Chapter 12: Tumours of the oropharynx

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The oropharynx is that part of the pharynx extending from the level of the hard palate above to the hyoid bone below. Its boundaries for the purposes of classification of tumours are shown. The subdivisions of the oropharynx are shown in Table 12.1.

Table 12.1 Oropharyngeal sites (UICC and AJC)

(1) Anterior wall (glosso-epiglottic area)
   (i) tongue posterior to the vallate papillae (base of tongue or posterior third)
   (ii) vallecula (UICC only)
   (iii) anterior (lingual surface of epiglottis (UICC only))

(2) Lateral wall
   (i) tonsil
   (ii) tonsillar fossa and faucial pillars
   (iii) glosso-tonsillar sulci

(3) Posterior wall

(4) Superior wall
   (i) inferior surface of soft palate
   (ii) uvula.

A further subdivision, into the palatine arch and the oropharynx proper is of practical importance because squamous carcinoma of the palatine arch is less aggressive and metastasizes later than that elsewhere in the oropharynx.

Two further points of surgical anatomy require emphasis. First, some authors include the retromolar trigone as part of the oropharynx while others do not. The retromolar trigone is included in the oral cavity in the UICC/AJC (Union Internationale Contre Le Cancer/American Joint Committee) definition, and tumours of the trigone should not be considered as oropharyngeal tumours. Second, tumours of the anterior (lingual) surface of the epiglottis and the vallecula are regarded as laryngeal tumours and are classified as such by the AJC. They behave and are treated in a similar way to such tumours. However, these structures are part of the oropharynx in the UICC classification.

The oropharynx contains three structures of importance for the development of tumours:

(1) a lining of squamous epithelium;
(2) the paired tonsils, and the collection of minor lymphoid tissue in the base of the tongue;
(3) collections of minor salivary tissue within the epithelium concentrated in the soft palate, the uvula and the capsule of the tonsil.

The surgical anatomy of the oropharynx including its lymphatic drainage is described in Volume 1, Chapter 10.
Pathology

Approximately one-third (35%) of pharyngeal carcinomata arise in the oropharynx. The oropharynx contains squamous, lymphoid and salivary tissues. Tumours may arise from each of these, and their relative incidence is shown in Table 12.2.

Table 12.2 Oropharyngeal tumours

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous carcinoma</td>
<td>70%</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphoma</td>
<td>25%</td>
</tr>
<tr>
<td>Salivary tumours</td>
<td>5%</td>
</tr>
</tbody>
</table>

Epithelial tumours

benign tumours such as papillomata arise from squamous epithelium but are of little pathological interest. The most important epithelial tumour is the squamous carcinoma; the lymphoepithelioma, which is a variant of this, will also be discussed.

Squamous carcinoma

The age and sex incidence of squamous carcinoma of the oropharynx are shown. As might be expected in an area with a rich lymphatic drainage, lymph node metastases are common and may be the presenting feature.

Bilateral nodes are less common than fixed nodes in this disease (fixation is, of course, a subjective assessment varying from one examiner to another). Enlargement of lymph nodes in squamous carcinoma is not influenced by the histological type of the tumour, and is as common in anaplastic tumours as in well-differentiated lesions.

The detection of lymph node metastases is very inaccurate because of differences between examiners, and because some palpable nodes do not contain tumour, whereas some impalpable nodes do. The level of the lymph nodes in the neck is shown.

The sites of origin of squamous carcinoma are listed in Table 12.3. Tumours of the oropharynx are staged under the UICC/AJC scheme, with the following conditions:

(1) the classification applies only to carcinoma. It is not clear whether the classification includes all carcinomata or only squamous carcinoma

(2) there must be histological verification of the disease. The histological features are variable: keratinization may be present or absent, and the degree of differentiation ranges from poorly differentiated or anaplastic tumours to well-differentiated examples reminiscent of normal structures. Spindle and basal cell variants are occasionally seen

(3) the extent of disease must be assessed clinically, radiographically and endoscopically. The T classification for both UICC and AJC is shown in Table 12.4, and that for classification of nodes in Table 12.5.
Table 12.3 Site incidence of squamous cell carcinoma of the oropharynx

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonsil/faucial pillars</td>
<td>50%</td>
</tr>
<tr>
<td>Base of tongue</td>
<td>20%</td>
</tr>
<tr>
<td>Soft palate</td>
<td>10%</td>
</tr>
<tr>
<td>Vallecula and lingual epiglottis</td>
<td>10%</td>
</tr>
<tr>
<td>Posterior wall</td>
<td>5%</td>
</tr>
<tr>
<td>Lateral wall</td>
<td>5%</td>
</tr>
</tbody>
</table>

Another primary tumours in the upper alimentary tract or lung is found in about 10% of cases of squamous cell carcinoma of the mouth and oropharynx.

