

Phaeochromocytoma and Paraganglioma Histopathology Reporting Guide



Family/Last name

Date of birth

Given name(s)

Patient identifiers

Date of request

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

indicates multi-select values indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (select all that apply) (Note 1)

- Information not provided
- Hormonal status
 - Biochemically functioning (select all that apply)
 - Metanephrine and/or adrenaline
 - Normetanephrine and/or noradrenaline
 - Methoxytyramine and/or dopamine
 - Other, *specify*
 - Biochemically silent
 - Biochemical analysis not performed
 - Cannot be determined (testing status not known)

Imaging findings, *specify*

Relevant biopsy/cytology results, *specify*

Previous therapy (including pre-operative embolization, chemotherapy, radiotherapy, targeted therapy, immunotherapy), *specify*

Relevant familial history, *specify*

Presence of endocrine or other tumours, *specify*

Germline mutation or familial syndrome, *specify mutation if known*

Other, *specify*

OPERATIVE PROCEDURE (select all that apply) (Note 2)

- Not specified
- Biopsy (core needle, incisional, excisional), *specify*
- Open resection, *specify procedure, including other organs if present (e.g., adrenal resection and liver biopsy)*
- Laparoscopic
- Organ-sparing
- Other (e.g., conversion, laparoscopic to open), *specify*

SPECIMEN(S) SUBMITTED (select all that apply) (Note 3)

- Not specified
- Adrenal gland
 - Left Right
- Biopsy tissue, *specify site(s) and laterality*
- Lymph nodes, *specify biopsy/dissection, site(s) and laterality*
- Other (e.g., right neck mass, midline abdominal mass), *specify site(s) and laterality*

TUMOUR FOCALITY (Note 4)

- Unifocal
- Multiple
 - Multifocal (separate tumours in the same organ), *specify number of tumours*
 - Multiple tumours in separate organs,^a *specify number of tumours*
- Indeterminate
- Cannot be assessed, *specify*

^a If multiple tumours from different organs are present, separate datasets should be used to record all following elements for each tumour.

TUMOUR SITE^a (select all that apply) (Note 5)

(Specify number of tumours at any site containing more than one tumour)

 Not specified Adrenal Left Right Other abdominal or pelvic Paraaortic Urinary bladder Other, specify Thorax Paraaortic Cardiac Other, specify Head and neck Carotid body Left Right Middle ear (jugulotympanic) Left Right Vagal Left Right Laryngeal Left Right Other, specify site(s) and laterality**SPECIMEN INTEGRITY** (Note 6) Specimen intact Fragmented specimen Cannot be assessed, specify**TUMOUR DIMENSIONS** (Note 7)

Maximum tumour dimension (largest tumour)

mm

Additional dimensions (largest tumour)

mm

x

mm

 Cannot be assessed, specify**MEDULLARY HYPERPLASIA** (Note 8)

(Applicable to adrenal specimens only)

Medullary nodules (microphaeochromocytoma) (<10 mm) Present Absent Indeterminate Cannot be assessed, specify**Diffuse hyperplasia** Present Absent Indeterminate Cannot be assessed, specify**HISTOLOGICAL TUMOUR TYPE** (select all that apply) (Note 9)

(Value list from the World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of Endocrine Organs (2017))

 Pheochromocytoma Extra-adrenal paraganglioma Composite pheochromocytoma Neuroblastoma, specify

%

 Ganglioneuroblastoma, specify

%

 Ganglioneuroma, specify

%

 Malignant peripheral nerve sheath tumour, specify

%

 Composite paraganglioma Neuroblastoma, specify

%

 Ganglioneuroblastoma, specify

%

 Ganglioneuroma, specify

%

 Malignant peripheral nerve sheath tumour, specify

%

 Other, specify

%

EXTENT OF INVASION (select all that apply) (Note 10) Cannot be assessed Microscopic transcapsular penetration of tumour capsule within an organ Microscopic transcapsular penetration of organ capsule Invasion into peritumoural soft tissue Invasion into adjacent structure(s)/organ(s), specify

LYMPHOVASCULAR INVASION (Note 11)

