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

Tissue pathways for oral and head and neck pathology

October 2023

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Unique document number	G077
Document name	Tissue pathways for oral and head and neck pathology
Version number	4
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Date active	October 2023 **(to be implemented within 3 months)**
Date for full review	October 2028
Comments	In accordance with the College's pre-publications policy, this document was on the Royal College of Pathologists' website for consultation from 11 July to 8 August 2023. Responses and authors' comments are available to view on publication of the final document. **Dr Brian Rous** **Clinical Lead for Guideline Review**

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Registered charity in England and Wales, no. 261035

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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 25 July 2017. 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 automatically be deemed negligent or a failure of duty of care. Pathologists should be prepared to justify any departure from the guidelines.

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

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

The information used to develop this tissue pathway was obtained by undertaking a systematic search of PubMed. Key terms searched included laboratories/standards; pathology, surgical/standards; specimen handling/methods for both mouth diseases and otorhinolaryngologic diseases. Dates searched were between January 2012 and October 2022; 17 studies met the selection criteria and were considered for review. Published evidence was evaluated using modified SIGN guidance (see Appendix A). Consensus of evidence in the guideline was achieved by expert review. Gaps in the evidence were identified by College members via feedback received during consultation

A formal revision cycle for all tissue pathways takes place on a 5-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 2 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 section of the College website.

The pathway has been reviewed by the Professional Guidelines team, Working Group on Cancer Services and Lay Advisory Group and was placed on the College website for consultation with the membership from 11 July to 8 August 2023. All comments received from the Working Group and membership were addressed by the authors to the satisfaction of the Chair of the Working Group and the Clinical Lead for Guideline Review.

This pathway was developed without external funding to the writing group. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

This document deals with the handling of specimens in relation to benign and 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 non-neoplastic and 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 RCPath datasets on head and neck cancers are based on the 7th edition and are currently under review.[2] The tissue pathways should be used in conjunction with American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) 8th Edition TNM Classification of Malignant Tumours.[2,3]

1.1 Target users of this guideline

The target primary users of the dataset are trainee and consultant cellular pathologists, and, on their behalf, the suppliers of IT products to laboratories. The secondary users are biomedical scientists, clinicians in secondary and primary care in the NHS and members of the head and neck multidisciplinary team.

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 its functions. At least 2 pathologists in a unit should be competent in the reporting of specimens from the head and neck. If neither is an oral and maxillofacial pathologist with expertise in oral mucosal biopsies and 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 RCPath's Continuing Professional Development or alternative 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. RCPath's *Guidelines on Staffing and Workload for Histopathology and Cytopathology Departments* is a guide and currently under review.[4] Workload may vary considerably according to the nature of the specimens received. Pathologists undertaking a significant amount of oncology and specialist referral 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 accredited for compliance with standards in best practice (e.g. ISO 15189) and that they will participate in national EQA schemes (UK NEQAS) for cellular pathology techniques and for immunocytochemistry as appropriate.

Details of the facilities needed and of appropriate techniques can be found in appropriate texts.[5] In general, laboratories should have access to the full range of routine laboratory facilities, including access to immunocytochemistry (including immunofluorescence), electron microscopy and molecular diagnosis, which may be off-site. Facilities for dissection 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 and an appropriate balance needs to be reached between slower decalcification for optimal morphology and more rapid decalcification to facilitate patient management (see Bancroft and Gamble, 2002).[5] 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, 5–10% formic acid is an appropriate decalcifying agent. The end point can be confirmed by palpation and/or ammonium hydroxide or by radiography.[5] 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 a secure electronic database that has facilities to search and retrieve specific data items and is indexed according to Systematised Nomenclature of Medicine (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 that, if applicable, is suitable for mapping to Healthcare Resource Groups.

2.3 Specimen submission

Most specimens are received in the laboratory in formalin as routine diagnostic or resection 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 in a suitable transport medium (Michel's transport medium is ideal).

The guidelines for the handling and dissection of head and neck specimens vary according to the type of specimen.[1,6]

3 Mucosal biopsies

3.1 Specimen dissection

Most of these specimens are small and should be measured in 3 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 slicing across the short axis (transversely).