Table 12.4 Classification of the primary tumour (UICC and AJC)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>Pre-invasive carcinoma (carcinoma in situ)</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour 2 cm or less in its greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour more than 2 cm but not more than 4 cm in its greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour more than 4 cm in its greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour with extension to bone, muscle, skin, antrum, neck etc</td>
</tr>
<tr>
<td>Tx</td>
<td>The minimum requirements to assess the primary tumour cannot be met</td>
</tr>
</tbody>
</table>

Table 12.5 Nodal classification

(A) **UICC Classification**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Regional lymph nodes</td>
</tr>
<tr>
<td>N0</td>
<td>No evidence of regional lymph node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Evidence of involvement of movable homolateral regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Evidence of involvement of movable contralateral or bilateral regional lymph nodes</td>
</tr>
<tr>
<td>N3</td>
<td>Evidence of involvement of fixed regional lymph nodes</td>
</tr>
<tr>
<td>Nx</td>
<td>The minimum requirements to assess the regional lymph nodes cannot be met</td>
</tr>
</tbody>
</table>

(B) **AJC**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Minimum requirements to assess the regional lymph nodes cannot be met</td>
</tr>
<tr>
<td>N0</td>
<td>No clinically positive node</td>
</tr>
<tr>
<td>N1</td>
<td>Single clinically positive homolateral node 3 cm or less in diameter</td>
</tr>
<tr>
<td>N2</td>
<td>Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter or multiple clinically positive homolateral nodes, none more than 6 cm in diameter</td>
</tr>
<tr>
<td>N2a</td>
<td>Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter</td>
</tr>
<tr>
<td>N2b</td>
<td>Multiple clinically positive homolateral nodes, none more than 6 cm in diameter</td>
</tr>
<tr>
<td>N3</td>
<td>Massive homolateral node(s), bilateral nodes, or contralateral node(s)</td>
</tr>
<tr>
<td>N3a</td>
<td>Clinically positive homolateral node(s), one more than 6 cm in diameter</td>
</tr>
<tr>
<td>N3b</td>
<td>Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately - N3b: right, N2a: left, N1)</td>
</tr>
<tr>
<td>N3c</td>
<td>Contralateral clinically positive node(s) only.</td>
</tr>
</tbody>
</table>
**Lymphoepithelioma**

The term lymphoepithelioma was first used by Regaud and Schmincke independently but simultaneously in 1921. The tumour is widely permeated by lymphocytes: the Regaud type contains nests of non-keratinizing squamous cells and the Schmincke type exhibits isolated transitional cells (hence the alternative term of transitional cell carcinoma).

The important clinical characteristics of this tumour are its extreme radiosensitivity, its tendency to metastasize and its sites - the nasopharynx, the tonsil and the base of the tongue. Quick and Cutler recognized it in 1927 as a subdivision of squamous carcinoma, and evidence for and acceptance of this view have grown steadily since. Sometimes these tumours may be confused with lymphoma, as the squamous cell component may be extremely undifferentiated. Immunohistology using the leucocyte common and cytokeratin antibodies may be helpful in doubtful cases. Surface marker studies of the lymphocyte population in lymphoepithelioma have shown these cells to be reactive, because they are composed of B cells, T-helper and T-suppressor cells and show no evidence of monoclonality or phenotypic restriction. Post-mortem studies on patients who died of this disease also show that the tumour is a variant of squamous cell carcinoma, with a coincidental lymphocytic content, because metastases to non-lymphatic sites, particularly the liver, contain tumour cells resembling the primary tumour only and do not contain lymphocytes.

**Aetiology**

Squamous cell cancer is uncommon before the age of 50 but increases in frequency thereafter. Men are affected about five times more often than women. Keratosis with dysplasia is well recognized as a precancerous condition in the mouth, but it seldom occurs in the oropharynx except on the palatine arch. As with oral cancer, tobacco and alcohol are thought to be important causal factors: however, those who believe this fail to answer the embarrassing question as to why the incidence of oral cancer has fallen to 10% of its former incidence in the last 50 years, at a time when the use of tobacco and alcohol have increased. The mucosal atrophy associated with iron-deficiency anaemia might be the precursor of oropharyngeal cancer in women. Syphilis and dental sepsis are no longer important factors in the UK.

**Tumours of lymphatic origin**

Hodgkin's disease is very rare in the oropharynx. Non-Hodgkin's lymphoma accounts for about 15% of tumours in this site, and most cases are of B-cell type. These have features in common with other tumours of MALT (mucosa associated lymphoid tissue) sites, remaining localized to the MALT sites longer than nodal lymphomata. The commonest type of B-cell lymphoma in the oropharynx is the large cell lymphoma of high grade malignancy.

**Aetiology**

As for most lymphomata, the aetiology is largely unknown. Certain associations are recognized, such as the development of lymphoma, often of lymphocytic or immunocytic type (*see below*), in long-standing cases of Sjögren's disease. African Burkitt's lymphoma, a B-cell high grade lymphoma of lymphoblastic type, shows a well-known association with
immunosuppression due to chronic malaria infection. Epstein-Barr virus is present in nearly all cases, and the lymphoma appears to favour sites of current epithelial proliferations: the odontogenic tissues in the young child, and the breast in pregnant women. T-cell lymphomata, rare in the oropharynx, show the well-documented association with human T-lymphotropic virus type I (HTLV-I), especially in Japan and the Caribbean countries.