- Not identified
- Present (select all that apply)
- Periadrenal or peritumoral for extra-adrenal tumours, specify
- Intracapsular Extracapsular
- Adrenal vein
- Vena cava
- Other (e.g., adrenal central vein and tributaries), specify

MARGIN STATUS (Note 12)

- Not involved (R0)
- Distance of tumour to closest margin mm
- Closest margin, specify if possible
- Involved
- Extent**
- R1 (microscopic), specify if possible mm
- R2 (macroscopic), specify if possible mm
- Location of involved margin(s), specify if possible
- Cannot be assessed, specify

PROLIFERATIVE FRACTION (Note 13)

- Mitotic count /2 mm²
- AND/OR
- Ki-67 %
- Cannot be assessed

LYMPH NODE STATUS (Note 14)

- No nodes submitted or found
- Lymph node biopsy, specify site(s), if applicable
- Number of lymph nodes examined
- Not involved
- Involved
- Number of positive lymph nodes
- Number cannot be determined
- Extranodal extension (ENE)**
- Not identified
- Present
- Number of nodes with ENE
- Cannot be determined
- Maximum dimension of largest lymph node metastasis mm

ADVERSE FEATURES (select all that apply) (Note 15)**Histological features**

- Necrosis
- Comedonecrosis
- Other, specify
- Growth pattern
- Large and irregular nests
- Diffuse
- Pseudorosette (even focal)
- Cellularity
- Moderate (150–250 cells/U)
- High (>250 cells/U)
- Indeterminate
- Cytologic features
- Spindle cells
- Other, specify
- Other, specify

Other features

- Extra-adrenal abdominal or mediastinal location
- Size >50 mm
- Negative staining for SDHB
- Biochemical testing showing high levels of methoxytyramine

ANCILLARY STUDIES (select all that apply) (Note 16)

- Not performed
- Immunohistochemistry performed
- Chromogranin A, specify result
- Synaptophysin, specify result
- S-100, specify result
- SDHB, specify result
- Tyrosine hydroxylase, specify result
- Other, specify
- Molecular testing performed, specify result(s) if available
- Other, specify

HISTOLOGICALLY CONFIRMED DISTANT METASTASES

(Note 17)

- Not identified
- Not assessed
- Present, *specify site(s)*

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PATHOLOGICAL STAGING (AJCC TNM 8th edition)^b (Note 18)

TNM Descriptors (only if applicable) (select all that apply)

- m - multiple primary tumours
- r - recurrent
- y - post-therapy

Primary tumour (pT)

- TX Primary tumour cannot be assessed
- T1 Pheochromocytoma <5 cm in greatest dimension, no extra-adrenal invasion
- T2 Pheochromocytoma ≥5 cm or paraganglioma-sympathetic of any size, no extra-adrenal invasion
- T3 Tumour of any size with invasion into surrounding tissues (e.g., liver, pancreas, spleen, kidneys)

Pheochromocytoma: within adrenal gland

Paraganglioma sympathetic: functional

Paraganglioma parasympathetic: often non-functional, and located in the head and neck

Note: Parasympathetic paragangliomas are not staged.

Regional lymph nodes (pN)

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

^b Used with the permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2016) published by Springer Science+Business Media.

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the NHMRC levels of evidence¹). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the expert committee. An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the Dataset Authoring Committee.

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Scope

The dataset has been developed for the pathology reporting of adrenalectomy/partial adrenalectomy specimens for pheochromocytoma, other excisions for paragangliomas and biopsies of related specimens.

Sarcoma, lymphoma and metastasis to the adrenal medulla are not covered in this dataset. Neuroblastoma and ganglioneuroblastoma are also not covered in this dataset. Adrenal cortical tumours are dealt with in a separate dataset.

Anatomic sites of paraganglia

Paraganglia are neural crest-derived neuroendocrine organs that produce catecholamines as their usual hormonal product. They are typically divided into 2 groups, associated with sympathetic or parasympathetic nerves. Sympathetic paraganglia, also-called sympathoadrenal paraganglia, are divided into 2 subgroups: the adrenal medulla, and extra-adrenal sympathetic paraganglia. Tumours arising from the adrenal medulla are termed pheochromocytomas, while tumours arising from extra-adrenal locations are called paragangliomas regardless of their sympathetic or parasympathetic origins. Parasympathetic paragangliomas are also known as head and neck paragangliomas, and most often arise in, or near the carotid body or middle ear. However, sympathetic paragangliomas occasionally arise from the cervical sympathetic chain.