[Level of evidence – GPP.]

3.2 Sectioning

Routinely a single section is usually sufficient for diagnostic purposes. Whenever possible and if sufficient tissue is available in the block, lesions where dysplasia is suspected or needs to be excluded will normally require additional levels.

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 periodic acid-Schiff (PAS) with or without diastase pre-treatment to help identify the fungal hyphae.

3.4 Further investigations

These are occasionally needed to confirm a diagnosis and are requested, as necessary. Examples include histochemical stains such as Congo red for amyloid, immunocytochemistry for suspected lymphomas or melanomas or in situ hybridisation for demonstration of mRNA, e.g. Epstein-Barr virus-encoded small RNAs (EBER) in oral hairy leukoplakia.

3.4.1 Immunofluorescence

Fresh samples submitted for suspected vesiculobullous disorders should be stained for a range of target antigens, primarily IgG, IgA and C3. This may include IgM and fibrinogen as well.[7]

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). Fungal and viral infective agents or dysplastic features (graded according to World Health Organization (WHO) guidelines) must be highlighted in the report.[8] 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; for example, a large cyst apparently encompassing the root of a tooth could not be regarded as a radicular cyst arising from that tooth if the pulp is shown to be vital.

Occasionally a clinical diagnosis of a tooth disorder requires histological confirmation; for example, for idiopathic resorption, structural and developmental disorders.[9]

Tooth notation, site, morphology, presence of caries and filling material are recorded. Enamel and dentine structure including colour, transparency, banding, erosion and abrasion are assessed. 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 that may need to be referred to specialist units. In this case, the tooth is bisected in a band saw and a ground section taken from 1 half and the other half submitted for decalcification.

[Level of evidence – GPP.]

4.2 Sectioning

Teeth are normally sectioned in the bucco-lingual/palatal plane.

4.3 Staining

Ground sections are viewed using Canada balsam or a resin 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 the following details: description of the enamel, including thickness, structure, presence of the enamel matrix and appearance of the amelodentinal junction; details about the dentine, including the appearance and presence of the mantle zone, pre-dentine, primary, secondary, tertiary and inter-globular dentine; the appearance and presence of dentine tubules, including their relative width and orientation, as well as the location of dysplastic dentine. The presence and appearance of cementum also merits comment.

[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.[10,11] Most of these specimens are small, soft and fragmented. The number of pieces and dimensions of the largest piece should be recorded. 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 may require levels, as well as further sampling.

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 (or cyst wall) should be described, particularly the presence or absence of an inflammatory cell infiltrate 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.[12]

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 3 dimensions and can be bisected in the longitudinal plane. For excision specimens, dissection is in planes appropriate to sample the closest excision margins. 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's 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 1 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:

- 1 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. PAS, Alcian blue or mucicarmine, are useful for identifying subtle extravasation of mucin and in the diagnosis of salivary gland tumours.

Immunohistochemistry is useful for the diagnosis of salivary gland tumours. Genomic testing, often in the form of fluorescence in situ hybridisation (FISH) or polymerase chain reaction (PCR), is increasingly used in 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's syndrome:

- the number of lobules examined
- the general features and presence of inflammation, etc
- the presence or absence of lymphocytic foci
- whether the criteria to support a diagnosis of Sjögren's syndrome have been met
- a focus score according to current guidelines may be used.[13,14]

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.

Unsuspected malignancy is reported according to the RCPath datasets on head and neck cancers.[2]

[Level of evidence – D.]

7 Major salivary glands

7.1 Specimen dissection

Submandibular glands are usually removed entirely as a result of obstructive symptoms, e.g. from a stone. Sublingual glands are usually removed to control a recurrent or deep extravasation cyst. 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 may 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 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 comprise:

- 1 block per 10 mm diameter (or part thereof) 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 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, e.g. for light and heavy chain restriction.

Increasingly, genomic testing, mostly FISH or PCR analysis, is being used in the diagnosis of salivary gland tumours.

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[8]
- distance of tumour from the nearest peripheral margin

- distance of tumour from the deep margin
- presence of a capsule and any breach.

Malignancy must be reported according to the guidelines in the relevant RCPath cancer dataset.[2]

[Level of evidence – D.]