Many of the lymphomata of the oropharynx are primary in the sense that there is no demonstrable deposit elsewhere in the body at the time of diagnosis. Sometimes, however, they appear to be secondary to, or coincident with deposits at other sites. These may include the gastrointestinal tract, lung and testis.

**Classification**

Until the early 1970s, classification of lymphomata was based on morphological features only. A bewildering variety of schemes was used, the best known being that of Rappaport (Rappaport, 1966). When immunological data on the cellular immunoglobulins, and later surface markers, of the lymphoma cells became available, it was apparent that the morphological criteria did not always correspond with the cells' immunological functional characteristics. In particular, Rappaport's 'histiocytic' group of large cell lymphomata was found to be principally of B-cell type, not of the macrophage origin implied by the term. The Kiel classification (Lennert et al, 1975, 1978) is widely used in Europe, and incorporates immunological and morphological data (*Table 12.6*). In over 10 years of use, only minor modifications have been required. The conceptually similar classification of Lukes and Collins (1974) is more widely used in the USA.

**Table 12.6 Kiel classification of non-Hodgkin's lymphomata (simplified from Lennert et al, 1978)**

1. Low grade malignant lymphomata
   a. lymphocytic lymphoma (B cell, T cell, hairy cell leukaemia, mycosis fungoides and Sézary's syndrome, T-zone lymphoma)
   b. immunocytoma
   c. plasmacytoma
   d. centrocytic lymphoma
   e. centroblastic/centrocytic lymphoma (follicular or diffuse)

2. High grade malignant lymphomata
   a. centroblastic lymphoma
   b. lymphoblastic lymphoma (B or T)
   c. immunoblastic lymphoma (with or without plasmablastic differentiation, B and T).

NB: Centroblastic and immunoblastic lymphomata may be difficult to distinguish and are sometimes grouped together as 'large cell lymphomata'.
Table 12.7 Histological types of non-Hodgkin's lymphoma of the oropharynx (based on a personal series of 100 patients)

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low grade</td>
<td></td>
</tr>
<tr>
<td>Centroblastic/centrocytic B-cell lymphoma</td>
<td>16%</td>
</tr>
<tr>
<td>Immunocytoma</td>
<td>13%</td>
</tr>
<tr>
<td>T-cell low grade</td>
<td>7%</td>
</tr>
<tr>
<td>Lymphocytic lymphoma</td>
<td>2%</td>
</tr>
<tr>
<td>Centrocytic lymphoma</td>
<td>2%</td>
</tr>
<tr>
<td>High grade</td>
<td></td>
</tr>
<tr>
<td>Other B-cell lymphomata (lymphoblastic immunoblastic)</td>
<td>3%</td>
</tr>
<tr>
<td>Centroblastic lymphoma</td>
<td>53%</td>
</tr>
<tr>
<td>T-cell high grade</td>
<td>4%</td>
</tr>
</tbody>
</table>

The commonest types of lymphoma in the oropharynx (Table 12.7) are centroblastic (high grade) and centroblastic/centrocytic (low grade) (CB/CC). The centroblastic lymphoma is composed predominantly of large follicle centre transformed lymphocytes with prominent nucleoli, together with variable numbers of infiltrating reactive T cells. This tumour behaves in a highly aggressive manner, but if at an early stage (I and II) may be curable by local treatment. The low grade lymphomata are less aggressive, and contain mixtures of B cells of various types: follicle centre cells in CB/CC lymphoma, lymphocytes in lymphocytic lymphoma and immunocytes (lymphoplasmacytoid cells) in immunocytoma. All types also contain T cells, presumably of reactive nature. Paradoxically, these low grade tumours may be less curable than high grade lymphoma because, even though they progress more slowly, they are frequently disseminated by the time of diagnosis (stage III and IV).

The relative site incidence of non-Hodgkin's lymphoma of the head and neck and the staging system (AJC) are shown in Tables 12.8 and 12.9.

Table 12.8 Site incidence of non-Hodgkin's lymphoma of the head and neck

<table>
<thead>
<tr>
<th>Site</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes</td>
<td>25%</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>45%</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>15%</td>
</tr>
<tr>
<td>Nose and sinuses</td>
<td>10%</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>5%</td>
</tr>
</tbody>
</table>

Salivary gland tumours

Salivary gland tumours can occur in the oropharynx, but it is obvious from all reported series that few oropharyngeal tumours are of salivary origin, and that only a small proportion of all salivary tumours arise in the oropharynx.

In a large series of 530 minor salivary gland tumours, 3% affected the oropharynx, almost all of them arising in the tonsillar area. It is difficult to draw up a histological classification because of the small numbers involved, the different histological terms, and different referral patterns, but at least one-half of the salivary gland tumours of the
oropharynx are malignant, adenoid cystic carcinoma forming the vast majority. At this site the tumour behaves in the same way as elsewhere: it spreads by permeation along nerve sheaths, metastasizes to lymph nodes, bone and lung and has a very poor long-term prognosis.

