The Royal College of Pathologists
Pathology: the science behind the cure

Tissue pathways for head and neck pathology

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NICE accredited
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NICE has accredited the process used by The Royal College of Pathologists to produce its Cancer Datasets and Tissue Pathways guidance. Accreditation is valid for 5 years from July 2012. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: www.nice.org.uk/accreditation.

Foreword

The tissue pathways published by The Royal College of Pathologists (RCPath) are guidelines that enable pathologists to deal with routine surgical specimens in a consistent manner and to a high standard. This ensures that accurate diagnostic and prognostic information is available to clinicians for optimal patient care and ensures appropriate management for specific clinical circumstances. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be carefully considered by the reporting pathologist; just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not be deemed negligent or a failure of duty of care.

The guidelines themselves constitute the tools for implementation and dissemination of good practice.

The information used to develop this tissue pathway was collected from electronic searches of the medical literature, previous recommendations of the RCPath, and local guidelines in the United Kingdom. The level of evidence was either grade C or D, or met the GPP/good practice point criteria. Consensus of evidence in the tissue pathways was achieved by expert review.

No major organisational changes or cost implications have been identified that would hinder the implementation of the tissue pathways.

A formal revision cycle for all tissue pathways takes place on a four-yearly basis. However, each year, the College will ask the author of the tissue pathways, in conjunction with the relevant sub-specialty adviser to the College, to consider whether or not the document needs to be updated or revised. A full consultation process will be undertaken if major revisions are required. If minor revisions are required, an abridged consultation process will be undertaken whereby a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the pathways and the full revised version (incorporating the changes) will replace the existing version on the publications page of the College.

The pathway has been reviewed by the Working Group on Cancer Services and was placed on the College website for consultation with the membership from 10 February to 10 March 2014. All comments received from the Working Group and membership were addressed by the author to the satisfaction of the Working Group Tissue Pathway Coordinator and the Vice-President for Advocacy and Communications.

This pathway was developed without external funding to the writing group. The College requires the authors of tissue pathways to provide a list of potential conflicts of interest. The authors of this document have declared that there are none.

1 Introduction

This document deals with the handling of specimens in relation to non-neoplastic lesions of the head and neck, and replaces the previous versions of the tissue pathway. The purpose of this document is to assist cellular pathologists to provide a high standard of care for patients in the reporting of benign head and neck specimens. The tissue pathways are important as they provide a consistent approach to managing histological samples in head and neck pathology, highlighting ancillary techniques when appropriate. There is very little literature on the management of samples for diagnosis of non-neoplastic disorders, but a good overview and clear guidance can be found in Slootweg and de Groot (1999).[1] The tissue pathways should be used in conjunction with the datasets on head and neck cancers (www.rcpath.org/publications-media/publications/datasets/datasets-TP.htm).[2]

Target users of this guideline

The target primary users of the tissue pathway are trainee and consultant cellular pathologists. It is recommended that each department should have a lead for head and neck pathology.

2 Staffing, workload and facilities

2.1 Staffing and workload

The diagnostic laboratory should have sufficient pathologists, biomedical scientists and clerical staff to cover all of its functions. At least two pathologists in a unit should be competent in the reporting of specimens from the head and neck. If one of these is not an oral and maxillofacial pathologist with expertise in oral mucosal biopsies and of the special tooth-related and odontogenic pathology of the jaws, then access to this expertise should be ensured.

Pathologists reporting head and neck specimens should participate in an appropriate external quality assurance (EQA) scheme and The Royal College of Pathologists' CPD scheme. Lead pathologists should participate in a specialist head and neck EQA scheme.

There are no agreed minimum workload figures for a full-time head and neck pathologist. The Royal College of Pathologists' *Guidelines for Staffing and Workload in Histopathology and Cytopathology Departments* are a guide.[3] Workload may vary considerably according to the nature of the specimens received. Pathologists undertaking a significant amount of oncology work will be able to report fewer cases per year than a pathologist dealing primarily with non-neoplastic specimens. Pathologists in general pathology laboratories should have access to specialist referral opinions on a local network or national basis.

2.2 Laboratory facilities

It is good practice and normally expected that laboratories will be CPA accredited and that they will participate in National External Quality Assurance Schemes (UKNEQAS) for Cellular Pathology Techniques and for Immunocytochemistry as appropriate.