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Note 1 – Clinical information (Core)

Clinical data provide important guidance to pathologists for establishing a diagnosis and for assisting clinicians in planning patient management. Optimally, information should be provided on biochemical function, individual and family history, multiple tumours and the presence of additional endocrine or non-endocrine tumours that may be components of a syndrome.² Almost 50% of phaeochromocytomas/paragangliomas are hereditary, making them the most hereditarily determined of all human tumours, and at least 15 hereditary susceptibility genes are now associated with their development.³ Distinct correlations exist between genotype, biochemical phenotype,⁴ tumour distribution, prognosis, and syndromic associations.^{5,6}

Most phaeochromocytomas and sympathetic paragangliomas are capable of synthesizing catecholamines and are also associated with clinical signs and symptoms related to catecholamine excess. In contrast, parasympathetic paragangliomas are rarely symptomatic and often lack tyrosine hydroxylase, the enzyme required for catecholamine synthesis, making them biochemically as well as clinically silent.⁷ There is overwhelming evidence that biochemical testing for phaeochromocytoma/paraganglioma should include metanephrines, measured either in plasma or urine, as these are superior to measurements of catecholamines.⁸ Many clinically silent paragangliomas, particularly of the sympathoadrenal type, will produce metanephrines and/or methoxytyramine and therefore are amenable to biochemical testing.^{3,4}

Similarly to other neuroendocrine neoplasms, phaeochromocytomas and extra-adrenal paragangliomas are also capable of producing and secreting peptides that can cause clinical syndromes.⁹ Production of adrenocorticotrophic hormone, β -endorphin, corticotropin-releasing hormone, calcitonin gene-related peptide, vasoactive intestinal peptide, growth hormone-releasing hormone, neuropeptide Y, peptide YY, insulin-like growth factor-1, galanin, adrenomedullin, serotonin, somatostatin, and gastrin like neuropeptide have been reported.⁵

As with other tumours, previous procedures can alter the microscopic appearance of a tumour, and should be recorded. Fine needle aspiration or core needle biopsy may cause tumour infarction or interfere with assessment of invasion. Preoperative embolization is an established cause of necrosis in head and neck paragangliomas.⁷ Partial adrenalectomy, which is increasingly utilized in treating patients with pheochromocytomas,¹⁰ might also be expected to cause long term changes in histology of the residual adrenal.

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Note 2 – Operative procedure (Core)

Laparoscopic surgery is frequently used and this may lead to some disruption or fragmentation of the gland/tumour. This may cause problems in assessing tumour size, integrity of the tumour capsule and completeness of excision and may also cause distortion of vascular channels, making assessment of lymphovascular invasion difficult. In the rare cases where the specimen has been morcellated, tumour size should be obtained from either the surgeon or from pre-operative cross-sectional imaging studies.

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Note 3 – Specimen(s) submitted (Core)

All anatomical structures removed or biopsied as part of the procedure should be identified. Examples of “other” specimens may include additional tissues or organs (e.g., kidney, larynx), or deposits of recurrent or metastatic tumour.

Laterality information is needed for correct identification of specimens. The designation of laterality may include right, left or midline.

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Note 4 – Tumour focality (Core)

The presence of multiple or multifocal tumours is an important clue to the presence of hereditary disease.¹¹ Multifocality is defined as separate foci of tumour in the same organ, in contrast to multiple tumours in separate organs (e.g., two or three removed paragangliomas or a paraganglioma and a pheochromocytoma). These designations apply to primary tumours, not metastases, and require histologic confirmation that tumour is present. In some cases it may not be possible to determine whether a specimen represents a metastasis or a separate primary (e.g., a suspected lymph node with no residual lymph node architecture or a solitary pulmonary nodule¹²). Similarly, it may not be possible to determine whether a fragmented specimen is multifocal. These examples would be classified as indeterminate. Specimens should be carefully examined both macroscopically and microscopically to determine whether multiple or multifocal tumours are present. In most cases multifocality specifically applies to the adrenal gland. However, occasional adrenal specimens may contain both a pheochromocytoma and a nearby extraadrenal paraganglioma.