**Staging classification of non-Hodgkin's lymphoma**

Stage I  
Involvement of a single lymph node region (I) or of a single extralymphatic organ site or site (IE)

Stage II  
Involvement of two or more lymph node regions (number to be stated) on the same side of the diaphragm (II); or, localized involvement of an extralymphatic organ or site of one or more lymph node regions on the same side of the diaphragm (IIE)

Stage III  
Involvement of lymph node regions on both sides of the diaphragm which may also be accompanied by local involvement of extralymphatic organs or site (IIIE) by involvement of the spleen (IIIIS), or both (IIIE + S)

Stage IV  
Diffuse or disseminated involvement of one or more extralymphatic organ tissues with or without associated lymph node enlargement. The reason for classifying the patient as stage IV is identified further by specifying the site.

**Clinical features**

**Symptoms**

In 10% of patients the presenting symptom is a lymph node metastasis in the neck. Other symptoms include sore throat, pain on swallowing and referred earache. Large tumours of the base of the tongue give the voice a curious muffled quality. The routine clinical examination of the upper respiratory tract and the neck, not forgetting the axilla, groins, liver and spleen in patients with a lymphoma will not be discussed further.

**Clinical examination**

Two main clinical types of squamous cell carcinoma may be recognized: the exophytic and the ulcerative. The exophytic type spreads superficially and the ulcerative type infiltrates deeply, but exceptions do occur. An adenocarcinoma presents as a smooth non-ulcerated swelling and the malignant lymphomata as enlargements in the tonsillar fossae or base of the tongue. Ulceration eventually supervenes.

The growths can be easily seen provided that good lighting is used, though for those originating in the base of the tongue a laryngeal mirror is needed. Fixation of the palate or tongue should be noted and the area should be palpated with the forefinger to estimate the extent of infiltration. A postnasal mirror should be used to detect extension into the nasopharynx or onto the upper surface of the soft palate. Sometimes a carcinoma may occur deep in the base of the tongue which may not be associated with any abnormality of the surface mucosa. The presenting symptoms may be pain, possibly of the glossopharyngeal neuralgic type, or a node in the neck. It is important to remember that a carcinoma of the
The base of the tongue cannot be excluded merely by inspection with a spatula or a laryngeal mirror - it is essential to palpate the tongue as well if growths of this type are not to be missed.

The neck must be examined carefully for lymph nodes both from in front and, most particularly, from behind the patient using the tips of the fingers. Another primary tumour should be looked for in the upper respiratory tract.

**Investigation**

Radiological examination includes the chest, but radiographs of the pharynx are mandatory for staging carcinoma under the UICC/AJCC scheme. What is to be achieved by this is not clear: tumours of the tonsil have no specific radiographic features and rarely invade the mandible. Computerized tomographic (CT) scans are more useful for showing the extent of the tumour, extension into the pterygoid fossa, and the presence of lymph nodes. The radiological assessment is described more fully elsewhere (Chapter 2). The assessment of the non-Hodgkin's lymphomata is unclear at the moment and is changing rapidly. Broadly speaking investigations should follow routes given below.

**Biopsy**

A biopsy is necessary to confirm the diagnosis and to establish the histology of the growth, since this is of importance in planning treatment. In most cases the biopsy can be performed under topical analgesia, but a general anaesthetic may be needed for lesions of the base of the tongue and to allow the extent of the growth to be determined by palpation. The biopsy specimen needs to be of adequate size to give a reasonable area of tissue for assessment of architecture, as well as cytological detail; needle biopsies are therefore not generally suitable. The lymph node must not be traumatized during removal or subsequent handling: the node consists of a delicate framework containing a fluid population of lymphocytes, and requires more care than perhaps any other pathological specimen. This also applies to biopsies from extranodal lymphoma sites. Fixation must be adequate: the authors' preference is to slice the tissue about 2 mm thick with a sharp, new blade, and then fix it for 24 hours in formalin with added 2% acetic acid (Curran and Gregory, 1980). Embedding is preferably done by a vacuum method, and cutting carried out with a sharp knife to give sections 2-3 microm thick. Plastic sections are not essential, but may add detail in certain cases, notably T-cell lymphomata.

Part of the biopsy should be snap frozen, unfixed in liquid nitrogen or carbon dioxide/isopentane, then stored at below -70°C for immunocytochemical studies (Nash, 1986). Few antibiotics work satisfactorily on fixed tissue; the availability of frozen tissue enables diagnosis in many otherwise difficult cases. Appropriate precautions must be taken to safeguard staff from infection when handling such material. Immunostaining can then be carried out when convenient, usually after the paraffin sections are available. The preferred current antibody panel is listed in Table 12.10. In the future, increasing use of gene probes will no doubt allow characterization of lymphomata according to gene re-arrangement and oncogene expression: stored frozen material is also suitable for these studies.
Table 12.10 Monoclonal antibodies used in the study of lymphomata

**B-cell related**
- Pan-B
- Immunoglobulins (IgA, IgG, IgD, IgM, kappa and lambda light chains)
- Dendritic reticulum cell
- Common leukaemia antigen
- HLA-Dr(Ia)

**T-cell related**
- Pan-T
- E-receptor
- Mature thymocyte
- Prethymic cells
- T-helper
- T-suppressor

**Other**
- Leucocyte common antigen
- Epithelial antigens (various)
- Macrophage.

**Blood investigation**

This should include complete blood count, erythrocyte sedimentation rate (ESR) urinalysis, liver function tests, plasma proteins and immunoglobulins.

