THYROID CYTOLOGY
STRUCTURED REPORTING
PROTOCOL
(1st Edition, 2014)
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The Royal College of Pathologists of Australasia ("College") has developed these protocols as an educational tool to assist pathologists and others in reporting relevant information for specific specimens. While each protocol includes "standards" and "guidelines" which are indicators of ‘minimum requirements’ and ‘recommendations’, the protocols are a first edition and have not been through a full cycle of use, review and refinement. Therefore, in this edition, the inclusion of "standards" and "guidelines" in each document are provided as an indication of the opinion of the relevant expert authoring group, but should not be regarded as definitive or as widely accepted peer professional opinion. The use of these standards and guidelines is subject to the clinician’s judgement in each individual case.

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Scope

This protocol contains standards and guidelines for the preparation, interpretation and reporting of thyroid cytology material obtained by fine needle aspiration biopsy (FNA). The aspirates may be direct aspirations or radiologically guided aspirations.

The aim is to improve quality of the final cytopathology report that is issued to clinicians, and in particular to improve the decision for management of thyroid lesions. However this reporting format allows flexibility in the report to reflect any specific issues as appropriate and to include additional information as free text.
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ASC</td>
<td>Australian Society of Cytology</td>
</tr>
<tr>
<td>ATC</td>
<td>Anaplastic thyroid carcinoma</td>
</tr>
<tr>
<td>BSCC</td>
<td>British Society of Clinical Cytology</td>
</tr>
<tr>
<td>FNA</td>
<td>Fine Needle Aspiration</td>
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<tr>
<td>FVPTC</td>
<td>Follicular variant of papillary thyroid carcinoma</td>
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<tr>
<td>IHC</td>
<td>Immunohistochemistry</td>
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<td>LBC</td>
<td>Liquid based cytology</td>
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<tr>
<td>MTC</td>
<td>Medullary thyroid carcinoma</td>
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<tr>
<td>NCI</td>
<td>National Cancer Institute</td>
</tr>
<tr>
<td>NZSP</td>
<td>New Zealand Society of Pathologists</td>
</tr>
<tr>
<td>PAP</td>
<td>Papanicolaou</td>
</tr>
<tr>
<td>PBS</td>
<td>Pharmaceutical Benefits Scheme</td>
</tr>
<tr>
<td>PTC</td>
<td>Papillary thyroid carcinoma</td>
</tr>
<tr>
<td>QA</td>
<td>Quality Assurance</td>
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<tr>
<td>QI</td>
<td>Quality improvement</td>
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<tr>
<td>RACS</td>
<td>Royal Australasian College of Surgeons</td>
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<tr>
<td>RANZCR</td>
<td>Royal Australasian and New Zealand College of Radiologists</td>
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<tr>
<td>RCPA</td>
<td>Royal College of Pathologists of Australasia</td>
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<tr>
<td>TBSRTC</td>
<td>The Bethesda System for Reporting Thyroid Cytopathology</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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</table>
Definitions

The table below provides definitions for general or technical terms used in this protocol. Readers should take particular note of the definitions for 'standard', 'guideline' and 'commentary', because these form the basis of the protocol.

Ancillary study  An ancillary study is any pathology investigation that may form part of a cancer pathology report but is not part of routine cytological assessment.

Clinical information  Patient information required to inform pathological assessment, usually provided with the specimen request form, also referred to as "pre-test information".

Commentary  Commentary is text, diagrams or photographs that clarify the standards (see below) and guidelines (see below), provide examples and help with interpretation, where necessary (not every standard or guideline has commentary).

Commentary is used to:
- define the way an item should be reported, to foster reproducibility
- explain why an item is included (e.g., how does the item assist with clinical management).
- cite published evidence in support of the standard or guideline
- state any exceptions to a standard or guideline.

In this document, commentary is prefixed with 'CS' (for commentary on a standard) or 'CG' (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (e.g., CS1.01a, CG2.05b).

General commentary  General commentary is text that is not associated with a specific standard or guideline. It is used:
- to provide a brief introduction to a chapter, if necessary
- for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).

Guideline  Guidelines are recommendations; they are not mandatory, as indicated by the use of the word "should". Guidelines cover items that are not essential for clinical management, but are recommendations.

Guidelines include key observational and interpretative findings that are fundamental to the interpretation, diagnosis and conclusion. Such findings are essential from a clinical governance perspective, because they provide a clear,
evidentiary decision-making trail.

Guidelines are not used for research items.

In this document, guidelines are prefixed with ‘G’ and numbered consecutively within each chapter (eg G1.10).

Microscopic findings

In this document, the term ‘microscopic findings’ refers to cytological/morphological assessment.

Prognostic factor

A *prognostic factor* is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.

Standard

Standards are mandatory, as indicated by the use of the term ‘must’. Their use is reserved for core items essential for the clinical management, and key information (including observations and interpretation) which is fundamental to the diagnosis and conclusion. These elements must be recorded and at the discretion of the pathologist included in the pathology report according to the needs of the recipient of the report.

The summation of all standards represents the minimum dataset for the cancer.

In this document, standards are prefixed with ‘S’ and numbered consecutively within each chapter (eg S1.02).

Structured report

A report format which utilises standard headings, definitions and nomenclature with required information.

Synoptic report

A structured report in condensed form (as a synopsis or precis).

Synthesis

Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new.

The Oxford dictionary defines synthesis as “the combination of components or elements to form a connected whole”.

In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information.
Introduction

On clinical examination, about 5% of the population are found to have thyroid nodules and with ultrasound examination, 25% have nodules. Fifty percent of people with clinically detected solitary nodules have additional nodules when examined further by ultrasonography. About 5% of thyroid nodules are likely to be malignant.\textsuperscript{1,2} The incidence of thyroid cancer is increasing, particularly in women, where it is among the top ten cancers diagnosed in Australia. In 2007, 1787 new cases of thyroid cancer were reported compared to 859 new cases in 1997—a twofold increase in 10 years.\textsuperscript{3}

Fine-needle aspiration is currently considered to be the best test for triaging thyroid nodules. The goal of cytological assessment is to provide guidance for patient management. The decision to assess the nodule by FNA is largely guided by clinical and radiological findings.

In Australia, a survey by Royal College of Pathologists of Australasia (RCPA) QA programme demonstrated that radiologists perform approximately - 65% of aspirations while pathologists perform only 11%. The quality and the quantity of smears and other material provided to the pathologist are therefore largely dependent on the skills of radiologists performing the procedure, and others who are involved in sample preparation before the specimen arrives in the laboratory.

If well-established and stringent diagnostic criteria are used, a majority of thyroid nodules can be safely and accurately categorised by cytological assessment. Often a specific diagnosis, such as a colloid goitre, thyroiditis, or a specific thyroid malignancy (eg papillary, medullary, anaplastic carcinoma) can be made. In some cases the use of ancillary techniques may enhance diagnostic accuracy.

Some aspirates are non-diagnostic due to technical issues such as insufficient cellularity, poor quality of sample preparation or technical artefacts due to blood staining, ultrasound gel etc. In others, the distinction between benign and malignant nodules may not be possible due to interpretative difficulties. To ensure the best possible assessment of thyroid nodules some guidance on sampling, preparation of material, interpretation and reporting is warranted.

The RCPA QA survey showed that thyroid FNAs constitute between 0-62% of the total workload of cytology laboratories. Of 143 labs surveyed, 60 used no defined classification system for reporting thyroid FNAs, 53 used the Bethesda system, and 14 used other systems for reporting thyroid cytology. Results of the survey revealed an overwhelming consensus for a uniform reporting system suitable for Australasia.

In an attempt to develop a more standardised reporting system for thyroid FNAs, the RCPA and the Australian Society of Cytology (ASC) formed a working party of cytopathologists, cytologists and clinicians with an interest and expertise in this field. The aim of the group was to prepare guidelines in an effort to standardise FNA techniques and smear preparation. It also sought to create a uniform approach to terminology, reporting, and management recommendations. In addition, information regarding the value of using ancillary techniques to improve diagnostic accuracy is provided. It is hoped that the document, by providing a more standardised reporting system, will enhance laboratory quality assurance programs and allow for the future development of appropriate performance measures as well as being of educational and research value to all those involved in the assessment and management of thyroid nodules.
Importance of cytopathology reporting

The role of the Cytopathologist and cytologist in the management of thyroid nodules is to provide guidance to clinicians in planning further management. While accurate assessment of cytology material is vital, translation of the pathological assessment and interpretation into a report is an equally important exercise. The reporting categories, system and terminology should be reproducible, predictive of outcome, and translate to clear management guidelines. The “inconclusive/grey” area should thus be within an acceptable range.