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Note 5 – Tumour site (Core)

This element is defined as the site from which the surgeon has removed tumour tissue, and requires histologic confirmation that tumour is present.

The anatomic location of a paraganglioma has important clinical correlations with predictive value concerning genotype, hormonal function, likelihood of additional and syndromically associated tumours, and risk of metastasis.¹³

Metastatic sites such as bone, liver, lung, lymph node, etc. should specifically indicate which bone(s)/which lung(s)/which lymph node(s), and the number of tumours, independently for each site.

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Note 6 – Specimen integrity (Core)

Tumour fragmentation often results from laparoscopic surgery and may cause problems in assessing tumour size, integrity of the tumour capsule, lymphovascular invasion and completeness of excision.

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Note 7 – Tumour dimensions (Core and Non-core)

Tumour measurements should not include adjacent fat or other non neoplastic tissue. The dimensions recorded should be the most complete as determined by accurately assessing gross and microscopic measurements.

Large tumour size (>50 mm) correlates to metastatic potential in some, but not all studies, although possibly not as an independently useful criterion.^{14,15} However, tumour size ≥ 50 mm is included as a staging criterion in the American Joint Committee on Cancer (AJCC) TNM 8 Staging Manual.^{16,17}

Tumour sampling for microscopy should represent all variations in the gross appearance and consistency of the tumour, as well as margins and other specific features of interest. The general guideline of at least 1 section per cm of tumour should be considered.

In the rare cases where the specimen has been morcellated, tumour size should be obtained from either the surgeon or from pre-operative cross-sectional imaging studies.

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Note 8 – Medullary hyperplasia (Core)

Adrenal medullary nodules either coexisting with pheochromocytoma/paraganglioma, or in a background of diffuse adrenal medullary expansion are an important clue to the presence of hereditary disease.¹¹ They most often are associated with MEN2, but have recently been described in other disorders.¹⁸ Historically, nodules <1 cm have been arbitrarily called hyperplastic nodules or nodular adrenal medullary hyperplasia. Current molecular evidence suggests they are more appropriately considered microphaeochromocytomas.¹⁹

Adrenal gland (or glands) received for diagnosis of possible microphaeochromocytoma or adrenal medullary hyperplasia should be oriented and dissected clean of as much fat/connective tissue as possible and then accurately weighed. Because this would preclude evaluation of the fat for microscopic involvement by a tumour, it should not be done in cases where invasive tumour is a consideration. Sequential sections of roughly equal thickness are made in the transverse plane to display the distribution and amount of medullary tissue in the general regions - head, body and tail.²⁰ Medulla is normally present only in the head and body of the gland, with only minimal extension into the alae but not into the tail. The presence of substantial adrenal medullary tissue in the tail or alae strongly suggests adrenal medullary hyperplasia. Normal medulla usually does not represent more than one-third of the gland thickness, with cortex on each side comprising the other two thirds. However, anatomic variants exist, and definitive diagnosis of medullary hyperplasia in the absence of nodules may require quantitative morphometric analysis.²¹

Although it is sometimes difficult to define the tail of an adrenal gland distorted by a pheochromocytoma, it should be remembered that adrenal medullary nodules²¹ and pheochromocytomas can occur in adrenals in MEN2 syndrome without an obvious background of diffuse hyperplasia. The adrenal gland adjacent to an apparently sporadic pheochromocytoma should therefore be sectioned as above and carefully examined for small nodules.⁵

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Note 9 – Histological tumour type (Core)

All tumours of the adrenal medulla and extra-adrenal paraganglia should be given a type based on the most recent edition of the World Health Organization (WHO) Classification of Tumours of Endocrine Organs.² A composite tumour is defined as a tumour that combines morphological features of paraganglioma or pheochromocytoma with those of a developmentally related neurogenic tumour including, ganglioneuroma, ganglioneuroblastoma, neuroblastoma or malignant peripheral nerve sheath tumour.² There is no specified percentage of the second tumour type.² However, complete histoarchitecture of the second tumour type is required. Scattered neuron-like cells often seen in pheochromocytomas are not sufficient. This designation is separate from mixed corticomedullary neoplasms, which would be included in “other”.