**Bone marrow aspiration and biopsy**

The bone marrow biopsy is a vital part of lymphoma staging, and it is important that a trephine be taken as well as an aspirate: the proportion of positives in bone marrow aspirates from patients with CB/CC lymphoma may be as low as 10%, while trephines give a figure of at least 50%. The bone marrow is handled in a similar manner to the tumour biopsy specimen, but decalcification is required. EDTA has been used for this purpose, which although slower than strong acids, gives much better morphology. Bone marrow may also be examined by immunocytochemical methods on frozen sections where appropriate.

Bone marrow involvement by lymphoma may take several forms (Bartl et al, 1984). In involvement by lymphocytic and immunocytic lymphoma, the pattern is frequently diffuse, which makes minimal involvement difficult to detect. Some small nodules may be seen: these must not be confused with the lymphoid nodules frequently present in normal marrow, especially in elderly people. CB/CC lymphoma frequently gives a nodular picture in the marrow, but these are large pale nodules containing follicular centre cells, and are clearly abnormal. A diffuse pattern may also occur, and this does not seem closely related to the presence of nodularity in the primary lymphoma. Centroblastic lymphoma is less frequently seen in the marrow, but forms clumps or sheets of the large transformed follicle centre cells. Individually scattered centroblasts are less frequently seen and, if present in small numbers, might be confused with myeloid precursors.
Percutaneous liver biopsy

While a wedge biopsy at the time of laparotomy gives the best results, an early percutaneous needle biopsy gives such a high yield of positive results that it usually precludes the need for laparotomy.

Radiology

This should include chest radiograph, skeletal survey, gastrointestinal series.

Pedal lymphography

Laparotomy was a standard procedure in the management of Hodgkin's disease but it certainly has no place in the management of the non-Hodgkin's lymphomata. Exploratory laparotomy with splenectomy may reveal disseminated disease, but this can usually be performed by simpler means, notably by lymphography the accuracy of which is about 95%.

Treatment of squamous carcinoma of the oropharynx

At least six forms of management are available for oropharyngeal tumours: no specific treatment; radiotherapy; surgery; combined surgery and radiotherapy; chemotherapy; and cryosurgery.

No specific treatment

It is noticeable, but perhaps not surprising, that very few accounts of the treatment of any head and neck cancer contain a clear definition of those patients not treated, the reasons for withholding treatment, and the fate of those who do not receive specific therapy. Yet a fairly large proportion of patients with any head and neck cancer are not treatable with any prospect of success - about 20% of patients with oropharyngeal carcinoma in the authors' experience. The question of untreatability of carcinoma is inevitably coloured by personal philosophy; the authors' contraindications to surgery are shown in Table 12.11, but it is realized that there may be controversy over these indications. Patients with one of the first four conditions shown have a very poor chance of survival: 10% or less at 1 year, and 5% or less at 5 years, and it is doubtful whether they should be offered an operation. Radical surgery inevitably mutilates and deprives the patient of important functions. Is it, therefore, justifiable to operate on the many who do not survive, for the sake of those few who do? Each surgeon must decide this for himself.

Table 12.11 Contraindications to surgery of oropharyngeal tumours

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Anaplastic tumours</td>
</tr>
<tr>
<td>Fixed bilateral neck glands</td>
</tr>
<tr>
<td>Trismus</td>
</tr>
<tr>
<td>Horner's syndrome</td>
</tr>
<tr>
<td>Distant metastases</td>
</tr>
<tr>
<td>Patient's refusal</td>
</tr>
<tr>
<td>Advanced age (over 75 years)</td>
</tr>
<tr>
<td>Poor general condition.</td>
</tr>
</tbody>
</table>
The temptation to give 'palliative treatment' for the patient who has an incurable tumour must also be mentioned. Usually all that is palliated is the surgeon's inability to accept reality! Of course, there are occasional unexpected successes, and young patients should seldom be denied the chance of treatment, but it should be remembered that radiotherapy causes a very sore mouth and a general upset lasting for months. The authors' figures show that the average period of survival of a patient with a head and neck cancer which is not suitable for radical treatment is 11 weeks. This is rather less than the period taken for the radiotherapy reaction to settle, so that the net result of palliative radiotherapy may be in fact an increase in the patient's discomfort. It should also be remembered that the vast majority of the general population is well aware of the site and significance of the regional radiotherapy unit. If such a unit pursues a frequent policy of giving palliative therapy which is followed rapidly by death, the local population can be forgiven for regarding the regional radiotherapy centre with dread.