Details of the facilities needed and of appropriate techniques can be found in appropriate texts.[4] In general, laboratories should have access to the full range of routine laboratory facilities, including access to immunocytochemistry (including immunofluorescence) and electron microscopy, which may be off site. Facilities for sectioning of hard tissue are required, including an appropriate saw (e.g. a band saw or diamond-coated saw) for dissection of bone resections of the jaws, expertise in decalcification and preparation of specimens of bones and teeth. Fixation in formalin for 24–48 hours after slicing bone, and before decalcification, may improve morphology. Facilities and expertise for the preparation of ground sections of teeth are also sometimes necessary (or should be available off site).

Detailed protocols for decalcification are beyond the scope of this document (see Bancroft and Gamble)[5] and an appropriate balance needs to be reached between slower decalcification for optimal morphology and more rapid decalcification to facilitate patient management. Some decalcifying protocols may interfere with immunocytochemistry and excessive decalcification affects the morphology. In general, strong acids, e.g. nitric acid, are best avoided as decalcification is rapid and difficult to control. For most purposes, 5% formic acid is an appropriate decalcifying agent. The end point can be confirmed by palpation and/or ammonium hydroxide[5] or by radiography. Unless the tissue is likely to fragment or otherwise be distorted, it is recommended that bone is trimmed to approximate block size before decalcification. This should allow decalcification to be completed in 1–10 days, although very dense bone and teeth will take longer.

Reports should be held on an electronic database that has facilities to search and retrieve specific data items, and that is indexed according to Systematised Nomenclature of Medicine Clinical Terms (SNOMED) T, M and P codes or SNOMED-CT. It is acknowledged that existing laboratory information systems may not meet this standard; however, the ability to store data in this way should be considered when laboratory systems are replaced or upgraded.

Workload data should be recorded in a format that facilitates the determination of the resources involved and which, if applicable, is suitable for mapping to Healthcare Resource Groups (HRGs).

2.3 Specimen submission

Most specimens are received in the laboratory in formalin as routine diagnostic or therapeutic specimens according to standard procedures. For most specimens, special facilities are not required for specimen dissection and preparation, with the exception of bone and teeth as mentioned above. It is good practice to photograph large specimens so that a permanent record of the macroscopic appearance and location of blocks can be recorded and filed in the patient records. Specimen dimensions should be measured in mm.

Fresh tissue specimens are occasionally required primarily for the diagnosis of vesiculobullous lesions using direct immunofluorescence. In these cases, a mucosal biopsy is submitted fresh to the laboratory, either immediately wrapped in damp gauze or in a suitable transport medium.

The guidelines for the handling and dissection of head and neck specimens vary according to the type of specimen.[1,4]

3 Mucosal biopsies

3.1 Specimen dissection

Most of these specimens are small and should be measured in three dimensions. Identify and describe the colour and texture of the mucosa as well as any identifiable lesion, e.g. polyp, ulceration. Incisional biopsies of sufficient size are bisected through the long axis, and may be inked to indicate orientation for embedding purposes. For excision specimens, the closest excision margins are often best sampled by sectioning across the short axis (transversely).

[Level of evidence GPP]

3.2 Sectioning

Routinely a single section is usually sufficient for diagnostic purposes. Lesions where dysplasia is suspected or needs to be excluded, or from high risk sites (e.g. floor of mouth, non-homogeneous leukoplakia), should have three levels cut at 100 µm intervals.

3.3 Staining

Haematoxylin and eosin (H&E) stained sections are required for all cases. White lesions and dysplastic lesions, which are often infected with Candida species, may be stained using PAS with prior diastase digestion to help identify the fungal hyphae and spores.

3.4 Further investigations

These are occasionally needed to confirm a diagnosis and are requested as necessary. Examples include stains for amyloid and immunocytochemistry for suspected lymphoma or melanoma.