The most common second component of composite tumours is ganglioneuroma (70-80% of cases) followed by ganglioneuroblastoma (15-20%). Although the latter is morphologically comparable to paediatric ganglioneuroblastoma, it differs in molecular and clinical perspectives and confers only a low risk of metastases.^{2,20}

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Note 10 – Extent of invasion (Core)

Invasion is a reported risk factor for development of metastases when considered in conjunction with other adverse features. However, invasion is currently categorized and weighted inconsistently.¹¹ Precise descriptions of the nature and extent of invasion are required in conjunction with other adverse factors in order to optimally guide patient management.

As pheochromocytomas usually do not have a capsule,²⁰ the adrenal capsule becomes the capsule of the tumour in most cases. Within other organs an encapsulated tumour may be more likely. If a tumour capsule is present, invasion of the organ capsule and tumour capsule should be documented separately. Capsular invasion is not assessed in a biopsy.

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Note 11 – Lymphovascular invasion (Core)

Vessel invasion is a reported risk factor for development of metastases when considered in conjunction with other adverse features.¹¹ Precise descriptions of the nature and extent of vascular invasion are required in conjunction with other adverse factors in order to optimally guide patient management.¹¹

There are currently no firm data for pheochromocytoma or paraganglioma to assess whether metastatic risk increases progressively with involvement of small to larger vessels, although extrapolation from other tumours would suggest that is the case. In the adrenal, invasion of one or more tributaries of the central vein may be an important event leading to involvement of the adrenal vein and the vena cava. This may be facilitated by the normal anatomy within the adrenal where arcades of mural smooth muscle provide gaps through which normal cortex and/or medulla or tumours derived from them can protrude into the vascular space(s).²⁰

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Note 12 – Margin status (Core and Non-core)

Incomplete excision has been associated with local recurrence.²² Positive margins are defined both grossly, as tumour obviously transected and microscopically as “tumour on ink”, if the surface is inked. Adrenalectomy specimens especially are frequently damaged and very irregular, often precluding both the application of ink, and reliable gross assessment. In these cases the margins cannot be assessed.

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Note 13 – Proliferative fraction (Core)

Mitotic count and/or Ki-67 proliferation index is now widely utilized in risk stratification for other neuroendocrine tumours. A high proliferative fraction based on either mitoses²³ or Ki-67²⁴ is a reported risk factor for development of metastases for pheochromocytoma and paraganglioma.

Mitotic count should be performed in a minimum area of 2 mm², which is equivalent to approximately 10 high power fields (HPFs) in many microscopes. There is currently no standard approach to scoring a Ki-67 labelling index in pheochromocytoma and paraganglioma and this has been emphasised. On the basis of established methodology for other neuroendocrine tumours,² it is recommended that the Ki-67 index should be reported as percentage of positive tumour cells per 40x field HPF (0.2 mm²) in area of highest nuclear labelling.^{5,24} Counts should ideally be based on manual counts of printed images or appropriately validated automated image analysis; visual estimates have proven less accurate for multiple tumour types.²

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Note 14 – Lymph node status (Core and Non-core)

Regional lymph nodes are found within the anatomic area in which a tumour is located and receive lymphatic drainage from that area. They are, therefore, anatomically related to the tumour and may be the earliest sites of lymph node metastases.

In keeping with practices applied to other tumours to stratify risk of early nodal involvement, the pathology report should state the total number of lymph nodes examined and the number of nodes with metastases. Size of tumour deposit within the lymph node may be correlated with outcome, and thus it is recommended to report the greatest tumour dimension identified within the lymph node dissection/biopsy sample.

Lymph node biopsies are sometimes received as intact resections and sometimes as multiple fragments. In the latter, the number of nodes will be known only if specified by the surgeon and otherwise is undetermined.

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Note 15 – Adverse features (Non-core)

While the cumulative summary of adverse features may be clinically helpful it is not a required component of the pathology report and is therefore listed as non-core. Individual features (tumour size and location) that are core are so listed in other sections.