Radiotherapy

Radiotherapy is undoubtedly the treatment of choice for non-Hodgkin's lymphoma without disseminated disease, and for many squamous carcinomata. Reviews of treatment of large series of squamous carcinomata are available.

Ledermann's series extends over a longer period from 1933 and shows an overall survival of 20% (Ledermann, 1967), whereas Fletcher and Lindberg's (1966) series from the USA, starting in 1954, shows 5-year survival of 35% for tonsillar carcinoma, and of 50% for palatal tumours. The chance of control of the primary tumour increased by about 20% with the introduction of supervoltage therapy, although this increase may not be reflected in an increased survival rate. Probably the greatest improvement over the last few decades has been the extension of first-class facilities to cover the whole population in the western countries - a political and not a medical achievement.

Surgery

Surgery was first described for tonsillar carcinoma at the end of the 19th century but, at that time, must have been a fearful undertaking for both patient and surgeon. There is little wonder that, when radiotherapy became available, surgery was abandoned by all but a few.

Until antibiotics became available it was impossible to open the neck and the pharynx at the same time because of the danger of infection. It was thus impossible to treat most of these patients surgically because of the presence of enlarged lymph nodes.

In the 1940s sulphonamides and then penicillin became available, and Hayes Martin was thus able to extend the operation of hemimandibulectomy and resection of the floor of the mouth to the treatment of tonsillar carcinoma, and to put the operation on a safe permanent footing. In his textbook published in 1957 he described how the term commando operation came to be used for this operation: the technical definition of the operation was too long-winded for everyday use and was therefore shortened to commando (combined neck dissection, mandibulectomy and resection of the oropharynx). At that time the commandos were recruited for aggressive warfare in difficult circumstances. His house staff borrowed the term and applied it to the operation (perhaps the analogy was close!).
Now that surgery can provide a cosmetically and functionally satisfactory end-product, what should be its place in treatment of carcinoma of the oropharynx, particularly of the tonsil? The patients who should not be offered surgery, for example those with trismus or fixed bilateral neck glands, have been mentioned above (see table 12.11). Furthermore, most patients with an oropharyngeal tumour without a palpable lymph node of the neck do tolerably well when treated by radiotherapy and should be offered this form of treatment initially. There thus remain two types of patients who should have surgery: those who have failed to benefit from radiotherapy, and those with a tonsillar carcinoma and a palpable gland in one side of the neck. Although the latter patient is treated in many centres by radiotherapy followed by a radical neck dissection, in the authors' experience the gland in the neck may become inoperable by the time the radiotherapy reaction has settled, and such a policy gives poor results; a 5-year survival of 12.5% for instance in Ledermann's series. It has been shown fairly clearly that surgery achieves better results than radiotherapy for larger tumours with nodes in the neck: 60% compared with 0%.

For tumours of the lingual surface of the epiglottis, supraglottic laryngectomy gives very good results. Tumours at this site are uncommon but treatment with radiotherapy is not very successful; a recent series did not contain a single survivor at 5 years. Better results are obtained with supraglottic laryngectomy, and this form of treatment deserves wider use and recognition for this tumour; tumours at this site must certainly be treated surgically.

**Treatment of neck nodes**

Few surgeons would disagree that palpable unilateral nodes should be treated by radical neck dissection. Many would treat bilateral nodes similarly but the results are not good. Fixed nodes are occasionally worth resecting, but the natural history of the disease can rarely be affected in the presence of bilateral fixed nodes. The treatment of the neck in patients with no palpable nodes must also be discussed. It is well known from pathological studies that a proportion of such patients have lymph nodes which contain tumour but which are not palpable. On this fact rests the policy of prophylactic neck dissection or prophylactic neck irradiation. Sadly, it has been shown by controlled trials that neither policy improves the survival rate compared to a 'wait and see' policy, although the local control rate might be improved.

**Combined surgery and radiotherapy**

An analysis of the failures of radiotherapy shows that there is a high incidence of local recurrence, and this has led some surgeons and radiotherapists to wonder if combined treatment would offer better results. As surgery fails at the periphery and radiotherapy at the centre of the tumour, a combination of the two might do better than either. Much of the early scientific work on preoperative radiotherapy was done by Powers and Tolmach (1964) who showed that a very high proportion of viable cells in a tumour (as many as 99% or more) were killed by 1000 cGy, higher doses being necessary to achieve eradication because of the exponential relationship between cure and dose. The argument advanced was that low dose preoperative radiotherapy, because it killed nearly all of the viable cells, should drastically reduce the chances of local implantation and dissemination, and at the same time not increase the morbidity. Powers and Tolmach investigated this in mice and showed that a low dose of
preoperative radiotherapy led to a significant increase in survival after surgery for a variety of induced tumours.