Immunofluorescence

Immunofluorescence to identify IgG, IgA, IgM, C3 and fibrinogen may be performed on fresh samples submitted for suspected vesiculobullous disorders.[6]

3.5 Report content

The report specifically refers to the overlying epithelium, lamina propria and other identified tissues including an indication of the depth of the biopsy (e.g. by reference to muscle on the deep aspect). Any infective agents or dysplastic features (graded according to the WHO guidelines)*[Level of evidence D]*[7] must be highlighted in the report. For excision specimens of oral leukoplakia, the presence and grade of dysplasia at surgical margins must be noted (this is not relevant for small, incisional mucosal biopsies) *[Level of evidence D]*.

4 Teeth

4.1 Specimen dissection

Teeth are received in formalin often with odontogenic cysts or as part of a resection specimen and may require histological examination to determine the vitality of the pulp. This can inform the pathogenesis of a periapical lesion.

Occasionally a clinical diagnosis of a tooth disorder requires histological confirmation – for example for idiopathic resorption, or developmental disorders.[8]

Tooth notation, site, morphology, presence of caries, and filling material are recorded. Assess enamel and dentine structure including colour, transparency, banding, erosion, abrasion and relative hardness. Root number, morphology and presence of resorption are identified.

Teeth are usually decalcified before dissection and sectioning. However, for diagnosis of enamel defects, a ground section is required. In this case, the tooth is bisected in a band saw and a ground section taken from one half and the other half submitted for decalcification.

[Level of evidence GPP]

4.2 Sectioning

Incisors, canines and premolar teeth are sectioned in the bucco-lingual plane. Molar teeth are sectioned mesiodistally.

4.3 Staining

Ground sections are viewed using Canada balsam as an embedding agent, as this has a similar refractive index to normal enamel.

Decalcified sections are stained using H&E.

4.4 Further investigations

Accurate clinical information including family history, extent of teeth affected, presence of metabolic bone disorders and examination of radiographs is required for accurate diagnosis of developmental disorders.

Disorders of tooth structure require the availability of polarised light microscopy.

4.5 Report content

The report should provide details about the enamel including thickness, structure, presence of enamel matrix and appearance of amelodentinal junction, and about the dentine including the appearance and presence of mantle zone, pre-dentine, primary, secondary, tertiary and inter-globular dentine; specifically, the appearance and presence of dentine tubules including relative width and orientation as well as the location of dysplastic dentine *[Level of evidence GPP].*

Pulp examination includes assessment of the root apex, vitality, inflammation, relative size and location.

5 Cysts: odontogenic and non-odontogenic

5.1 Specimen dissection

A detailed approach to the diagnosis of cysts of the head and neck has been previously published.[9] Most of these specimens are small, soft and fragmented. Record the number of pieces and dimensions of the largest piece. Small hard tissue fragments are common and decalcification overnight is often sufficient. Large fragments of bone and identifiable teeth or tooth fragments should be described, decalcified and blocked separately. The relationship to the tooth such as attachment to the cement-enamel junction or root apex is recorded. Tooth notation, caries status and the presence of restorations should be documented.

Large cysts require a description of the wall and the presence of mural thickening or nodules. Examination of the cyst lumen and its contents may reveal thickenings or intraluminal nodules. Thick creamy keratinous contents suggest a keratinising cyst and a shimmering appearance is often associated with the presence of cholesterol crystals.

Small fragmented specimens must be embedded in their entirety. Small intact cysts can be bisected. For large cysts, representative transverse slices are best. Care should be taken to sample any nodules or mural thickenings.

[Level of evidence GPP]

5.2 Sectioning

For small curetted specimens, a single section is usually sufficient for diagnostic purposes. For large specimens, multiple blocks may be needed to ensure adequate sampling of the wall including areas of thickening or nodules.

5.3 Staining

H&E stains are required for all cases.

5.4 Further investigations

Clinical information and preferably examination of radiographs is required for accurate diagnosis since it is often important to know the relationship to the teeth. Unusual findings require three levels at 100 µm intervals, as well as further representative samples.

PAS, alcian blue or mucicarmine stains may be useful in the diagnosis of glandular odontogenic cysts.

5.5 Report content

The report should specifically describe the cyst lining and the type and nature of the epithelium, e.g. the presence of keratinisation or basal palisading, mucous metaplasia,

hyaline (Rushton) bodies, or atypical features. The capsule must be described, particularly the presence or absence of inflammation and features such as daughter cysts, calcifications, odontogenic rests or foreign material. *[Level of evidence GPP]*

6 Minor salivary glands

6.1 Specimen dissection

Most of these specimens are relatively small and less than 15 mm.[10]

Mucoceles are usually fluctuant and may be covered by mucosa. The presence of minor salivary gland tissue should be identified.