Benefits of standard/uniform reporting

It is not uncommon to find inconsistencies in approaches to handling and reporting of thyroid cytology within a single institution, across organisations, states, and countries. An effective way to overcome this situation is to create a standardised approach that will ensure that the aspirated material is optimally prepared, and key features observed, interpreted, and translated into the report to guide clinicians in further management of the lesion. It is also desirable to document important features, for the purposes of audits, QA and QI purposes. The recently introduced Bethesda system for Reporting Thyroid Cytopathology (TBSRTC)⁴, Papanicolaou Society Classification⁵ and British Thyroid Association Terminology⁶ provide standard reporting and terminology guidelines. There are several systems in use in Australasia⁷-⁹ either in their original form or modified to suit local needs. Our aim is to generate a standard approach not limited to reporting terminology, but including sampling, preparation and recommendations incorporating relevant available evidence-based information. The most widely utilised system, the Bethesda system, was used as the framework to prepare Australasian reporting guidelines. It is important to note that these guidelines are not restricted to reporting terminology alone, but incorporate other essential pre-analytical and post-analytical aspects of thyroid cytology. The guidelines are aimed at modifying aspects of Bethesda terminology to suit the Australasian setting, and reconciling any inconsistencies between terminologies that are currently in use within the Bethesda framework. These guidelines will evolve further when evidence and data on their merits and shortcomings become available. It is hoped that a standard approach to all aspects of thyroid cytology will allow optimal management of thyroid lesions by clinicians.

Design of this protocol

This protocol defines the relevant information to be assessed and recorded in cytology reporting of thyroid lesions. Mandatory elements (standards) are differentiated from those that are not mandatory but represent best practice (guidelines). The structure provided in the following chapters, headings and subheadings describe the elements of information and their groupings, but does not necessarily represent the format of either a pathology report (Chapter 7) or a checklist (Chapter 6). These, and the structured pathology request form (Appendix 1) are templates that represent information from this protocol, organised and formatted differently to suit different purposes.
Key documentation

- Guidelines for Authors of Structured Cancer Pathology Reporting Protocols\textsuperscript{10}
- The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Provider\textsuperscript{11}
- Guidelines of the Papanicolaou Society of Cytopathology for fine needle aspiration procedure and reporting\textsuperscript{5}
- Techniques for Thyroid FNA: A Synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference\textsuperscript{12}

Changes since the last edition

Not applicable.
Authority and development

This section provides details of the committee involved in developing this protocol and the process by which it was developed.

Protocol developers

This protocol was developed jointly for the RCPA and ASC by the following expert committee.

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Acknowledgements

The thyroid cytology expert committee wish to thank Dr Andrew Field for his excellent contributions to the preparation of this document. In addition, the committee wish to thank the following for their valuable feedback:

- Anthony Gill
Alistair Lochhead
Christopher Toon
Jason Stone
Sanjiv Jain
William Murray

Stakeholders

ACT Health
Anatomical Pathology Advisory Committee (APAC)
Australian Association of Pathology Practices Inc (AAPP)
Australian Cancer Network
Australian Commission on Safety and Quality in Health Care
Australian Society of Cytology
Cancer Australia
Cancer Control New Zealand
Cancer Council ACT
Cancer Council NSW
Cancer Council Queensland
Cancer Council SA
Cancer Council Tasmania
Cancer Council Victoria
Cancer Council Western Australia
Cancer Institute NSW
Cancer Services Advisory Committee (CanSAC)
Cancer specific expert groups – engaged in the development of the protocols
Cancer Voices
Clinical Oncology Society of Australia (COSA)
Department of Health and Ageing
Grampians Integrated Cancer Services (GICS)
Independent Review Group of Pathologists
Health Informatics Society of Australia (HISA)
Medical Software Industry Association (MSIA)
National Coalition of Public Pathology (NCOPP)
National E-Health Transition Authority (NEHTA)
National Pathology Accreditation Advisory Council (NPAAC)
National Round Table Working Party for Structured Pathology Reporting of Cancer.
New Zealand Guidelines Group (NZGG)
New Zealand Ministry of Health
New Zealand Society of Gastroenterology (NZSG)
NSW Department of Health
Peter MacCallum Cancer Institute
Queensland Cooperative Oncology Group (QCOG)
Representatives from laboratories specialising in anatomical pathology across Australia
Royal Australasian College of Physicians (RACP)
Southern Cancer Network, Christchurch, New Zealand
Southern Melbourne Integrated Cancer Service (SMICS)
Standards Australia
The Medical Oncology Group of Australia
The Royal Australasian College of Surgeons (RACS)
The Royal Australian and New Zealand College of Radiologists (RANZCR)
The Royal Australian College of General Practitioners (RACGP)
The Royal College of Pathologists of Australasia (RCPA)
Victorian Cooperative Oncology Group (VCOG)
Western Australia Clinical Oncology Group (WACOG)

Secretariat

Meagan Judge, Royal College of Pathologists of Australasia

Development process
This protocol has been developed following the nine-step process set out in Guidelines for Authors of Structured Cancer Pathology Reporting Protocols.10

Where no reference is provided, the authority is the consensus of the expert group.
1 Pre-analytical

This chapter relates to information that should be recorded on receipt of the specimen in the laboratory.

Clinical information is a prerequisite for accurate diagnosis. Some of this information may be received on generic pathology request forms; however, the additional information required by the pathologist specifically for the reporting of Thyroid FNA is outlined in Appendix 1. Appendix 1 also includes a standardised request information sheet that may be useful in obtaining all relevant information from the requestor.

Collection procedures affect the quality of the specimen and recommendations for appropriate collection are included in Chapter 2.

S1.01 All demographic information provided on the request form and with the specimen(s) must be recorded.

CS1.01a The Royal College of Pathologists of Australasia (RCPA) The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers must be adhered to.13 This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

CS1.01b The patient’s ethnicity must be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.

CS1.01c The patient’s health identifiers may include the patient’s Medical Record Number as well as a national health number such as a patient’s Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

S1.02 All information as documented on the request form must be recorded verbatim in the final pathology report.

CS1.02a The request information may be recorded as a single text (narrative) field or it may be recorded in a structured format.

S1.03 The pathology accession number of the specimen must be recorded.

S1.04 The principal clinician involved in the patient’s care and responsible for investigating the patient must be recorded.

CS1.03a Knowledge of the clinical presentation is an essential part of the WHO classification yet it may not be available for a number of reasons:

- The clinical assessment and staging may be incomplete at the time of biopsy.
- The pathology request is often authored by the clinician performing the FNA (eg radiologist) rather than the clinician who is investigating and managing the patient.
• The identity of this clinician is often not indicated on the pathology request form

In practice therefore, it is important in such cases that the reporting pathologist should be able to communicate with the managing clinician for clarification.

G1.01 Any clinical information received in other communications from the requestor or other clinician should be recorded.
2 FNA collection and preparation of material

This chapter relates to the collection and preparation of FNA material.

Prior to collection

- Local guidelines for obtaining consent should be followed and the usual risks of the procedure (bleeding, tenderness, infection) explained to the patient. Special considerations may be required for paediatric patients.

Collection of Thyroid FNA samples

- A detailed discussion of the general principles of performance of fine needle aspiration biopsy and all technical requirements is outside the scope of this document. Readers are referred to publications by the NCI, Papanicolaou Society and BSCC\textsuperscript{5,12,14} for detailed reviews of the published literature.

The procedure may be a palpation-guided aspiration by a pathologist or a clinician or an ultrasound guided aspiration performed by a radiologist. The following are generally accepted guidelines relating to specimen procurement, either with or without ultrasound guidance:

1. The patient may be in a sitting or lying position, but with the neck extended to facilitate access to the thyroid.
   
   Most aspirators recommend 25 or 27 gauge needles with a long or regular bevel. When draining a cystic lesion, a 23 gauge needle may be beneficial.

2. Sampling may be performed with aspiration utilising a syringe, with or without a pistol-grip device, or without aspiration by needle alone. No statistically significant improvement in adequacy rates has been demonstrated with aspiration over non-aspiration sampling, however some authors prefer the increased tactile sensation non-aspiration provides and claim it causes less bleeding.\textsuperscript{5,15} Alternatively, aspiration by an assistant via a connecting tube allows maintenance of tactile sensation. Aspiration may be particularly helpful to drain cysts or following unsuccessful needle-only sampling.\textsuperscript{16} Larger gauge needles with aspiration may be required to drain viscous colloid cysts.

3. Ultrasound gel used in ultrasound – guided aspirations should be thoroughly removed prior to aspiration to prevent gel artefact which may seriously impede interpretation.

4. Cellular material is obtained by the cutting action of the trailing edge of the needle (heel of the bevel) and is retained in the needle lumen by forward motion and capillary tension.

5. The needle should be oscillated back and forth approximately three times per second and withdrawn after 3-5 seconds, following release of any aspiration pressure applied. Longer dwell times result in capillary blood contamination and clotting within the needle. Appropriate haemostasis should be applied by local
pressure between each pass.

There is no clear scientific evidence to indicate the optimum number of passes. A pragmatic recommendation, based in part on the Papanicolaou Society Task Force review of the literature, is as follows:

a) **FNA with rapid interpretation by on site evaluation available**: one or two passes from different areas of the lesion, smeared onto an appropriate number of slides with a representative slide stained for adequacy. No more tissue is needed if (1) a cyst is completely drained and no residual mass is identified, (2) a specific malignancy is identified (and no ancillary tests are deemed necessary), or (3) the aspirate appears adequate.