The causes of failures due to surgery and radiotherapy are as follows:

**Surgical failures**

(1) The primary tumour may be cut across because some carcinomata proliferate along tissue planes

(2) regional spread in the lymphatics may not be encompassed by the operated field

(3) distant undetected vascular spread may have occurred before operation

(4) surgical manipulation may spread neoplastic cells into the lymphatics, blood vessels or the wound.

**Radiation failures**

(1) The central portion of the primary tumour may be relatively anoxic, and hence most radioresistant. While peripheral, better oxygenated tumour might be killed, the central portion could regain its malignant potential after a period of quiescence

(2) metastases to lymph nodes are relatively radioresistant

(3) local or distant spread outside the treated field may have taken place before therapy, and radiation then does not encompass the lesion

(4) the tumour may be radioresistant. That is, may be better able to resist ionizing radiation than surrounding vital tissue.

If these factors are considered together it seems possible that radiation followed by surgery planned to encompass the original estimated extent of the tumour may offer higher survival rates. For example, the peripheral extensions of malignant cells at the primary site inadvertently left behind by the surgeon in the unirradiated patient may be eliminated by the combined approach. The core of poorly oxygenated neoplasms destined to recrudescence in irradiated patients (after lurking undetected beneath an intact mucosa) may be eliminated by surgery. Furthermore, lymphatic metastases leading to failure of radiotherapy are removed by combined therapy. Cells spilled at operation after radiation therapy may be less plentiful because the greater part of the tumour has been killed, and less able to resume production. Finally, radiation may 'seal off' lymphatic channels and thus reduce the chance of manipulative dissemination of tumour cells.

It must also be recognized that there are patients who cannot be helped by preoperative radiotherapy, including patients with metastases (evident or unrecognized) and patients with a non-recurring carcinoma, for example, small skin tumours.
One of the main criticisms of preoperative irradiation is that the optimal dose and the benefit, if any, have seldom been investigated by rigidly controlled, randomized prospective trials. Most investigators have contented themselves with comparing survival rates at different times in their own institutions or retrospectively with other institutions. Since survival rates can vary widely depending on referral patterns, philosophy, selection, skill and many other factors, such a 'trial' produces no evidence of any value.

Only one controlled trial has been carried out and sadly this showed that preoperative radiotherapy does not increase survival (Strong et al, 1978).

**Reconstruction after surgery**

There have been four phases of repair of the surgical defect: using *local* flaps, *axial* flaps, *musculocutaneous* flaps, and *free* flaps.

*Local* cervical flaps tend to be of poor viability; one flap in three is lost partially or completely because of necrosis; furthermore, the use of these flaps leads to a temporary fistula on the neck, and possibly exposure of the carotid vessels. This method has now been abandoned.

*Axial* flaps include the *temporal* and *deltoid* flaps. The *temporal* flap has few of the disadvantages of *cervical* flaps. The flap is virtually always viable; the temporary fistula does not leak saliva because it is placed high in the mouth, and the carotid sheath is not exposed. The main disadvantage of this method is the very obvious defect on the forehead. Visible defects of this sort make many patients self-conscious and may even make some reclusive. 'Surgery scars not only the face but also the mind'.

The *deltoid* flap can be used for repair after excision of tumours of the oropharynx. The flap is led in through a temporary fistula and sewn to the edges of the defect. Three weeks later the flap is divided; the distal end is rearranged in the mouth and pharynx; the proximal end of the flap is returned to the chest, and the fistula is closed. It is important at the primary operation to protect the carotid sheath with a levator scapulae muscle graft and to close the lower compartment of the neck. This technique gives quite good results. The necrosis rate of the flap is less than 10% if proper precautions are taken while lifting it; the functional result for speaking and swallowing is good and the appearance of the patients is satisfactory. However, axial flaps have now been largely abandoned.

*Musculocutaneous* flaps are now one of the two standard methods of repair. Much the commonest for repair of tonsillar defects is the pectoralis major flap. At the end of the excisional phase a pectoralis major flap is raised in the standard manner (Volume 1, Chapter 24) and led through the neck into the oropharynx, where it is sutured in place.

*Free* vascularized flaps have also been described, the commonest being the foream flap. The flap is raised during or at the end of the excisional phase (Volume 1, Chapter 24) and is then transferred to the oropharynx. Its artery and at least two veins are reanastomosed in the neck, the facial artery and vein often being convenient sources. This flap is not as
reliable in most surgeons' hands as the pectoralis major flap. Furthermore, the latter flap
provides bulk, and it remains the workhorse of reconstruction for tumours at this site.

Chemotherapy

In contrast with the rosy picture in the lymphomata, the results of chemotherapy for
carcinomata are still disappointing. Chemotherapy may be used for the sole treatment of
advanced/recurrent (end stage) disease or as an adjunct to radiotherapy or surgery. Both types
of treatment have been used in numerous phase II trials, that is where the response of the
tumour is measured, but the survival of the patient is not. Such trials show that 25-50% of
head and neck cancers respond to a wide variety of agents. Sadly these trials do not contain
untreated controls. Only rarely have phase III trials been carried out, that is with untreated
controls and with measurement of the patients' survival. These have shown that only cisplatin
is effective, and that some agents actually reduce survival besides being toxic and expensive.
Furthermore, the prolongation of median survival by cisplatin in patients with end stage
disease is only 3 months. The results of phase III trials of adjuvant chemotherapy with
radiotherapy for treatable tumours have been even more depressing: a high proportion of
tumours respond but there is no effect on survival.

