that the hearing was impaired on both sides. In June, 1930, a curettage was performed and the hearing improved. The patient was admitted to the Western Infirmary in December, 1930, and another curettage performed. The deafness immediately reappeared, there was now pain in the left ear and buzzing noises in the head.

On examination a fleshy mass was found in the nasopharynx, almost completely filling it and incorporated with the upper surface of the soft palate. The cervical glands were palpable.

*Treatment.*—A Stockholm box containing radium was passed into the affected region. About five hours later the patient swallowed the box. Recovery from the œsophagus proved unsuccessful and the box passed into the stomach, from which it was recovered by gastrotomy. Five weeks later she was re-admitted and another box was passed into the nasopharynx. The growth was found to have caused further adhesions of the soft palate. Under radium treatment the growth disappeared rapidly and after a further ten weeks the patient's condition was very much



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improved, there being little or no sign of active tumour growth, but adhesions in the nasopharynx were plentiful.

One gynæcological applicator was tied into the nasopharynx and a further dosage of radium given.

*Subsequent History.*—She complained from time to time of pain and discomfort in the ears and also of some abdominal discomfort but the condition of the nasopharynx has remained satisfactory. In 1936 symptoms of gall-bladder disease appeared and cholecystectomy was performed. There was no evidence of metastases in the abdomen and she made a good recovery. The patient has since re-married.

*Pathological Specimen.*—Only a very small fragment of the tumour was received for examination. Microscopically it consists of round and oval cells closely packed together with numerous lymphocytes among them. The tumour cells are larger than lymphocytes and their nuclei are less rich in chromatin: in places they form poorly defined columns (Fig. 15) but in most parts lie diffusely without obvious arrangement. Silver impregnation, however, reveals a poorly defined carcinomatous structure with a delicate reticular stroma separating the cell masses into distinct alveoli. The surface squamous epithelium is invaded by groups of tumour cells spreading intra-epithelially. The growth is considered to be a lympho-epithelioma.

CASE V.—J.S., male, æt. 60. There was a history of frequent attacks of tonsillitis and once a right-sided quinsy. On admission he complained of pain and a feeling of fullness in the throat for about ten weeks with pain and difficulty in swallowing; hoarseness had recently become progressively worse. On examination the tonsils were enormously enlarged and of fiery red colour. The pillars of the fauces were also much engorged, but the pharyngeal wall was not congested. The accessory nasal sinuses were clear to transillumination. The glands of the neck on both sides were enlarged. They were very hard but not adherent to surrounding structures.

*Treatment.*—Bilateral tonsillectomy by dissection was carried out and radium was stitched into both tonsil beds. A radium collar was applied externally for five days, a total dosage of 20,000 milligram hours being given. The patient was discharged a week later feeling well, with instructions to report for examination in a few weeks' time.

*Subsequent History.*—When next seen after a few weeks a small nodule was observed in the right tonsil bed; this was removed for microscopical examination and proved to be of similar structure to the tonsillar growth previously removed. The patient became very depressed and went downhill rapidly; death occurred at home about six weeks later, not apparently due to the local condition in

LYMPHO-EPITHELIOMA.

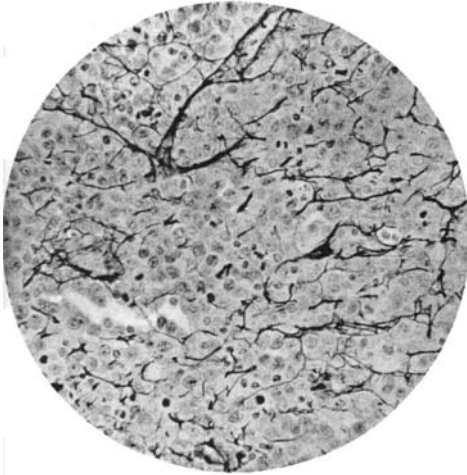


FIG. 18.

Case V. Silver impregnation of sarcoma-like area showing alveolar structure. Mitoses numerous.  $\times 190$ .