Several categories of histological features are putative risk factors for development of metastases in multiple publications and overlap in the two major proposed scoring systems for risk stratification, PASS²⁵ and GAPP.²⁴ However, the individual parameters within the categories are assessed and weighted differently in the two systems. No scoring system is currently required or endorsed, but histologic features may be considered in conjunction with other data for cumulative risk stratification in order to optimally guide patient management. Comedonecrosis and growth pattern are the most readily recognized and possibly the most predictive parameters, while cellularity is potentially highly subjective. To reduce subjectivity, it was recommended that cellularity be quantitated by counting the number of cells within an area (U) encompassed by a square grid in a 10x ocular viewed with a 40x HPF, corresponding to 0.0625 mm.^{3,24} Necrosis does not include ischemic necrosis secondary to therapeutic embolization or spontaneous infarction.

PASS was designed for pheochromocytomas, while GAPP was intended for both pheochromocytomas and sympathetic paragangliomas. No scoring system currently applies to head and neck paragangliomas, although individual parameters may provide useful information for those tumours.²⁶ Use of either scoring system is optional. A 2019 meta-analysis of multiple papers employing PASS or GAPP, concludes that a low score with either histological system is a strong predictor of low metastatic risk but that high scores have little predictive value in the absence of additional features including genotype and biochemical testing.²⁷ Poor concordance between expert pathologists has been noted in a PASS study.²⁸

Coarse nodularity is a gross finding reported to be associated with metastatic risk.²⁹

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Note 16 – Ancillary studies (Non-core)

The differential diagnosis of pheochromocytoma or paraganglioma often requires use of generic immunohistochemical markers to establish the neuroendocrine nature of a tumour together with additional more specific markers to confirm the diagnosis or exclude other entities, including other neuroendocrine neoplasms.^{7,30,31} The most frequently utilized positive generic markers in most contexts are chromogranin A (CgA) and synaptophysin. However, synaptophysin is expressed in adrenal cortex and must not be used to distinguish pheochromocytomas from cortical neoplasms. Additional useful positive markers include tyrosine hydroxylase to demonstrate capacity for catecholamine synthesis, and S100 to demonstrate sustentacular cells. Useful negative markers include keratins and inhibin. A caveat is that head and neck paragangliomas are often completely negative for tyrosine hydroxylase and also negative or only focally positive for CgA and synaptophysin.⁷ In those cases the presence of sustentacular cells can be particularly helpful; however, sustentacular-like cells can also be found in other neuroendocrine tumours and are therefore not diagnostic. Additional potentially useful positive markers that have been proposed include dopamine beta-hydroxylase,³² INSM1,³³ NKX2.2³⁴ and GATA-3.^{31,35}

In addition to aiding diagnosis, immunohistochemistry is increasingly used as a genetic screen. This particularly applies to staining for loss of SDHB, which also serves as a prognostic marker.^{36,37}

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Note 17 – Histologically confirmed distant metastases (Core)

A diagnosis of metastasis is appropriate when pheochromocytoma or paraganglioma is present in a site where normal paraganglia do not exist. The only such sites *a priori* are bone and histologically confirmed lymph node. It is crucial to remember the normal anatomic distribution of paraganglia in order to consider the possibility of multiple primary tumours.³¹ The assessment of distant metastasis can be particularly challenging in some cases because primary paragangliomas do also occur in rare anatomic sites such as thyroid, pituitary, gallbladder, liver and lung. Therefore, tumour in these rare locations should not automatically be considered metastatic. In addition, due to the ease of performing needle core biopsies of various organs, metastatic disease is now increasingly seen histologically and in many cases biopsies may be the only tissue sample available due to the advanced nature of the primary tumour or the comorbidities associated with surgical resection.

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Note 18 – Pathological staging (Core)

The AJCC staging system for pheochromocytomas and sympathetic paragangliomas was implemented in 2017 in order to guide clinicians in determining the therapies and follow-up that patients require.¹⁶ It is expected that extensive staging and survival data to be collected will also lead to increased understanding of these tumours and to future improvements in patient care.^{16,17}

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