Additional FNA is recommended if (1) there is a residual mass after draining a cyst, (2) cellularity is inadequate or, (3) to enrich a sample for cell block preparation, flow cytometry, molecular techniques or electron microscopy.

Attendance at the FNA procedure by a cytopathologist, scientist or cytotechnologist is valuable in determining specimen adequacy and achieving optimal preparation and handling of the specimen. There is a high level of concordance between the on-site evaluation provided by cytology staff and the final diagnosis. On-site evaluation generally requires fewer passes than predetermined clinical protocols and achieves higher adequacy rates.

Following the preparation of direct smears from each pass, the needle may be rinsed in saline or cell transport medium to harvest any residual material. Although cell yield is often low, needle washout samples may be useful for adjunctive testing such as flow cytometry for suspected lymphoproliferative disorders. However, if the requirement for ancillary tests is anticipated, a dedicated pass for cell block (for immunohistochemical stains) or flow cytometry is recommended. Further cytology preparations may also be made but are rarely contributory.

b) **FNA without rapid interpretation by on site evaluation available**: two to five passes from different sites within the lesion with representative material from each pass smeared onto an appropriate number of slides and the remaining tissue rinsed into a collection tube with cell transport medium (eg Hanks, RPMI) without fixative (unless delay in immediate processing is expected).

c) **Liquid based cytology (LBC)**: LBC preparations are appropriate for assessing needle wash material and may be preferred by some laboratories when specimens are collected by staff with no expertise in smear techniques, but their use as a replacement for direct smears is to be strongly discouraged. There is no consistent evidence supporting use of liquid based
preparation methods for thyroid cytology samples, either as an adjunct or a replacement for direct smears, in terms of adequacy rates and the data is variable in assessing accuracy of diagnosis.\textsuperscript{21,22}

Direct smears are essential if on-site adequacy assessment is required and air-dried preparations are not possible with LBC methods. Direct smears provide important diagnostic information which can be lost in LBC material and at the time of this publication LBC alone is not regarded as ideal for diagnosis. There are also subtle differences in the appearance of the cytological material following LBC preparation which require experience for reliable interpretation.

6. Smears should be clearly labelled in lead pencil (on the side of the smeared material) with at least two identifiers (patient’s name/date of birth/unit record number) and the site of aspirate and labelled as to whether air-dried or alcohol fixed.

7. Air dried smears should be transported in a container separate from the alcohol – fixed preparations and also separate from any formalin fixed specimens as the vapours may create artefacts.

**Preparation of aspirate material obtained**

- Laboratories should have available written instructions detailing their recommendations for specimen handling.

- The FNA material, including visible tissue fragments, should be smeared over one or two slides per pass to allow preparation of both air dried and alcohol fixed smears. Excessive blood contamination can make smearing of material obtained from the thyroid difficult, and more slides may be required to adequately smear the material. There are a variety of techniques available to produce a near-monolayer of cells and gently tease apart tissue fragments while preserving architectural and cellular detail. A number of these are detailed and illustrated at http://www.papsociety.org/fna.html and in texts on the subject, such as Orell, Sterrett and Whitaker.\textsuperscript{23} Thin, well spread smears facilitate rapid alcohol fixation or rapid air-drying, essential for optimal staining.

- The use of both alcohol-fixed and air-dried smears is optimal as the two techniques are complementary. However exclusive use of one type is acceptable. Slides can be alcohol fixed by either immersion in 95% ethanol or by spraying with a commercial fixative, and are then stained with either the Papanicolaou stain or haematoxylin and eosin. Air-dried slides are stained with a Romanowsky stain and the rapid modified Wright Giemsa (or ‘Diff Quik’) stain or similar is generally favoured.

- Cyst fluid may be assessed by making direct smears or prepared in the laboratory by centrifugation (eg for cell blocks) or LBC methods to concentrate the cellular material. The latter is useful to effectively sample large volume (>5 mL) specimens.
Record of Procedure

If the procedure is undertaken by a Cytopathologist then the following information should be recorded:

S2.01 The date of the FNA must be recorded.

S2.02 The identity of the FNA operator (pathologist, radiologist/other must be recorded.

CS2.02a It is not essential that this information be included in the final report, however the information must be readily available in the event that it is required.

S2.03 The location of each sampled nodule must be recorded.

G2.01 A description of the nodule(s) should be recorded.

CG2.01a The description should include the size of each nodule, whether calcification is present, the number of passes undertaken and whether the nodule was aspirated to dryness. If aspirated to dryness, any residual mass should be noted.

G2.02 If lymph nodes are sampled this should be recorded and include the location, size and cervical lymph node level.

CG2.02a Neat samples of cystic fluid or the supernatant or a needle rinse/wash of suspected metastases of papillary thyroid carcinoma (PTC) may be tested for thyroglobulin, or for parathyroid hormone when parathyroid tumours are suspected, if appropriate. Please refer to ancillary testing (chapter 4).

G2.03 The general appearance of the aspirate should be described.

G2.04 Any difficulties experienced with the aspiration may be recorded.

G2.05 If used, the level and type (including dose) of sedation should be recorded.

G2.06 Record any additional relevant information on the procedure.

Specimen information

The following standards and guidelines should be recorded about the specimen:

S2.04 The number of air dried and alcohol fixed slides and other specimens collected such as needle rinses must be reported.

S2.05 The distribution of biopsy material for investigational purposes must be reported.

CS2.04a This provides a checklist to indicate how many and what sort of ancillary tests may have been performed on a specimen in which results are still pending.
3 Terminology, microscopic findings, interpretation & recommendations

This section relates to purely cytological (morphological) assessment. Information derived from multiple investigational modalities, or from two or more chapters, is described in Chapter 5. The most widely known Bethesda system is used as the framework to prepare Australasian guidelines for reporting.

S3.01 The general classification (category descriptor) of the aspirate must be recorded.

CS3.01a Following general categorisation, a specific diagnosis must be stated, favoured or suggested, where applicable.

G3.01 The Bethesda System for Reporting Thyroid Cytopathology classification is included below in Table 1 with comments and recommendations for use in the Australasian setting. These are further discussed in detail in Table 2 under each general category.

CG3.01a Further information on interpretation, problems and issues and recommendations on each category as it pertains to the Australasian environment is explained in detail in Table 2.

CG3.01b A category descriptor should always be stated in a report with the category number when using the classification system in Table 1. The number should NOT be used without the descriptor to avoid any potential miscommunication with other numbered categories used for other sites eg breast.

S3.02 The report must include a summary of the cytological findings and, usually in a conclusion or comment, any recommendations as appropriate.

CS3.02a As the pathologist may not have the full clinical information (such as a previous indeterminate result), appropriate wording regarding the recommendation such as “consider in appropriate clinical context” may be used.

Any management recommendations should ideally be evidence–based.
Table 1: General categories with comparison to the Bethesda system and comments/recommendations

<table>
<thead>
<tr>
<th>Australasian Recommendations</th>
<th>Bethesda</th>
<th>Category number</th>
<th>Comments and recommendations *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-diagnostic</td>
<td>Non-diagnostic/Unsatisfactory</td>
<td>1</td>
<td></td>
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<tr>
<td>Benign</td>
<td>Benign</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Indeterminate OR</td>
<td>Atypia of undetermined</td>
<td>3</td>
<td>1. The use of the term</td>
</tr>
<tr>
<td>Follicular lesion of</td>
<td>significance/ Follicular lesion</td>
<td></td>
<td>atypia in the general</td>
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<tr>
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<td>of undetermined</td>
<td></td>
<td>diagnostic category is</td>
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<tr>
<td>significance</td>
<td>significance</td>
<td></td>
<td>discouraged.</td>
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<td></td>
<td></td>
<td></td>
<td>2. The word atypia is used</td>
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<td></td>
<td></td>
<td>to describe a cellular or</td>
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<td></td>
<td></td>
<td></td>
<td>architectural feature.</td>
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<td>3. Includes follicular and</td>
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<td></td>
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<td>non follicular lesions.</td>
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<td>4. Most cases will have a</td>
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<td>benign follow up.</td>
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<td>5. The choice of</td>
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<td>Follicular neoplasm or</td>
<td>4</td>
<td>The use of the term</td>
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<tr>
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<td>Suspicious for FN</td>
<td></td>
<td>suspicious is not</td>
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<td>recommended</td>
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<tr>
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<td>Suspicious of malignancy</td>
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</tr>
<tr>
<td>Malignant</td>
<td>Malignant</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

* See detailed discussion below under each general category.
1. Introduction

If the general category of Non-diagnostic (Category 1) is reported then a reason for this choice of category should also be included in the report.

For a thyroid aspirate to be adequately assessed and be reliably interpreted there must be sufficient well preserved cellular material, in order to prevent a false negative result. In the literature there is no definition of adequacy with level 1 evidence, but there are numerous definitions based on expert opinion (Level V).4,7,24,26 The most recent definition, and one which has been most accepted, is that of the Bethesda System for Reporting Thyroid Cytopathology:4 “greater than 6 groups of well-visualised follicular cells, with at least 10 cells per group (preferably on a single slide)”. The British Thyroid Association definition is very similar. This definition states that to be adequate “smears usually contain 6 or more groups of 10 or more thyroid follicular cells but the balance between cellularity and colloid may be more important”.