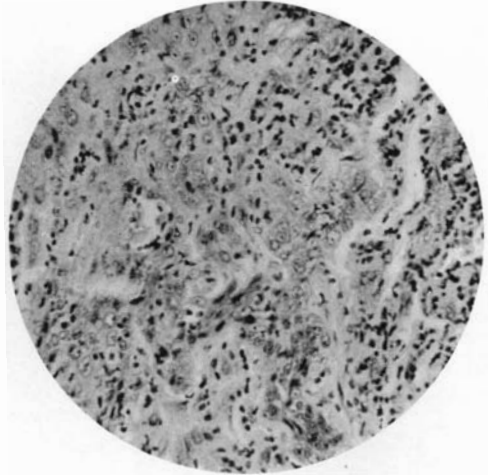


FIG. 19.

Case V. Strands of large pale cells with vesicular nuclei, resembling those in Figs. 13 and 14, numerous lymphocytes in stroma and among epithelial cells.  $\times 190$ .

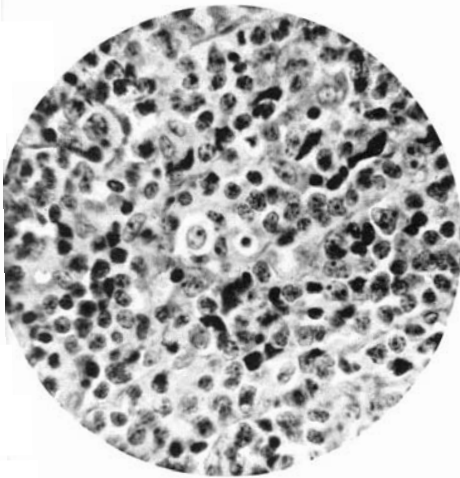


FIG. 20.

Case VI. Solid alveoli of pale-staining epithelial cells and lymphocytes.  $\times 380$ .



FIG. 21.

Case VII. The advancing edge of the neoplasm showing penetration of lymphoid tissue by large pale-staining epithelial cells.  $\times 190$ .

## The Pathology of Nasopharyngeal Tumours

the throat or to any extension from it. No post mortem examination was obtained.

*Pathological Specimen.*—Both tonsils were received for examination, they were greatly enlarged and of fairly firm consistence and showed superficial ulceration. The cut surface presented a uniform highly cellular appearance. In the affected portions the normal architecture of the tonsils is obliterated and replaced by a highly cellular new growth consisting chiefly of round or oval elements somewhat larger than lymphocytes, with scanty cytoplasm and nuclei of more open texture and less rich in chromatin (Fig. 17). These areas present a sarcomatous appearance but silver impregnation of the reticulum reveals a definitely alveolar arrangement throughout (Fig. 18). In such areas the cells occur in loosely packed masses without any clear architectural pattern but there are distinct trabeculae and epithelial-like cells from which the round cells appear to be derived by migration. The epithelial elements form an irregular network, in the meshes of which lie densely packed lymphocytes and also the large oval cells described above. Lymphocytic invasion of the trabeculae is sometimes prominent, occasionally large cells with convoluted nuclei occur singly or in small groups, these somewhat resemble the giant cells of Hodgkin's disease and this resemblance is increased by patches of eosinophil infiltration.

An unusual feature is the occurrence in both tonsils of infiltrating strands of clearly defined squamous epithelial cells, most of which show no keratinization (Fig. 19) but resemble closely the epithelial columns of Cases I and III. These are supported by a well-formed reticular stroma which does not penetrate between the individual cells but in places the marginal cells separate off and wander into the sarcoma-like areas through gaps in the reticular membrane.

CASE VI.—C.B., female, æt. 53. Admitted to the Dundee Royal Infirmary May 10th, 1933, complaining of swelling in the back of the throat and difficulty in swallowing. The patient had observed dryness and discomfort in the throat about three years previously, but at that time no obvious abnormality was detected. On examination a large fleshy mass of bright red colour was seen springing from the left tonsil; the right tonsil was also enlarged, but less so. The glands below and behind the angle of the jaw on the left side were enlarged to about the size of a bean. They were not painful or tender and were not attached either to the skin or to the deeper structures.