The specimen should be measured in three dimensions and can be bisected in the longitudinal plane. For excision specimens, dissection is in planes appropriate to sample the closest excision margins. If multiple lobules of minor salivary gland tissue are received, the collective area is measured. Certain sites such as the upper lip are at an increased risk of tumour development even though these may clinically and macroscopically appear to be mucoceles.

Labial gland biopsies are occasionally taken to assist in the diagnosis of Sjögren syndrome. Multiple small lobules of gland may be received. These should be counted and the collective area measured. All the lobules can be placed into one block.

Resection specimens are orientated as indicated by the surgeon on the request form. Deep and peripheral excision margins should be inked. Care must be taken to examine the capsule and record any areas where it is incomplete or ruptured. Where a tumour is suspected, describe its location, consistency (i.e. solid, cystic, gelatinous), capsule and circumscription.

Blocks required include:

- one block per 10 mm diameter of tumour for larger specimens; most specimens will be blocked in their entirety
- sufficient sampling to determine adequacy of surgical margins
- adjacent mucosa and normal salivary glands.

[Level of evidence GPP]

6.2 Sectioning

A single section from each block is usually sufficient for diagnostic purposes in cystic and inflammatory conditions.

6.3 Staining

H&E stains are required for all cases.

6.4 Further investigations

Mucin stains, e.g. for PAS, alcian blue or mucicarmine are useful for identifying subtle extravasation of mucin and in the diagnosis of benign salivary gland tumours.

Immunohistochemistry is occasionally useful for the diagnosis of salivary gland tumours.

6.5 Report content

Cysts:

- nature of cyst and lining, i.e. epithelium or connective tissue
- type of inflammatory infiltrate
- presence of atrophy, mucus extravasation, ductal ectasia and minor salivary gland tissue.

Labial gland biopsies for Sjögren syndrome:

- record the number of lobules examined
- describe the general features and presence of inflammation, etc.
- record the presence or absence of lymphocytic foci
- comment if the criteria to support a diagnosis of Sjögren syndrome are met, e.g. give a focus score according to current guidelines.[11]

Benign tumours:

- type of tumour as based on WHO guidelines *[Level of evidence D]*[7]
- distance of tumour from the nearest peripheral margin
- distance of tumour from the deep margin
- presence of a capsule and any breach.

Any unsuspected malignancy is reported according to the College datasets on head and neck cancers *[Level of evidence D]*.[2]

7 Major salivary glands

7.1 Specimen dissection

Submandibular and sublingual glands are usually removed entirely as a result of sialolithiasis. Radiographs may be used to identify a sialolith.

Parotid gland specimens most often comprise a superficial parotidectomy of the lower pole of the superficial lobe. Total parotidectomies are rare for benign disease but may be performed for deep lobe tumours. The superficial and deep lobes may be provided separately. Specimens should be orientated by the surgeon; in cases of doubt, the surgeon must be consulted.

Superficial parotidectomy specimens resemble a triangle, with the smooth surface representing the superficial surface and the shortest profile the superior margin.

Deep lobes of the parotid and sublingual glands are difficult to orientate and are best done at the time of surgery by the operating clinician.
The submandibular gland can be orientated by the indentation produced by the mylohyoid on the deep margin and by the duct at the anterior aspect.

Required measurements include:

- dimensions and weight (g) of the specimen
- dimension and number of cysts
- dimensions of any identifiable tumour
- distance to the nearest margins
- presence of a capsule and whether or not this is intact.

Describe the location of any swelling or tumour, its consistency (i.e. solid, cystic, gelatinous), capsule and circumscription.

Blocks required include:

- one block per cm diameter of tumour
- sufficient sampling to determine the adequacy of surgical margins
- adjacent mucosa and normal salivary glands
- proximal and distal aspect of nerves if identifiable
- any intra-glandular or adjacent lymph nodes.

[Level of evidence GPP]

7.2 Sectioning

Routinely a single section of each block is sufficient for diagnostic purposes in cystic, infective and inflammatory conditions.