Percentage of FNA cases falling in this category: 10-15%4,7,8

2. Interpretation

For the purpose of this document, the definition of adequacy is: “Greater than 6 groups of well-visualised follicular cells, with at least 10 cells per group (preferably on a single slide)”, as is defined in the Bethesda System for Reporting Thyroid Cytopathology.4

3. Cytological findings

The rationale behind this definition is that it is thought that a sheet of 10 cells is sufficient to exclude a microfollicular architecture, and therefore a categorisation as Indeterminate or Follicular lesion of undetermined significance.

Reasons for an inadequate smear

a) There are less than 6 well preserved groups of 10 follicular epithelial cells.

b) Cyst fluid containing only cyst macrophages without epithelial cells, where there is no history of complete aspiration of the cyst, may be deemed inadequate as a cystic neoplasm cannot be excluded.

c) If there is abundant material but the preservation is poor due to inadequate fixation or too much blood.

The reason for the inadequate smear should be clearly stated in the report.

4. Practical issues, problems

Exceptions

There are however several exceptions to the definition above, when the smears may be considered adequate:

a) A cyst aspirated to dryness without residual mass or atypical features by imaging should be categorised as benign even in the absence of
epithelium (please refer to the benign section).

b) Smears with abundant thick colloid may be accepted as indicating a benign colloid nodule even if the aspirate is paucicellular or acellular.

c) There is inflammation with specific features indicative of thyroiditis, such as Hashimoto’s thyroiditis or granulomatous thyroiditis. In this situation there may be no follicular epithelial cells but a background of inflammatory cells.

d) The smears are paucicellular but the cells present cannot be deemed benign with certainty. In this situation, these cases should be placed in the appropriate category with an appropriate recommendation (repeat aspiration or specialist surgical opinion should be sought).

5. Recommendation

A categorisation of non-diagnostic should trigger a repeat aspirate under ultrasound guidance. There is no level 1 evidence regarding the optimum interval for a repeat aspiration. A 3 month interval has been suggested to prevent false-positive misinterpretations due to reactive/reparative changes. However the repeat interval may be decided by the clinician depending on the clinical circumstances.28,29

BENIGN (CATEGORY 2)

1. Introduction

Most thyroid nodules are benign and by accurately and reliably identifying these lesions as such patients can avoid further unnecessary investigation and surgery (the introduction of FNA has reduced the number of thyroid operations by 35-75%).30

Percentage of FNA cases falling in this category: 40-60%4,7,8

2. Interpretation

Benign; where possible a specific diagnosis should be given:

- Colloid nodule/follicular nodule/multinodular goitre
- Cyst
- Diffuse hyperplasia (Graves disease)
- Lymphocytic thyroiditis (Hashimoto)
- Acute thyroiditis
- Granulomatous thyroiditis (palpation, de Quervain)

3. Cytological findings

Minimum diagnostic criteria required with no significant atypia.

a) Colloid nodule/follicular nodule/multinodular goitre
   i. Abundant colloid generally with low cell to colloid ratio. Colloid has varied appearance ranging from watery thin (almost invisible and detected by even spread of material across slide) to typical
‘cracked pavement’ to thick (cracked glass or globular appearance).

ii. Cytologically benign follicular epithelial cells including flat sheets and intact follicles. Hyperplasia and/or metaplasia may be present.

iii. Hypercellularity permissible and often present.

iv. Microfollicular regions may be present but do not predominate.

v. Often have cystic changes with foamy macrophages.

vi. Siderophages (previous bleeding) often present.

vii. Goitre is characterised by the combination of the above features. Fibrosis and (non-psammomatous) calcification may be present but not commonly observed in cytology preparations.

b) Cyst

i. Cystic fluid with benign epithelium is classified as such.

ii. A cyst aspirated to dryness without residual mass or atypical features by imaging can be categorised as benign in the absence of epithelium.

iii. Cyst fluid without epithelium, not aspirated to dryness and without adequate clinical or radiological information should be assigned to Non-diagnostic (Category 1) (that is, if reporting pathologist has significant doubt about benignity then considered non-diagnostic).

c) Diffuse hyperplasia (Graves disease)

i. Hyperplasia is not synonymous with hypercellular (though both often co-exist).

ii. Cytological features of hyperplasia include follicular cells with pale, vacuolated cytoplasm and ‘fire-flares’. May be associated with some anisonucleosis and mild atypia including grooves.

iii. When considering a diagnosis of Graves disease an attempt should be made to correlate with thyroid function tests and autoantibodies.

d) Lymphocytic thyroiditis (Hashimoto)

i. Often hypercellular with reduced colloid.

ii. Lymphocytes present (by definition) but variable numbers from background cells to prominent with germinal centres (may overwhelm the epithelial component). Lymphocytes may be seen within epithelial cell groups. Plasma cells may or may not be present.

iii. Epithelial cells usually show oncocytic metaplasia (but not always); oncocytic cells usually have anisonucleosis.

iv. When considering a diagnosis of Hashimoto thyroiditis an attempt should be made to correlate with thyroid function tests and autoantibodies.

e) Acute thyroiditis

i. Characterised by acute inflammation: neutrophils, macrophages and cellular debris.

ii. Correlates with typical clinical features.
f) Granulomatous thyroiditis (palpation, de Quervain)
   i. Granulomatous inflammation
   ii. Consider differential diagnoses associated with granulomata (infection, etc.)

4. Practical issues, problems and suggestions for ancillary testing
   a) A confident diagnosis of a cyst without epithelium as benign requires clinicopathological/radiological correlation – the use of standardised request forms will facilitate provision of this information.
   b) A definitive diagnosis of autoimmune thyroiditis may be made with the knowledge of autoantibody results and thyroid function tests. These tests may not have been performed prior to FNA and a recommendation to perform these tests should be made.
   c) Colloid nodule/follicular nodule/multinodular goitre: These lesions may have variable features including some hypercellularity, minor nuclear "atypia" (often seen in areas of hyperplasia) and even a minor microfollicular component. The presence of these features is acceptable for benign categorisation.
   d) Dual benign pathology may be present eg colloid nodule and lymphocytic thyroiditis.
   e) False negative diagnoses: Assessment of all cytology specimens requires appropriate interpretation of "atypia"; for thyroid cytology this may be cytomorphological or architectural pattern or both. Well differentiated thyroid carcinomas often have minimal morphological atypia with the diagnosis primarily based on pattern. Nevertheless, the presence of atypia should not automatically result in non-benign categorisation. There should be awareness of the suboptimal reproducibility of the histological distinction between follicular nodule, adenoma and well differentiated follicular carcinoma (despite histology being considered the "gold standard"). It is noted that there is no reliable method of auditing the rate of false negative diagnoses.

5. Recommendation
   No specific recommendation based on cytology alone.

INDETERMINATE OR FOLLICULAR LESION OF UNDETERMINED SIGNIFICANCE (CATEGORY 3)

1. Introduction
   This category reflects some degree of uncertainty in the cytological findings. Some features of a colloid nodule or of a hyperplastic or follicular nodule are present, but other features raise the less likely possibility of a follicular neoplasm (adenoma or well differentiated carcinoma).
   The proportion of cases in this category should be in the range of approximately 10% of the total number of cases.
   Percentage of FNA cases falling in this category: 3-20%
The use of the term atypia in the general diagnostic category is strongly discouraged. The term “Atypical” conveys a greater degree of concern for neoplasia, and therefore could trigger surgery which, in most cases, is likely to be inappropriate for this category. The term atypia may be used to describe a cellular or architectural feature as appropriate but not in the general category. In this category, the descriptors "indeterminate" and "follicular lesion of undetermined significance" are equally acceptable and can be used interchangeably and appropriately.

2. Interpretation
The cytological findings are indeterminate such that distinction between a non-neoplastic nodule (including colloid nodule, hyperplastic or follicular nodule, or occasionally thyroiditis) and a follicular neoplasm cannot be made with certainty. This category may include cases in which cells showing a degree of cytological atypia are present in greater numbers than regarded as non diagnostic or suboptimal. Most cases in this category will have a benign outcome.

Estimated likelihood of malignancy: VERY LOW

3. Cytological findings
1. A mixed pattern, with some flat sheets, some microfollicles and scant to moderate colloid. The findings raise the possibility of a neoplasm rather than strongly suggesting its likelihood.
2. Findings that raise the possibility of thyroiditis (eg the presence of moderate numbers of lymphocytes or lymphoid tangles but with an accompanying predominant microfollicular pattern), especially when there is clinical or imaging concern about neoplasm.
3. A history of Hashimoto thyroiditis but with a prominent Hürthle (oncocytic) cell population (benign Hürthle cell nodule versus neoplasm), especially when there is clinical concern about neoplasm.
4. A predominant pattern of colloid nodule but with a subpopulation of cells that exhibit nuclear atypia (for example nuclear enlargement or pale chromatin or nuclear grooves, raising the possibility of a very low likelihood of a papillary lesion) in which a repeat FNA may be useful in excluding malignancy but not surgery.
5. A predominant lymphoid population with few follicular cells in worrying clinical setting (eg elderly patient, longstanding lymphocytic thyroiditis, enlarging goitre), some degree of monotony or concerning nuclear changes that may warrant repeat aspiration, with or without ancillary testing, but not surgery.