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.[15]

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; these 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 or dimensions of the largest piece should be recorded. Determining the relationship between resection specimens and separate fragments, e.g. with regard to excision margins, can be difficult, especially with maxillectomy specimens, 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 of larger resections are often useful to assess the extent of the lesion, tooth resorption and the presence of calcification.

Required measurements include:

- antero-posterior 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, bone limits, may be inked.

Small specimens can be decalcified in their entirety before sampling. For large resections, especially of the mandible, it is often helpful to take slices of 5–8 mm using an appropriate saw. It may also be possible to slice maxillary specimens but often these are very fragile and decalcification of the entire specimen before slicing and block selection 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.[6]

[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, reporting of hard tissue lesions benefits from the examination of radiographic images or the opinion of a radiologist.

Congo red, alizarin red or thioflavin 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. Molecular testing can be useful, e.g. for GNAS1 in cases of fibrous dysplasia.[16]

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 can be confirmed with special stains and is usually not associated with systemic amyloidosis.

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 RCPath cancer dataset.[2]

[Level of evidence – D.]

9 Nasal cavity and paranasal sinuses

9.1 Specimen dissection

Most of these specimens are small and fragmented. Specimens should be measured in 3 dimensions, and the colour and texture of the mucosa noted 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 but decalcification overnight may be

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. Levels 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

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; immunohistochemistry may be necessary to confirm the diagnosis in these cases.

Histochemical stains such as PAS and Grocott are useful when fungal disease is suspected, while Giemsa, Gram or Warthin-Starry stains may help detecting intracellular bacterial infections, e.g. rhinoscleroma. Stains for mycobacteria, such as Ziehl-Neelsen or Auramine O, are usually required in granulomatous conditions. If vasculitis is suspected, an elastic van Gieson stain may be helpful in identifying damaged vessels and further clinical information on the presence of positive MPO- or PR3-ANCA tests and the value of the erythrocyte sedimentation rate may be useful.

[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. The type of inflammatory infiltrate should be noted. Infective agents or dysplastic features (graded according to the WHO guidelines) must be highlighted.[8] The presence and grade of dysplasia at surgical margins must be noted for excision specimens, but this is usually not possible in fragmented samples.

[Level of evidence – D.]

Specific diagnoses should be provided for any polypoid lesion, e.g. 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 3 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.

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.

Laryngectomy specimens and major resections for benign disease are treated as for laryngeal malignancy.[2,5]

[Level of evidence – GPP.]

Tonsillectomy specimens:

- orientate (if possible) and ink the margins
- measure in 3 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 2 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. Up to 10% of tonsil carcinomas may metastasise to the contralateral side and 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.

Whenever possible and if sufficient tissue is available in the block, lesions from high-risk sites, i.e. non-homogeneous leukoplakia from the vocal cords, normally require additional levels

10.3 Staining

H&E stains are required for all cases. Lesions suspicious for Candida spp. infection should be stained with PAS with or without diastase pre-treatment.

10.4 Further investigations

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

Infections including leishmaniasis and lepromatous leprosy (including erythema nodosum leprosum) may sometimes be seen and can be confirmed with appropriate stains including PAS, Grocott, Giemsa and Gram stains, which are all useful for detecting fungal and bacterial infections. Mycobacterial stains, such as Ziehl-Neelsen or Auramine O, are required in granulomatous conditions

10.5 Report content

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

Infective agents or dysplastic features (graded according to the WHO guidelines) should be highlighted within the report.[8] 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.

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

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.[17]

For benign disease, most neck specimens are small excisional biopsies. Neck dissections must be handled as for malignant disease.[6,8]

[Level of evidence – D.]

11.1.1 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 2 or 3 representative slices embedded (see also *Tissue Pathways for Lymph Node, Spleen and Bone Marrow Trephine Biopsy Specimens*).[18]

[Level of evidence – GPP.]

11.1.2 Cysts

Measure in 3 dimensions. Thyroglossal cysts usually present as a cord of fibrous tissue surrounded by fat and muscle; part of the hyoid bone may be present at 1 end with an ellipse of skin at the other.