7.3 Staining

H&E stains are required for all cases.

7.4 Further investigations

Mucin stains, e.g. PAS, alcian blue or mucicarmine are helpful in the diagnosis of benign salivary gland tumours.

Immunohistochemistry is occasionally useful for the diagnosis of salivary gland tumours and for the differential diagnosis of benign lymphoepithelial lesions from extranodal marginal zone (MALT) lymphoma. This can be supplemented by molecular analysis for light and heavy chain restriction.

7.5 Report content

Cysts:

- nature of cyst and lining, i.e. epithelium or connective tissue
- type of inflammatory infiltrate
- presence of atrophy, mucus extravasation and ductal ectasia
- presence of salivary gland tissue.

Benign tumours

- type of tumour as based on WHO guidelines[7]
- distance of tumour from the nearest peripheral margin
- distance of tumour from the deep margin
- presence of a capsule and any breach.

Any malignancy must be reported according to the guidelines in the relevant RCPath cancer dataset *[Level of evidence D]*.[2]

8 Jaw lesions

8.1 Specimen dissection

This category includes a number of benign and non-neoplastic lesions that necessitate resective surgery. This includes ameloblastomas, 'mixed odontogenic tumours' and odontomes, as well as the fibro-osseous lesions.[12]

The presentation of jaw specimens is variable and includes enucleated specimens composed of fragmented pieces of soft tissue or bone as well as bone resections. When examining curetted or fragmented specimens. care should be taken to identify any fragments of bone or teeth; if necessary, the fragments can be decalcified separately or the specimen can undergo a short decalcification in its entirety.

If multiple fragments are included, the number of pieces, total dimensions and dimensions of the largest piece should be recorded. It is important to determine the relationship between resection specimens and separate fragments, especially with regard to excision margins. This is particularly relevant to maxillectomy specimens and fibro-osseous lesions, which may become fragmented during removal.

If the sample is small, it should all be processed, otherwise representative sections are usually sufficient.

Some odontogenic tumours and hamartomas are cystic in nature. If associated with teeth, the relationship should be documented. In addition, examination of the cyst lumen can reveal the presence of mural or luminal nodules in unicystic ameloblastomas.

For larger specimens, identification of the type of operation and orientation are required. Photographs should be used and carefully labelled to indicate orientation and the origin of blocks. Radiographs are essential to assess the extent of the lesion, tooth resorption and the presence of calcification.

Required measurements include:

- antero-posterior diameter along the alveolar ridge
- maximum bone height, i.e. ramus
- dimensions of tumour
- distance and location of the nearest margin.

Surgical margins, e.g. mucosal, deep, superior limit of ramus etc. may be inked.

Small specimens can be decalcified in their entirety before sampling or blocking out. For large resections, especially of the mandible, it is often helpful to takes slices of 5–8 mm using an appropriate saw. It may also be possible to slice maxillary specimens. Sometimes these are very fragile and decalcification of the entire specimen helps sampling and preserves orientation.

As most lesions are intraosseous, dissection of soft tissue from bone is usually not necessary. However, evidence of cortical perforation requires close soft tissue examination and specimens should be handled in a similar way to resections for malignant disease.[4]

[Level of evidence GPP]

8.2 Sectioning

A single section of each block is usually sufficient for diagnostic purposes.

8.3 Staining

H&E stains are required for all cases.

8.4 Further investigations

Accurate clinical information is required for accurate diagnosis. In general, hard tissue lesions should not be reported without examination of radiographs and/or CT images.

Congo red, alizarin red or thioflavine T are useful for the detection of amyloid proteins in adenomatoid and calcifying epithelial odontogenic tumours.

Van Gieson stains are useful in identifying dentinoid material, e.g. in ghost cell lesions and the mixed odontogenic tumours and odontomes.

Immunohistochemistry is rarely required.

8.5 Report content

An accurate description of any epithelium, including the formation of duct–like structures, as well as the presence of atypical features such as mitotic figures is required. Atypical features such as pleomorphism are common in some odontogenic tumours, including the calcifying epithelial odontogenic tumour. If no odontogenic epithelium is identified, this must be stated. *[Level of evidence GPP]*

The appearance of the stroma must be described including the presence of enamel, dentine, bone or other calcified material. *[Level of evidence GPP]*

The presence of amyloid must be confirmed with special stains.