4. Practical issues, problems and suggestions for ancillary testing
This category includes a range of pathological entities. The suggested management guideline is to repeat the FNA after an appropriate interval. Surgery is generally not indicated.

Studies have shown that repeat FNA results in a more definitive cytological diagnosis in 62.2% to 80% of cases. The incidence of malignancy on follow-up in this category is very low.
Ancillary testing
In selected cases appropriate immunohistochemical tests or molecular tests may be applied.36-39

Cases in which the possibility of a low grade lymphoma is raised might benefit from a repeat FNA and sending cytological material for flow cytometry, in order to characterise the lymphoid population and assess for the presence of clonality. It should be noted, however, that false positive results of clonality may sometimes be obtained,40,41 and clinicopathological correlation is required.

5. Recommendation
Repeat FNA after 3 months or at a shorter interval depending on clinical circumstances. In cases where there are subsequent ‘indeterminate/FLUS’ results the patient should be referred for specialist opinion. There is no level 1 evidence regarding the optimum interval for a repeat aspiration. A 3 month interval has been suggested to prevent false-positive misinterpretations due to reactive/reparative changes. However the repeat interval may be decided by the clinician depending on the clinical circumstances.28,29

In cases with a concerning lymphoid population, repeat the FNA with material for flow cytometry. If there is a genuine suspicion of a lymphoma Suspicious of malignancy (Category 5) is more appropriate.

SUGGESTIVE OF A FOLLICULAR NEOPLASM (CATEGORY 4)

1. Introduction
This category includes nodules in which the cytological features strongly suggest neoplasm with a follicular architecture, but the suspicion of malignancy is not high. Therefore the term ‘suggestive’ is recommended over ‘suspicious’.

Percentage of FNA cases falling in this category: ~10%4,7,8

2. Interpretation
“Findings that strongly suggest a follicular neoplasm, in which malignancy cannot be excluded.”

The spectrum of entities range from benign to malignant and include cellular hyperplastic nodule, follicular adenoma, follicular carcinoma, Hürthle cell neoplasm and follicular variant of papillary thyroid carcinoma (FVPTC). Lesions that are highly suggestive of a neoplasm with minimal, subtle nuclear features which are insufficient to classify as Suspicious of malignancy (Category 5) are often included in this category. A proportion of these cases may be classical papillary thyroid carcinoma (PTC) on histology. Some of these cases may be controversial even at histology.8 However the presence of nuclear features that strongly suggest PTC should warrant classification in Suspicious of malignancy (Category 5).

There should be enough justification for these lesions to be surgically managed. Estimated likelihood of malignancy: LOW TO MODERATE4,8
3. **Cytological findings**

1. Suggestive of follicular neoplasm - Scant or absent colloid and abundant blood may be present. Cellularity may be variable with follicular elements arranged in one or more of three patterns: predominant, repetitive microfollicles, syncytial sheets or trabeculae.

2. Suggestive of Hürthle cell neoplasm – A predominant oncocytic cell population with no significant lymphoid background. Other clues to neoplastic Hürthle cell lesions include cell dissociation, monotony, presence of cherry red macronucleoli and traversing vessels in larger tissue fragments. Colloid is variable, ranging from scanty to moderate.

3. In some cases in this category there are epithelial cells with subtle nuclear atypia (enlargement, pleomorphism, irregularity or focal grooves). Papillary thyroid carcinoma may be a consideration but there are insufficient nuclear features to categorise as suspicious of PTC.

4. Rare variants of medullary carcinoma may present with a follicular pattern.

4. **Practical issues, problems and suggestions for ancillary testing**

Although a fairly narrow cytological spectrum forms this category, the histologic outcomes include several different neoplasms which in reality, are quite different in terms of clinical behaviour and diagnostic criteria (eg follicular adenoma, follicular carcinoma, PTC). Cytological findings and recommendations for management must be clearly stated.

**Ancillary testing**

Ancillary testing might be useful in this category, depending on the cytological findings and availability of resources and expertise. Please refer to chapter 4.

5. **Recommendation**

Refer to specialist surgeon.

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Microfollicle - small follicular groups of approximately 6-12 follicular cells in a ring-like or wreath like arrangement, which may or may not have a small central colloid droplet evident.

Syncytial group - three dimension groups of overlapping follicular cells appearing as crowded irregularly shaped groups distinguishable from macrofollicles by their lack of associated colloid and absence of an orderly / honeycomb cell arrangement.

Trabecular architecture - rounded and overlapping follicular cells forming ribbons or trabeculae.
SUSPICIOUS OF MALIGNANCY (CATEGORY 5)

1. Introduction
This category includes cases diagnosed as suspicious of malignancy and typically fall into two groups:
   a. Qualitative: cellular aspirates in which the cytological features are insufficient to make a definite diagnosis of malignancy.
   b. Quantitative: highly atypical cells, but insufficient in number for a definite diagnosis of malignancy.

Percentage of FNA cases falling in this category: 2-3%4,7,8

2. Interpretation
This category specifically excludes follicular neoplasms.

When using this category the cytopathologist may give an indication of which type of malignancy the features would favour, for example, “suspicious of malignancy, favour medullary carcinoma” or “suspicious of medullary carcinoma”.

Estimated likelihood of malignancy: HIGH

3. Cytological findings
   a. The most common diagnosis falling into this category is “suspicious of papillary carcinoma”. Paucicellular, cystic lesions with some nuclear or background features suspicious of papillary carcinoma (such as multinucleated giant cells, psammomatous calcifications or squamoid cells) may also be reported in this category.
   b. A similar approach is applied to other primary thyroid carcinomas (medullary, poorly differentiated and anaplastic) and metastases. These cases need to be carefully correlated with radiological and clinical findings with a clear recommendation for management.
   c. Lesions that show spindle cells or a predominant single cell population may raise the possibility of malignancy. These lesions are rare and include primary benign and malignant neoplasms, such as medullary carcinoma, metastatic malignancies or non-neoplastic lesions such as nodular fasciitis.

4. Practical issues, problems and suggestions for ancillary testing
   a. A repeat FNA may be appropriate to provide more conclusive evidence of malignancy and material for a cell block for ancillary studies.
   b. In selected cases other investigations (ie serum calcitonin assay for suspected medullary carcinoma) may be recommended.
   c. In cases where there is a suspicion of lymphoma, a repeat FNA with a recommendation for flow cytometry may establish a definitive diagnosis.
d. When ancillary tests are performed a supplementary report should be issued with relevant findings and additional information.
e. A more definitive classification may be obtained with consultation or further clinical information.

5. **Recommendation**
The recommendation for this category would be specialist referral.
In selected cases other investigations and repeat aspiration for ancillary testing (as described above) may be recommended.

**MALIGNANT (CATEGORY 6)**

1. **Introduction**
This category should be used when there is sufficient cytological evidence to support an unequivocal diagnosis of malignancy.
Patients with a diagnosis of malignancy on FNA will often proceed to definitive cancer therapy and care must be exercised to ensure that a cytological diagnosis of malignancy can be made confidently.
This category does not include a diagnosis of follicular carcinoma as the diagnostic features of malignancy in follicular carcinoma, such as vascular and capsular invasion, can only be assessed histologically. These lesions are included under Suggestive of a follicular neoplasm (Category 4).
Percentage of FNA cases falling in this category: 3-4%\(^4,7,8\)

2. **Interpretation**
Cytological features of malignancy are present. Where possible a specific malignancy should be stated, favoured or suggested.
Estimated likelihood of malignancy: VERY HIGH (99-100%)

3. **Cytological findings**
The cytological features of the various thyroid malignancies are well described in standard texts and the literature and will not be repeated here.\(^4,7,8\)
Lesions which can be diagnosed as malignant on FNA include:
1. Primary malignant tumours of the thyroid
   a. Papillary thyroid carcinoma
   b. Medullary carcinoma
   c. Poorly differentiated carcinoma
d. Anaplastic carcinoma
e. Lymphoma
2. Metastatic tumours to the thyroid.
   For specific diagnoses and subtyping ancillary testing may be indicated in particular for a specific diagnosis of a lymphoma or metastases. Please refer to
the chapter on ancillary testing.

4. **Practical issues, problems**
   a. If there are insufficient cytological features for a definitive diagnosis of PTC classify as Suspicious of malignancy (Category 5).
   b. If the FNA has been examined at the time of aspiration by a scientist or pathologist and there is suspicion of medullary carcinoma then collection of material for immunohistochemical staining for Calcitonin (on cell block or unstained smears) is recommended.
   c. A definitive diagnosis of lymphoma typically requires ancillary studies in combination with flow cytometry.