*Treatment.*—A portion of the tonsil was removed for microscopical examination and the following day radium was applied externally to the left side of the neck; thereafter a daily application of radium was given for ten days, a total of 6,600 milligram hours.

*Subsequent History.*—The swelling of the tonsils and of the glands

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of the neck disappeared with great rapidity and the patient has since remained perfectly well. She reports frequently for examination and there is no evidence of local or other recurrence to date; she has now remained well for over five years.

*Pathological Specimen.*—Several fragments of soft, friable, whitish tumour tissue were received. Microscopically, the tonsillar architecture is totally obliterated, being replaced by highly cellular new growth composed of round or oval cells densely packed together. Immediately beneath the surface epithelium the cells are larger with less deeply stained nuclei and are arranged in distinct trabeculae. In the deeper portion, these epithelial columns fade off insensibly into the masses of round and oval cells (Fig. 20). Mitotic figures are very numerous throughout the growth. Silver impregnation of the reticulum shows that a distinctly alveolar arrangement is present even in the more sarcoma-like areas. In this case the epithelial character of the cells is less obvious and it is difficult to demonstrate where the epithelial columns cease and lymphocytic cells begin, as all gradations can be traced between the larger cells in frankly alveolar formation and the small deeply stained cells densely packed in fine reticular stroma.

CASE VII.—M.B., female, age unstated. There was a history of swelling of the neck of nine weeks' duration, more on the right side and increasing rapidly in size. Six weeks prior to admission swelling of the right tonsil was noted; this was not painful and caused no difficulty in swallowing. On examination the right tonsil was found to be much enlarged and hard with ulceration on the internal aspect. Marked swelling was present in the submaxillary and submental regions. On November 27th, 1932, the tonsil was removed for examination and three weeks later deep X-ray therapy was instituted. The immediate improvement under radiation was striking and the patient has remained well up-to-date, the survival period being now over five years.

*Pathological Specimen.*—The right tonsil was sent for pathological examination. Microscopically, a portion of normal tonsillar tissue persists at one end of the specimen and the shape of the organ is in general preserved. The greater part of the tonsil is replaced by a neoplasm composed of fairly large cells loosely packed together; in places the cells are separate from one another but their cytoplasm is very poorly defined (Fig. 21). In other parts the cells are united to form a sort of syncytial network. In all parts the individual cells possess rather large vesicular nuclei and mitotic figures are fairly numerous. Lymphocytic infiltration is patchy, but occurs both in the stroma and throughout the masses of tumour cells. A prominent feature is the presence of a clear reticular network in the meshes of which the tumour cells lie in clearly defined alveolar

LYMPHO-EPITHELIOMA.

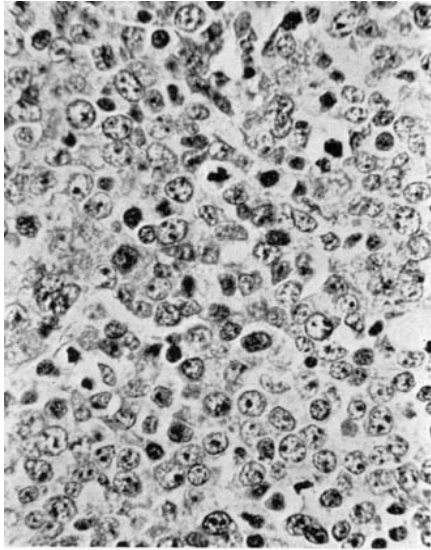


FIG. 22.

Case VII. Here the tumour cells are of frankly epithelial character and are arranged in trabeculae with lymphocytic infiltration throughout. Note resemblance to Fig. 23.  $\times 380$ .