The report should comment on the relationship to normal structures, e.g. teeth, bone, and the presence of a capsule and nature of the surgical margins recorded.

Malignant tumours must be reported according to the guidelines in the relevant College cancer dataset *[Level of evidence D]*.[2]

9 Nasal cavity and paranasal sinuses

9.1 Specimen dissection

Most of these specimens are small and fragmented. Specimens should be measured in three dimensions. Identify and describe the colour and texture of the mucosa as well as any identifiable lesion, e.g. polyp, ulceration. Small specimens should be measured and are usually embedded whole. Specimens of sufficient size are best bisected through the long axis. Larger samples and sinonasal polyps should have representative samples taken. Unilateral nasal polyps are usually blocked in their entirety because unilateral lesions have a slightly higher risk of being neoplastic than bilateral lesions. Small hard tissue fragments are common and decalcification overnight is often sufficient. Large fragments of bone should be described, decalcified and blocked separately.

[Level of evidence GPP]

9.2 Sectioning

A single section of each block is usually sufficient for diagnostic purposes. Three levels at 100 µm intervals may be indicated for more detailed examination of papillomas where dysplasia or invasive malignancy is suspected.

9.3 Staining

H&E stains are required for all cases.

9.4 Further investigations

PAS, Grocott's and Gram stains are useful for detecting fungal and bacterial infections. Mycobacterial stains are required in granulomatous conditions. If Wegener's granulomatosis is suspected, an elastic van Gieson stain may be helpful in identifying damaged vessels and further clinical information on the presence of positive c-ANCA tests and ESR is useful. Immunohistochemistry is usually not necessary in the diagnosis of benign nasal lesions. However, rare soft tissue tumours such as solitary fibrous tumour, pituitary gland neoplasms and meningioma may occur and immunohistochemistry may be necessary to confirm the diagnosis in these cases *[Level of evidence GPP]*.

Minor salivary gland tumours and fibro-osseous lesions should be reported, as indicated in the relevant sections.

9.5 Report content

The report may include details about the overlying epithelium, lamina propria and other identified tissues. Note the type of inflammatory infiltrate. Any infective agents or dysplastic features (graded according to the WHO guidelines)[7] must be highlighted *[Level of evidence D]*. The presence and grade of dysplasia at surgical margins must be noted for excision specimens, but this is usually not possible in fragmented samples.

Specific diagnoses should be provided for any polypoid lesion, i.e. allergic/inflammatory type, inverted papilloma, in view of the potential risk of malignant transformation in the latter.

10 Larynx, pharynx and tonsil

10.1 Specimen dissection

Most of these specimens are small or fragmented. Identify and describe the colour and texture of the mucosa as well as any identifiable lesion, e.g. polyp, ulcer. Measure in three dimensions. Specimens of sufficient size can be bisected through the long axis or sliced serially. Piecemeal resection specimens of the pharynx should be embedded in their entirety. *[Level of evidence GPP]*

Resection specimens should be orientated as indicated by the surgeon on the request form. Deep and peripheral excision margins should be inked. Care must be taken to examine the capsule and record any areas where it is incomplete or ruptured. Describe the location of the tumour, consistency (i.e. solid, cystic, gelatinous), capsule and circumscription. Dissection should be in planes appropriate to sample the closest excision margins. *[Level of evidence GPP]*

Laryngectomy specimens and major resections for benign disease are treated as for laryngeal malignancy.[4] *[Level of evidence GPP]*

Tonsillectomy specimens:

- orientate (if possible) and ink the deep margins
- measure in three dimensions and weigh
- examine grossly and cut into 4–5 mm transverse slices
- measure and describe any abnormality

- take representative blocks; if there is no macroscopic abnormality, then two blocks are sufficient.

[Level of evidence GPP]

Note: the ipsilateral tonsil is often the source of metastatic squamous cell carcinoma in the neck, particularly cystic metastases that can mimic branchial cysts. The primary lesion may be microscopic. In cases of tonsillectomy for patients who have proven or suspected metastasis in neck nodes and where tumour is not clearly identified within the tonsil at macroscopic examination, the tonsillectomy specimen must be blocked serially and examined in its entirety to exclude a microscopic primary in the tonsil itself.