5. **Recommendation**
   Specialist referral as appropriate.
4 Ancillary studies

Ancillary testing is not required for the majority of thyroid aspirates and is not recommended as part of routine practice. When appropriate, an adequate specimen should be available before proceeding to ancillary studies. Cell blocks are the most suitable for histochemistry and immunohistochemistry (IHC). Molecular testing can be performed on aspiration fluid, cyst fluid, cell blocks and liquid based preparations (LBP).8,26,36,44

The practice of using ancillary tests is essentially based on availability of resources and expertise as well as the clinical demand.

G4.01 The results of any ancillary tests performed should be incorporated into the pathology report.

CG4.01a Ancillary studies may be done in several situations:
1. To characterise cells in the aspirate
2. To confirm and classify a specific malignancy
3. To refine categorisation of a cytology sample
4. To detect genetic or molecular characteristics and provide prognostic information.

CG4.01b 1. Characterisation of cells in the aspirate

Cysts

A panel of cytokeratin stains may be useful to confirm the presence of epithelial cells. This exercise may be valuable when assessing specimens that may be deemed non-diagnostic due to paucity of cells.45,46

Primary thyroid origin

- TTF-1 and thyroglobulin are useful to establish thyroid origin. TTF1 is considered a sensitive marker for thyroid and lung carcinomas. However TTF1 does not have perfect specificity and rare neoplasms from other primary sites, such as breast, colon and prostate have been reported to express TTF-1.47-49 Thyroglobulin is more specific but interpretation of cytoplasmic positivity may be difficult due to background staining.
- PAX8 is another marker that shows consistent positivity in thyroid epithelial cells but is also expressed in renal, ovarian and pancreatic epithelium.50
- CDX2 is known to be positive in columnar cell variant of PTC.51
- Mucin production is not a feature of primary thyroid neoplasms with the exception of rare tumours such as mucoepidermoid carcinomas.
2. **Confirmation and classification of a specific malignancy**

Papillary, medullary and anaplastic carcinomas may be diagnosed with a very high degree of accuracy on cytomorphology alone. There are times when the cells are cytologically malignant but the subtyping is uncertain. In other situations the full complement of cytological criteria may be lacking leading to a suspicious rather than a definitive report. Judicious use of IHC may be valuable to arrive at a conclusive diagnosis.

**Papillary thyroid carcinoma (PTC)**

- CK19, HBME1 and Galactin combinations have been shown to be reliable in the diagnosis of classical PTC.\(^52\)-\(^55\)
- The V600E mutation of the BRAF kinase (BRAF) gene is a common event in PTC and the majority of classic (45-77%) and tall cell variants (80%).\(^56\),\(^57\) Detection of this mutation in aspirates should virtually confirm the diagnosis of PTC therefore can be used to confirm a diagnosis in suspicious cases.\(^58\),\(^59\),\(^36\),\(^60\)
- RET / PTC and PAX8 / PPARc gene abnormalities have been described in several thyroid neoplasms. However their use in thyroid cytology is not currently established.

**Medullary thyroid carcinoma (MTC)**

- IHC for calcitonin, CEA and neuroendocrine markers in cell block preparations may confirm medullary thyroid carcinoma.

**Anaplastic thyroid carcinoma (ATC)**

- Generally ATC does not show any specific IHC pattern. However metastatic malignancies would be the primary differential diagnosis and a negative reaction to site specific antibodies may be of help.

3. **To refine categorisation of a cytology sample**

- An aspirate categorised as suspicious of malignancy may be confirmed as PTC with a panel of IHC (HBME-1, CK19, Galectin and BRAF)\(^51\),\(^62\) and/or mutation testing for BRAF. However there is no universal acceptance of this in clinical practice.
- Commercially available molecular diagnostic kits for "inconclusive" categories are available including Afirma® Thyroid FNA Analysis (Veracyte Inc, San Francisco, CA) and miRInform® Thyroid (Asuragen®, Austin, TX). However the accuracy, advantages, cost effectiveness and use of these tests in routine practice needs further evaluation.\(^44\)
4. **To detect genetic or molecular characteristics and provide prognostic information**

A panel of mutations including those in the BRAF V600E and RAS genes and rearrangements involving RET / PTC and PAX8 / PPARc have been recommended in the management of thyroid nodules. Of these the BRAF mutation is the most evaluated marker for prognosis in relation to PTC as it appears to play a key role in the development and progression of this disease. PTCs with the BRAF V600E mutation are believed to be associated with advanced stage and aggressive biological behaviour although this notion is being questioned lately.63-65

The recent introduction of the selective BRAF V600E inhibitor PLX4032 in the management of melanomas harbouring the T1799A point mutation has renewed interest in the identification of BRAF mutated thyroid carcinomas as possible targets for alternative therapy for otherwise treatment-resistant BRAF T1799A-mutated PTC.

CG4.01c **Flow cytometry**

Cell surface marker analysis by flow cytometry is indicated in suspected lymphoproliferative disorders.

The decision to submit material for flow cytometry may have to be made at the time of aspiration with on site evaluation. This decision may be guided by the clinical circumstances in addition to the presence of suspicious or concerning cytological features. Flow cytometry enables characterisation of the lymphoid population with confirmation of clonality. It should be noted, however, monoclonality may occur in Hashimoto thyroiditis.40,41 The results should be interpreted in conjunction with the clinical and cytological findings.

CG4.01d **Thyroglobulin assay in lymph nodes**

Thyroglobulin assay in aspirates of suspected metastatic papillary thyroid carcinoma can be helpful in establishing a diagnosis. Aspiration samples, the supernatant of cyst fluid or a needle rinse may be tested for thyroglobulin levels.66-68

CG4.01e **Parathyroid hormone assay**

In lesions suspected of being parathyroid tumours or cysts, material can be sent for parathyroid hormone testing (needle washed in 0.1- 0.5ml of normal saline).69
5 Synthesis and overview

Information that is synthesised from multiple modalities and therefore cannot reside solely in any one of the preceding chapters is described here.

By definition, synthetic elements are inferential rather than observational, often representing high-level information that is likely to form part of the report ‘Summary’ or ‘Diagnosis’ section in the final formatted report.

Overarching case comment is synthesis in narrative format. Although it may not necessarily be required in any given report, the provision of the facility for overarching commentary in a cancer report is essential.

G5.01 A field for free text or narrative in which the reporting pathologist can give overarching case comment must be provided.

CG5.01a This field may be used, for example, to:
- list any relevant ancillary tests
- document any noteworthy adverse gross histological features in the cell block
- express any diagnostic subtlety or nuance that is beyond synoptic capture
- document further consultation or results still pending.

CG5.01b Use of this field is at the discretion of the reporting pathologist.
6 Structured checklist

The following checklist includes the standards and guidelines for this protocol which must be considered when reporting, in the simplest possible form. The summation of all “Standards” is equivalent to the “Minimum Data Set” for reporting thyroid FNA cases. For emphasis, standards (mandatory elements) are formatted in bold font.

S6.01 The structured checklist provided below may be modified as required but with the following restrictions:

a. All standards and their respective naming conventions, definitions and value lists must be adhered to.

b. Guidelines are not mandatory but are recommendations and where used, must follow the naming conventions, definitions and value lists given in the protocol.

G6.01 The order of information and design of the checklist may be varied according to the laboratory information system (LIS) capabilities and as described in Functional Requirements for Structured Pathology Reporting of Cancer Protocols.70

CG6.01a Where the LIS allows dissociation between data entry and report format, the structured checklist is usually best formatted to follow pathologist workflow. In this situation, the elements of synthesis or conclusions are necessarily at the end. The report format is then optimised independently by the LIS.

CG6.01b Where the LIS does not allow dissociation between data entry and report format, for example where only a single text field is provided for the report, pathologists may elect to create a checklist in the format of the final report. In this situation, communication with the clinician takes precedence and the checklist design is according to principles given in Chapter 7.

G6.02 Where the checklist is used as a report template (see G6.01), the principles in Chapter 7 and Appendix 2 apply.

CG6.02a All extraneous information, tick boxes and unused values should be deleted.

G6.03 Additional comment may be added to an individual response where necessary to describe any uncertainty or nuance in the selection of a prescribed response in the checklist. Additional comment is not required where the prescribed response is adequate.
Values in italics are conditional on previous responses.

Values in all caps are headings with sub values.

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<tr>
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<td><strong>Date</strong></td>
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<td>FNA operator (name, contact details, role ie radiologist/surgeon etc)</td>
<td><strong>Text</strong></td>
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<td><strong>Note:</strong> repeat for each aspirated nodule.</td>
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<td>Number of passes</td>
<td><strong>Numeric:</strong> ____</td>
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**Record of procedure (If FNA performed by Cytopathologist)**

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**Microscopic findings**

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<tr>
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<td>• Equivocal antibodies</td>
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<tr>
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<td>• Negative antibodies</td>
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<td>Text</td>
<td>Conditional</td>
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<td><em>Note:</em> Test result type, result and interpretive comment will need to repeat for each other test performed.</td>
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**Synthesis and overview**

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</table>

7 Formatting of pathology reports

Good formatting of the pathology report is essential for optimising communication with the clinician, and will be an important contributor to the success of cancer reporting protocols. The report should be formatted to provide information clearly and unambiguously to the treating doctors, and should be organised with their use of the report in mind. In this sense, the report differs from the structured checklist, which is organised with the pathologists’ workflow as a priority.