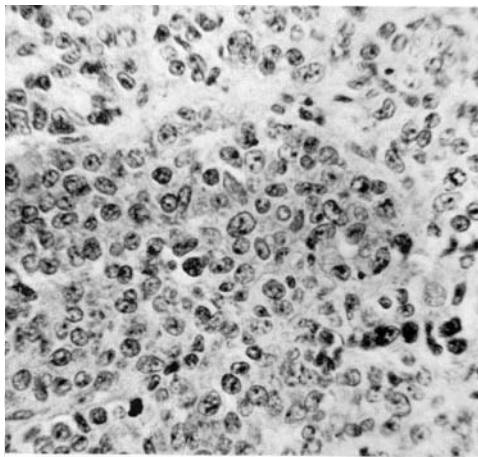


FIG. 23.

Case VIII. Groups of large epithelial cells without clearly defined cell boundaries; no keratinization, no intercellular bridges. Lymphocytic infiltration scanty. Transitional-cell carcinoma or lympho-epithelioma (cf. Fig. 22).  $\times 310$ .

## The Pathology of Nasopharyngeal Tumours

formation. Silver impregnation reveals a delicate network of reticular fibres separating the tumour cells into sharply defined alveoli. The lymphoid tissue of the tonsil is not totally destroyed but persists at one end of the specimen and here the separation of lymphoid and neoplastic cells is unusually distinct. This, together with the scantiness of lymphocytic infiltration, might justify removing this case from the group of lympho-epithelioma and classifying it along with the succeeding case as a transitional-celled carcinoma. An interesting finding is the occurrence, in one area, of invasion of the covering squamous epithelium of the tonsil by small groups of neoplastic cells, which appear to be living intra-epithelially.

CASE VIII.—W.C., male, æt. 60. About three months before admission the patient had a severe cold which culminated in otitis media; the throat then became painful and difficulty in swallowing appeared. More recently he had the feeling of something bursting in the throat and coughed up blood. He had been in poor health for some time and stated that he had lost about two stones in weight. There was also a complaint of pain in the right buttock radiating into the leg. On examination the patient was fairly well nourished. Speech was thick and the cervical glands on the left side were enlarged and hard. The epiglottis was pushed over to the right by a swelling in the left vallecula and arytenoid region, which prevented a satisfactory view of the cords. The left mastoid was opened and pus was obtained. By direct laryngoscopy a fungating tumour was found on the right side of the pharynx involving the epiglottis and extending some distance round the pharyngeal wall. A small portion was removed for microscopical examination. The patient's temperature continued to swing between 100° and 105° F. Death occurred two days later. Post mortem examination was not obtained.

*Pathological Specimen.*—The small portion of tissue received is covered by squamous epithelium, ulcerated at one end and extensively infiltrated by a cellular growth of carcinomatous type. The constituent cells are of fairly large size and have large vesicular nuclei; the cytoplasm is poorly defined and in many places the cell outlines cannot be distinguished (Fig. 23). In one area the overlying squamous epithelium is invaded by the tumour cells which are spreading intra-epithelially. Lymphocytic infiltration occurs in small patches here and there, chiefly in the stroma surrounding the tumour alveoli. Invasion of the epithelial columns by lymphocytes is not marked. The tumour cells show no tendency to keratinization and there are no intercellular bridges. This tumour is classified as a transitional-celled carcinoma but the illustration shows the striking resemblance to certain parts of the other tumours.

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Verf. berichtet über die Einteilung und das anatomische Vorkommen von 122 Neubildungen des Retronasalraumes, der Tonsillen und des Pharynx. 64% werden als Plattenepithelkrebs, 10% als Lympho-epitheliome und transitional-cell Karzinome bezeichnet; in 8% handelte es sich um Mischgeschwülste der Mundhöhle. Ein Fall betraf ein malignes Rhabdomyom. Hauptsächlich werden Lympho-epitheliome besprochen und ihre Reaktion auf Bestrahlung ausführlich beschrieben.

L'auteur présente la classification et la distribution anatomique de 122 néoformations du naso-pharynx, des amygdales et du pharynx. Soixante-quatre pour cent sont classifiés comme épithéliomes squameux, dix pour cent comme lymphoépithélioma et carcinome à cellules transitoires, et huit pour cent étaient des tumeurs mixtes parabucales. Il signale un cas de rhabdomyome malin. Il attire tout spécialement l'attention sur les lympho-épithéliomes et donne en détail leurs réactions à l'irradiation.