10.2 Sectioning

A single section from each block is usually sufficient for diagnostic purposes.

Lesions from high-risk sites, i.e. non homogeneous leukoplakia from the vocal cords should have three levels at 100 µm intervals.

Retention of unstained sections is desirable, if resources permit.

10.3 Staining

H&E stains are required for all cases. Lesions suspicious of Candida infection should be stained with PAS and diastase pre-treatment.

10.4 Further investigations

Immunohistochemistry is usually not required, although this may be beneficial for some rare diagnoses.

10.5 Report content

The report should specifically describe the overlying epithelium, lamina propria and other identified tissues.

Any infective agents or dysplastic features (graded according to the WHO guidelines)[7] should be highlighted within the report *[Level of evidence D]*. The presence and grade of dysplasia at surgical margins must be noted.

Salivary and other benign tumours should be reported as discussed in the relevant sections.

[The majority of data in this section is based on expert opinion – Level of evidence D.]

11 Neck lesions

11.1 Specimen dissection

Swellings of the neck can be associated with any closely related structures such as lymph nodes, thyroid, salivary glands, blood vessels, nerves or fat. A wide variety of diseases may present but most relate to cervical lymph node enlargement.[13]

For benign disease, most neck specimens are small excisional biopsies. Neck dissections must be handled as for malignant disease *[Level of evidence D]*.[7]

Lymph nodes: small nodes (up to 4 mm in maximum dimension) should be embedded whole. Nodes up to 10 mm in diameter across the short axis should be bisected longitudinally through the hilum (or 'bivalved') and embedded in total. Nodes larger than 10 mm in the equatorial plane should be serially sliced at approximately 4 mm intervals and have two or three representative slices embedded. *[Level of evidence GPP]*

Cysts: measure in three dimensions. Thyroglossal cysts usually present as a strip of fibrous tissue surrounded by fat and muscle.

Branchial cysts are typically submitted intact. Sufficient sampling of branchial cysts is required to rule out the possibility of a cystic metastatic carcinoma. Examine the cyst lumen for nodules and record the nature of contents and thickness of the cyst wall. Small specimens should be bisected or embedded intact, while larger specimens are serially sliced and representative blocks (2–4) taken.

Soft tissue tumours and carotid body paragangliomas: these are not usually orientated and may be fragmented. Ink the external surfaces and measure:

- dimensions of the specimen
- dimensions of the tumour (if different from those of the specimen)
- distance from tumour to the nearest surgical margin or to marked vessels and nerves.

Describe the tumour including the colour, whether encapsulated or infiltrative, and the presence of haemorrhage and necrosis. Paragangliomas should also be weighed. Serially slice the tumours into 4–5 mm sections. Representative blocks include one block per cm of tumour. Record the presence of necrotic and haemorrhagic areas.

[Level of evidence GPP]

11.2 Sectioning

A single section per block is usually sufficient for diagnostic purposes.

Lymph nodes: usually one section per block (see also *Tissue pathways for lymph node, spleen and bone marrow trephine biopsy specimens*).

11.3 Staining

H&E stains are required for all cases.

11.4 Further investigations

Immunohistochemistry may be useful for a range of neck lesions including for micro-metastases, to exclude lymphomas, and in the diagnosis of soft tissue tumours.

11.5 Report content

For cysts, the report should record:

- cyst lining, i.e. keratinisation, presence of atypical features and mitotic figures
- nature of the capsule such as fibrous, fibromyxoid and the degree of inflammation
- presence of foreign body reaction to ruptured cysts.

For tumours, the report should record:

- type
- tumour – tissue interface, i.e. infiltrative or encapsulated
- relationship to major vessels and nerves

- nearest surgical margin.

[Level of evidence GPP]

12 Electron microscopy

Electron microscopy is rarely used in diagnostic head and neck pathology. Although occasionally applied in tumour pathology, it has no role in non-neoplastic disorders.

13 Molecular investigations

At present, molecular investigation of histological samples is not used in a diagnostic setting for non-neoplastic lesions of the head and neck.