Uniformity in the format as well as in the data items of cancer reports between laboratories makes it easier for treating doctors to understand the reports; it is therefore seen as an important element of the systematic reporting of cancer. For guidance on formatting pathology reports, please refer to Appendix 2.
Appendix 1  Pathology request information

This appendix describes the information that should be collected before the pathology test. Some of this information can be provided on generic pathology request forms; any additional information required specifically for the reporting of a thyroid FNA may be provided by the clinician on a separate request information sheet. An example request information sheet is included below. Elements which are in bold text are those which cytopathologists consider to be required information. Those in non-bold text are recommended.

Also included in this appendix are the procedures that are recommended before handover of specimens to the laboratory.

Patient information

➤ Adequate demographic and request information should be provided with the specimen.

• Items relevant to cancer reporting protocols include:
  • patient name
  • date of birth
  • sex
  • identification and contact details of requesting doctor, who referred the patient to the radiologist or cytopathologist
  • date of request

• The patient’s ethnicity should be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.

➤ The patient’s health identifiers should be provided.

• The patient’s health identifiers may include the patient’s Medical Record Number as well as a national health number such as a patient’s Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

Clinical Information

➤ Any history of prior surgery, radiation to head and neck area and prior FNA will be important information to include in the request information.

➤ Results of any thyroid function tests eg T3, T4, TSH and Thyroid antibodies should be included. These are most helpful in cases of multiple nodules.

➤ The radiologic and ultrasonographic appearances of the nodule(s) (those to be sampled/sampled, and other nodules not sampled) and
surrounding thyroid should be described.
- The location and size of the nodule(s) should be described.
- The description of the nodules may include:
  - Cystic
  - Solid
  - Mixed
  - Other (describe)
- The presence or absence of any calcification should be included.
- Any other relevant clinical information should be recorded.
- Submission of a copy of the referring doctor’s letter to the radiologist and the radiology report with the request form are desirable.

**Procedural Information**

If the request is accompanied by biopsied material the following information on the procedure should be submitted with the request form:

- **The date of the FNA.**
- **The name, contact details and role (radiologist/surgeon/other) of the clinician who performed the procedure.**
- The method of aspiration ie direct by palpation or ultrasound guided.
- The number of passes undertaken.
- The general appearance of the aspirate.
- Whether or not the nodule(s) are aspirated to dryness ie completely aspirated. If aspirated to dryness, any residual mass should be noted.
- Whether lymph nodes are sampled and if so the location size and level should be recorded.
- Any difficulties experienced with the aspiration may be described.
- If used the level and type (including dose) of sedation.
Example Request Information Sheet

### Thyroid FNA Cytology Request Information

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#### Clinical Information

**History of prior surgery/radiation**

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**Thyroid function test results**

- T3
- T4
- TSH

**Thyroid antibodies**

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<th>Module Identifier</th>
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<th>Calcification</th>
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</table>

#### Other relevant information and comments

**Please attach a copy of the radiology report with the request form**

*Ver. 1.0 Request Information Thyroid FNA Cytology Structured Reporting Protocol 1st Edition*
PROCEDURAL INFORMATION (Please complete the following if biopsied material is submitted with the request form.)

Date of FNA: [DD - MM - YYYY]  
Direct ☐  Ultrasound guided ☐

FNA operator (name, contact details)

Radiologist: ☐  Surgeon ☐  Pathologist present ☐
Other: [Other details]

Sampled nodules

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<th>No. of passes</th>
<th>Residual mass</th>
<th>General appearance of aspirate</th>
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Lymph nodes

Not sampled ☐  Sampled ☑

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Any difficulties experienced with the aspiration


Sedation (level and type)


Vers. 1.0 Request Information Thyroid FNA Cytology Structured Reporting Protocol 1st Edition
Appendix 2  Guidelines for formatting of a pathology report

Layout

Headings and spaces should be used to indicate subsections of the report, and heading hierarchies should be used where the LIS allows it. Heading hierarchies may be defined by a combination of case, font size, style and, if necessary, indentation.

- Grouping like data elements under headings and using ‘white space’ assists in rapid transfer of information.\(^{71}\)

Descriptive titles and headings should be consistent across the protocol, checklist and report.

When reporting on different tumour types, similar layout of headings and blocks of data should be used, and this layout should be maintained over time.

- Consistent positioning speeds data transfer and, over time, may reduce the need for field descriptions or headings, thus reducing unnecessary information or ‘clutter’.

Within any given subsection, information density should be optimised to assist in data assimilation and recall.

- Configuring reports in such a way that they ‘chunk’ data elements into a single unit will help to improve recall for the clinician.\(^{71}\)
- ‘Clutter’ should be reduced to a minimum.\(^{71}\) Thus, information that is not part of the protocol (eg billing information, Snomed codes, etc) should not appear on the reports or should be minimized.
- Injudicious use of formatting elements (eg too much bold, underlining or use of footnotes) constitutes clutter and may distract the reader from the key information.

Where a structured report checklist is used as a template for the actual report, any values provided in the checklist but not applying to the case in question must be deleted from the formatted report.

Reports should be formatted with an understanding of the potential for the information to mutate or be degraded as the report is transferred from the LIS to other health information systems.

As a report is transferred between systems:

- text characteristics such as font type, size, bold, italics and colour are often lost
- tables are likely to be corrupted as vertical alignment of text is lost when fixed font widths of the LIS are rendered as proportional fonts on screen or in print
- spaces, tabs and blank lines may be stripped from the report, disrupting the formatting
- supplementary reports may merge into the initial report.
Appendix 3  Examples of cytopathology reports

Examples of full reports

Example 1: Benign (category 2)

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**Thyroid FNA STRUCTURED REPORT**

FNA of right upper lobe nodule

CONCLUSION: Benign (category 2); colloid nodule

CYTOLOGICAL FINDINGS (Microscopic):
The smears are moderately cellular and contain benign appearing follicular epithelial cells with background thin colloid that contains abundant macrophages; some features of hyperplasia are noted. There is no significant nuclear atypia and there is no prominent microfollicular pattern. The features suggest a colloid nodule with some cystic degeneration.

CLINICAL
Clinical information provided: Copy of radiology report submitted

RECORD OF PROCEDURE
Date of FNA: 2/9/2013
FNA operator: DB Massid

SPECIMEN INFORMATION
Specimen types/slides: 2 air dried smears, 2 fixed smears
Distribution of biopsy material: Not applicable

Reported by Dr Maria Giuseppe  
Authorised 4/9/2013
Example 2: Suggestive of follicular neoplasm (category 4)

Thyroid FNA STRUCTURED REPORT

FNA of Left thyroid nodule

CONCLUSION: Suggestive of follicular neoplasm (category 4)

CYTOLOGICAL FINDINGS (Microscopic):
Moderately cellular smears show a predominant, repetitive microfollicular pattern admixed with some syncytial sheets of follicular cells. No significant nuclear atypia is present. Scant colloid is noted in the background.

Recommendation:
Referral to specialist surgeon for lobectomy.

CLINICAL
Clinical information provided: Copy of radiology report submitted

RECORD OF PROCEDURE
Date of FNA: 2/9/2013
FNA operator: S. J. Johns

SPECIMEN INFORMATION
Specimen types/slides: 2 air dried smears, 2 fixed smears
Distribution of biopsy material: Not applicable

Reported by Dr F. Singh

Authorised 4/9/2013
Examples of abbreviated reports

Each report requires a conclusion with the descriptor and category number. A brief statement with further clarification is often required. Several options and examples are given below. These example reports are only guides.

**NON DIAGNOSTIC (Category 1)**

**Example 1**

US FNA left thyroid lobe  
**CONCLUSION:**  
NON-DIAGNOSTIC (Category 1); inadequate cellularity for assessment.

**CYTOLOGICAL FINDINGS (MICROSCOPIC):**  
(insert as appropriate)

**RECOMMENDATION:**  
Repeat aspiration in 3 months or as clinically indicated.

**Example 2**

US FNA left thyroid lobe  
**CONCLUSION:**  
NON-DIAGNOSTIC (Category 1); smears are heavily blood stained with a few scattered poorly preserved cells.

**CYTOLOGICAL FINDINGS (MICROSCOPIC):**  
(insert as appropriate)

**RECOMMENDATION:**  
Repeat aspiration in 3 months or as clinically indicated.

**Example 3**

US FNA left thyroid lobe  
**CONCLUSION:**  
NON-DIAGNOSTIC (Category 1); unsatisfactory smears with poor preservation and smearing artifacts.