Cryosurgery

The destructive properties of freezing have been known for a long time, but
cryosurgery has been used clinically only in the last decade, and cryosurgical units for clinical
use are now available. Cryosurgery appears to achieve its effective by rupture of nuclear and
cellular membranes, alterations in the lipoprotein components of cell membranes, pH changes,
toxic concentration of electrolytes, polymerization and denaturation of proteins, and vascular
stasis and microthrombi leading to ischaemia. It appears that there must be rapid repeated
freezing and thawing with sufficient duration of freezing to a temperature of at least -20°C
for a good iceball to form. The advantages claimed for cryosurgery are relative avascularity
with little or no postoperative bleeding, minimal tissue response, pain relief mediated by
destruction of sensory nerve endings, resistance of some tissues such as bone to the effect of
freezing and possibly an immunological effect due to the altered antigenicity of the tumour
tissue.

Cryosurgery does have a place in the treatment of tumour of the oral cavity and
oropharynx, but this is mainly for benign lesions, hyperkeratosis, haemangioma and
tonsillectomy in haemophiliacs, for instance. Small salivary tumours may respond well in
unfit patients and small recurrences of squamous carcinoma will also sometimes resolve. But,
for the average large recurrence of squamous carcinoma cryosurgery can at best achieve
reduction in size of the tumour and pain relief. For the vast majority of patients with
squamous carcinoma this form of treatment is at best only palliative.

Treatment of non-Hodgkin's lymphoma

Localized lymphoma is potentially curable by radiotherapy. The use of radiotherapy
followed by chemotherapy is another approach to treatment, and the available data show an
advantage for patients treated by the combined approach compared with radiotherapy alone.
For disseminated non-Hodgkin's lymphomata, the treatment of choice is systemic chemotherapy.

**Single agent chemotherapy**

A wide variety of agents is active in non-Hodgkin's lymphomata. They include the alkylating agents (nitrogen mustard, cyclophosphamide and chlorambucil), the vinca alcaloids (vincristine and vinblastine), procarbazine and prednisone, bleomycin, doxorubicin and the nitrosoureas (BCNU and CCNU). The response to single agent chemotherapy, the duration of response and the overall survival, vary with histological type, results consistently being superior in patients with nodular lymphomata in contrast to those with diffuse disease. Single agent chemotherapy with an alkylating agent may be the treatment of choice in patients with advanced 'favourable' histology.

**Combination chemotherapy**

Combination chemotherapy is the treatment of choice in patients with unfavourable histological types which, in contrast to the favourable histology lymphomata, show a rapidly progressive and fatal course unless complete remission is achieved. Once complete remission has been maintained for 2 years, the probability of relapse is low, suggesting that a cure is possible. A partial response in these histological types conveys little survival benefit.

The first successful combination regimen for non-Hodgkin's lymphomata was cyclophosphamide, vincristine and prednisone, forming the CVP and COP regimens. CVP consists of short pulses of chemotherapy at 21-day intervals with cyclophosphamide on days 1-5 at a dose of 400 mg/m² per day. The Southwest Oncology Group called their regimen COP and administered cyclophosphamide at a dose of 800 mg/m² every 2 weeks for six courses. Other modifications have included cyclophosphamide on day 1 only, a day 1-8 schedule or on a day 1-4 schedule. CVT and COP produce complete responses in 60-90% of patients with favourable histology lymphomata and may be used as an alternative to single agent therapy in this group, although the superiority of combination therapy has not been established.

In an attempt to improve results in the unfavourable histological types more aggressive regimens including MOPP and C-MOPP (cyclophosphamide replacing mustine), and regimens developed by adding bleomycin and doxorubicin to the CVP regimen to form BACOP, have been tested. Each of these regimens have complete response rates of more than 40%.

The Southwest Oncology Group (SWOG) added doxorubicin to a modified COP to produce the CHOP regimen. In a study comparing CHOP to COP, the complete remission rate of 67% achieved with CHOP was superior to the 60% remission rate on COP for patients with diffuse lymphomata. The addition of bleomycin does not appear to improve the results of treatment.

Involvement of the central nervous system is a common problem in lymphomata, being the site of first relapse in 26% of the patients in one series. It is suggested that, in parallel with acute lymphoblastic lymphoma, prophylactic intrathecal therapy should be a component

**Treatment of salivary tumours**

Benign salivary tumours are almost exclusively pleomorphic adenomata, and are treated by local excision with a generous margin. Malignant tumours, generally adenoid cystic carcinomata, are treated by radical surgery as for a squamous carcinoma, followed by appropriate reconstruction. Radiotherapy has no place in the primary treatment of these disease, but is very useful if tumour remains at the surgical margins, and may be useful for palliation.