14 Cytology

Fine needle aspiration cytology is widely used in the diagnosis of salivary gland tumours and for neck lumps. This is almost exclusively for the diagnosis and management of neoplasms and for staging head and neck cancer. Occasionally FNA cytology will reveal non-neoplastic lesions, but this is not its primary purpose.

Cytology is still occasionally used on aspirates from cystic lesions of the jaws. The primary purpose of this is to differentiate inflammatory cysts from keratocystic odontogenic tumour (odontogenic keratocyst) by searching for evidence of keratin in the specimen. However this has a high rate of insufficient specimens or false negatives, and is therefore rarely used.[14]

14.1 Specimen preparation

The aspirate is smeared onto 3–4 slides and stained for Papanicolaou and H&E. Sections may also be stained with PAS and a water-mounted section can be prepared for polarised light microscopy.

14.2 Report content

The report should describe the cells present and their relative proportions. The presence of epithelial cells is not diagnostic, but particular note should be made of the presence of keratinising cells, which suggest an odontogenic keratocyst. Many inflammatory cells suggest an inflammatory cyst but are not diagnostic. Polarised light microscopy may reveal cholesterol crystals, which are suggestive of an inflammatory cyst.

[Level of evidence GPP]

15 Criteria for audit of the tissue pathway

Other audits are also recommended by the RCPath as key performance indicators (KPIs) (see *Key Performance Indicators – Proposals for implementation* (July 2013) on www.rcpath.org/clinical-effectiveness/kpi/KPI):

- Cancer resections must be reported using a template or proforma, including items listed in the English COSD which are, by definition, core data items in RCPath cancer datasets. English Trusts are required to implement the structured recording of core pathology data in the COSD.

Standard: 95% of reports must contain structured data.

- Histopathology cases that are reported confirmed and authorised within 7–10 calendar days of the procedure.

  Standard: 80% of cases must be reported within 7 calendar days and 90% within 10 calendar days. Cases requiring prolonged decalcification are reasonably excluded.

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Appendix A AGREE compliance monitoring sheet

The tissue pathways of The Royal College of Pathologists comply with the AGREE standards for good quality clinical guidelines. The sections of this tissue pathway that indicate compliance with each of the AGREE standards are indicated in the table.

AGREE standard	Section
Scope and purpose	
1. The overall objective(s) of the guideline is (are) specifically described	Foreword
2. The clinical question(s) covered by the guidelines is (are) specifically described	Foreword Introduction
3. The patients to whom the guideline is meant to apply are specifically described	Foreword
Stakeholder involvement	
4. The guideline development group includes individuals from all the relevant professional groups	Foreword
5. The patients‟ views and preferences have been sought	N/A*
6. The target users of the guideline are clearly defined	Introduction
7. The guideline has been piloted among target users	Foreword
Rigour of development	
8. Systematic methods were used to search for evidence	Foreword
9. The criteria for selecting the evidence are clearly described	Foreword
10. The methods used for formulating the recommendations are clearly described	Foreword
11. The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword
12. There is an explicit link between the recommendations and the supporting evidence	3–11
13. The guideline has been externally reviewed by experts prior to its publication	Foreword
14. A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15. The recommendations are specific and unambiguous	2–15
16. The different options for management of the condition are clearly presented	2–15
17. Key recommendations are easily identifiable	Throughout
18. The guideline is supported with tools for application	Throughout
Applicability	
19. The potential organisational barriers in applying the recommendations have been discussed	Foreword
20. The potential cost implications of applying the recommendations have been considered	Foreword
21. The guideline presents key review criteria for monitoring and/audit purposes	15
Editorial independence	
22. The guideline is editorially independent from the funding body	Foreword
23. Conflicts of interest of guideline development members have been recorded	Foreword

* The Lay Advisory Committee (LAC) of The Royal College of Pathologists has advised that there is no reason to consult directly with patients or the public regarding this tissue pathway because it is technical in nature and intended to guide pathologists in their practice. The authors will refer to the LAC for further advice if necessary.

Appendix B Summary table – Explanation of grades of evidence

(modified from Palmer K *et al. BMJ* 2008; 337:1832)

Grade (level) of evidence	Nature of evidence
Grade A	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type. Or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Grade B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type. Or Extrapolation evidence from studies described in A.
Grade C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type. Or Extrapolation evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert Opinion. Or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.