Branchial cysts are typically submitted intact to the laboratory. Sufficient sampling is required to rule out the possibility of a cystic metastatic carcinoma, particularly from an occult primary in the tonsil. 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 taken.

11.1.3 Soft tissue tumours and 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. Serially slice the tumours into 4–5 mm sections. Representative blocks include 1 block per 10 mm diameter (or part thereof) of tumour diameter. Record the presence of necrotic and haemorrhagic areas. Paraganglioma of the carotid body may include portions of the carotid artery.

[Level of evidence – GPP.]

11.2 Sectioning

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

Lymph nodes: usually 1 section per block (see also *Tissue Pathways for Lymph Node, Spleen and Bone Marrow Trephine Biopsy Specimens*).[18]

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 micrometastases, to assist with the diagnosis or exclusion of lymphoma 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 abnormal mitotic figures, nature of the capsule such as fibrous, fibromyxoid and the degree of inflammation; presence of organised lymphoid components
- presence of foreign body reaction to ruptured cysts

- psammomatoid calcifications, which may raise the possibility of papillary carcinoma.

For tumours, the report should record:

- type (e.g. metastatic tumours, paraganglioma, soft tissue tumours)[19,20]
- tumour–tissue interface, i.e. infiltrative or encapsulated
- relationship to major vessels and nerves
- nearest surgical margin.

[Level of evidence – GPP.][18]

12 Electron microscopy

Electron microscopy is rarely used in diagnostic head and neck pathology. Although occasionally applied in tumour pathology, it has little role in non-neoplastic disorders.

13 Molecular investigations

At present, a priori molecular investigation of histological samples is not used in a diagnostic setting for non-neoplastic lesions of the head and neck but may follow histological findings. For example, the diagnosis of odontogenic keratocyst in a patient in their first decade may prompt investigation for Gorlin syndrome or a cystic radiolucency shown to be rich in osteoclastic giant cells may lead to a diagnosis of cherubism.

14 Cytology

Fine needle aspiration cytology is widely used to aid in the triage and diagnosis of swellings presenting in salivary glands and the neck including thyroid gland.[21,22] It may be used to inform clinical staging of head and neck cancers. In some units, cytology will be used in the context of a ‘1 stop clinic’ setting.[23,24] Cytology is not recommended for a definitive diagnosis of head and neck lymphoma, where a tissue biopsy is more appropriate. However, a FNA sample may provide valuable information for flow cytometry in providing an assessment of clonality but may guide the selection of appropriate lymph nodes for sampling.

Cytology is still occasionally used on aspirates from cystic lesions of the jaws. The primary purpose of this is to exclude a vascular lesion or to differentiate inflammatory cysts from odontogenic keratocyst by searching for keratin in the specimen. However,

this has a high rate of insufficient specimens or false negatives and is therefore rarely necessary.[25]

14.1 Specimen preparation

Commonly used stains are Papanicolaou, Giemsa and Diff-Quik.

Cytology specimens may further aid diagnosis of epithelial neoplasms and can be used for immunohistochemistry studies through the use of a liquid-based cytology system and clot/cell block construction.

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.

[Level of evidence – GPP.]

15 Criteria for audit

In addition to the above, the following are recommended by the RCPath as key indicators of quality in histopathology reports.[26,27]

The following are recommended by the RCPath as key assurance indicators (see *Key assurance indicators for pathology services*) and key performance indicators (see *Key performance indicators – proposals for implementation*):

- cancer resections are usually reported using a template or proforma, including items listed as core data items in RCPath cancer datasets (KPI 5.2)
- compliance with the agreement between the laboratory and users of the laboratory services on the proportion of cases reported within agreed turnaround times for this specific patient pathway (KAI 18).

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Appendix A 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 population 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 population 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 population 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.

Appendix B AGREE II guideline monitoring sheet

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

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Introduction
2 The health question(s) covered by the guideline is (are) specifically described	Introduction
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	N/A
6 The target users of the guideline are clearly defined	Introduction
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword and Introduction
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 or health issue are clearly presented	2–15
17 Key recommendations are easily identifiable	7 and 8
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	15
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline	Foreword
23 Competing interest of guideline development group members have been recorded and addressed	Foreword