**CYTOLOGICAL FINDINGS (MICROSCOPIC):**  
(insert as appropriate)

**RECOMMENDATION:**  
Repeat aspiration in 3 months or as clinically indicated.
Example 4

US FNA left thyroid lobe

CONCLUSION:
NON-DIAGNOSTIC (Category 1); a cystic lesion with no epithelial cells (please see comment).

CYTOLOGICAL FINDINGS (MICROSCOPIC):
The smears and cell block made of 5 ml fluid received contain foamy macrophages and granular debris. No intact epithelial cells or malignant cells are seen.

RECOMMENDATION:
Repeat aspiration in 3 months or as clinically indicated.

Comment: If the cyst was aspirated to dryness with no residual mass remaining this lesion may be considered benign. Please correlate with radiological appearance.

BENIGN (CATEGORY 2)

Example 1

FNA of right upper lobe nodule

CONCLUSION:
Benign (category 2); lymphocytic thyroiditis

CYTOLOGICAL FINDINGS (MICROSCOPIC):
The smears are moderately cellular and contains follicular epithelial cells with a mixed population of lymphocytes in background blood; colloid is difficult to discern. The epithelial cells are variable with some focal oncocytic change; these oncocytic cells have some irregularities of the nuclear membrane and very occasional grooves. The lymphoid population appears benign. The features suggest lymphocytic thyroiditis.

RECOMMENDATION:
Correlation with autoantibodies and thyroid function tests may be useful.

Example 2

FNA of right upper lobe nodule

CONCLUSION:
Benign (category 2); cellular colloid nodule

CYTOLOGICAL FINDINGS (MICROSCOPIC):
The smears are moderately cellular with abundant follicular epithelial tissue fragments and dispersed intact cells in a background of thin
colloid and blood. The epithelial cells are uniform; some stripped nuclei are present. There are some intact follicles and also occasional microfollicles though the latter feature does not predominate. There is no significant nuclear atypia. The features suggest a cellular colloid nodule.

RECOMMENDATION:
Nil

Example 3

FNA of right upper lobe nodule
CONCLUSION:
Benign (category 2); cyst

CYTOLOGICAL FINDINGS (MICROSCOPIC):
The aspirate contains abundant thin colloid with admixed macrophages. There is no epithelial sampling.

RECOMMENDATION:
Repeat aspiration if cyst re-accumulates.

Comment: This has been categorised as a benign cyst given the clinical information of no residual mass/no complex features by ultrasound.

INDETERMINATE (CATEGORY 3)

Example 1

US FNA right thyroid
CONCLUSION:
INDETERMINATE/ FOLLICULAR LESION OF UNDETERMINED SIGNIFICANCE (CATEGORY 3); Unable to differentiate between colloid nodule and neoplasm.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
The smears are heavily bloodstained and show scattered crowded clusters of thyroid epithelial cells. No colloid is seen. No features of papillary carcinoma are noted.

RECOMMENDATION:
Repeat aspiration in 3 months or as clinically indicated.
Example 2

Left thyroid nodule FNA

CONCLUSION:
INDETERMINATE/FOLLICULAR LESION OF UNDETERMINED SIGNIFICANCE (Category 3); features indeterminate between adenomatous nodule and follicular neoplasm

CYTOLOGICAL FINDINGS (MICROSCOPIC):
Relatively hypocellular smears show both flat sheets as well as microfollicular arrangements of follicular cells with no significant nuclear atypia. Minimal colloid is present in the background.

RECOMMENDATION:
Repeat aspiration in 3 months or as clinically indicated. Suggest correlation with clinical and radiological findings.

Example 3

Left thyroid nodule, FNA

CONCLUSION:
INDETERMINATE (Category 3); microfollicular pattern with lymphocytic infiltrates, raising the possibility of thyroiditis

CYTOLOGICAL FINDINGS (MICROSCOPIC):
Smears show prominent microfollicular arrangements of follicular cells, accompanied by a background lymphoid population composed predominantly of small lymphocytes, admixed with larger, more activated forms. Minimal colloid is identified. No significant nuclear atypia is noted.

RECOMMENDATION:
Repeat aspiration in 3 months and correlate with clinical, biochemical and relevant serological investigations.

Comment: The findings raise the possibility of a lymphocytic thyroiditis.

Example 4

Left thyroid nodule, FNA

CONCLUSION:
INDETERMINATE/FOLLICULAR LESION OF UNDETERMINED SIGNIFICANCE (Category 3); Features indeterminate between adenomatous nodule and follicular neoplasm.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
Relatively hypocellular smears show both flat sheets as well as microfollicular arrangements of follicular cells with no significant nuclear atypia. Minimal colloid is present in the background.

**RECOMMENDATION:**
Repeat FNA after an appropriate interval and correlation with clinical and radiological findings.

Comment: The likelihood of malignancy is low.

---

**Example 5**

Left thyroid nodule, FNA

**CONCLUSION:**
**INDETERMINATE (Category 3);** Microfollicular pattern with lymphocytic infiltrates, raising the possibility of thyroiditis

**CYTOLOGICAL FINDINGS (MICROSCOPIC):**
Smears show prominent microfollicular arrangements of follicular cells, accompanied by a background lymphoid population composed predominantly of small lymphocytes, admixed with larger, more activated forms. Minimal colloid is identified. No significant nuclear atypia is noted.

**RECOMMENDATION:**
Repeat FNA after an appropriate interval and correlate with clinical, biochemical and relevant serological investigations.

Comment: The likelihood of malignancy is low. The findings raise the possibility of a lymphocytic thyroiditis.

---

**SUGGESTIVE OF A FOLLICULAR NEOPLASM (CATEGORY 4)**

**Example 1**

US FNA right thyroid

**CONCLUSION:**
**Suggestive of a follicular neoplasm (Category 4);** favour follicular neoplasm

**CYTOLOGICAL FINDINGS (MICROSCOPIC):**
The smears are heavily bloodstained and cellular showing many equal sized repetitive rounded microfollicles, some of which contain colloid in the central lumen. No thin colloid is seen. No features of papillary carcinoma are noted.

**RECOMMENDATION:**
Suggest referral to specialist surgeon/excision.
Example 2

US FNA right thyroid

CONCLUSION:
Suggestive of a follicular neoplasm (Category 4)

CYTOLOGICAL FINDINGS (MICROSCOPIC):
The smears are cellular and a mixture of monolayered sheets and crowded aggregates of heavily bloodstained and cellular showing many equal sized repetitive rounded microfollicles, some of which contain colloid in the central lumen. No thin colloid is seen. No features of papillary carcinoma are noted.

RECOMMENDATION:
Suggest referral to specialist surgeon/excision.

SUSPICIOUS OF MALIGNANCY (Category 5)

Example 1

US FNA left thyroid lobe

CONCLUSION:
SUSPICIOUS OF MALIGNANCY (Category 5); suspicious of medullary carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist surgeon +/- repeat FNA for ancillary testing as appropriate. Serum calcitonin assay may be of value.

Example 2

US FNA left thyroid lobe

CONCLUSION:
SUSPICIOUS OF MALIGNANCY (Category 5); favour papillary carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist surgeon +/- repeat FNA for ancillary testing.
Example 3

US FNA left thyroid lobe

CONCLUSION: SUSPICIOUS OF MALIGNANCY (Category 5); features are highly suggestive but not diagnostic of papillary carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC): (as appropriate)

RECOMMENDATION: Referral to specialist surgeon.

Example 4

US FNA left thyroid lobe

CONCLUSION: SUSPICIOUS OF MALIGNANCY (Category 5); features are highly suggestive but not diagnostic of papillary carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC): (as appropriate)

RECOMMENDATION: Referral to specialist surgeon.

Comment: Cell block was insufficient for further assessment and ancillary testing.

Example 5

US FNA left thyroid lobe

CONCLUSION: SUSPICIOUS OF MALIGNANCY (Category 5); some features favour a poorly differentiated thyroid carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC): (as appropriate)

RECOMMENDATION: Referral to specialist surgeon.

Example 6

US FNA left thyroid lobe

CONCLUSION: SUSPICIOUS OF MALIGNANCY (Category 5); features are highly suggestive of a lymphoma.
CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist management.
A repeat FNA for ancillary testing and flow cytometry would be helpful.

Example 7

US FNA left thyroid lobe
CONCLUSION:
SUSPICIOUS OF MALIGNANCY (Category 5); it is difficult to further characterise the neoplasm.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist management. A repeat FNA for ancillary testing may be helpful.

MALIGNANT (CATEGORY 6)

Example 1

US FNA left thyroid lobe
CONCLUSION:
MALIGNANT (Category 6); papillary thyroid carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist surgeon.

Example 2

US FNA left thyroid lobe
CONCLUSION:
MALIGNANT (Category 6); papillary thyroid carcinoma with focal poorly differentiated features.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist surgeon.

Example 3

US FNA left thyroid lobe

CONCLUSION:
MALIGNANT (Category 6); papillary thyroid carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist surgeon.

Example 4

US FNA left thyroid lobe

CONCLUSION:
MALIGNANT (Category 6); medullary thyroid carcinoma.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist surgeon.

Comment: Suggest clinicopathological correlation.

Example 5

US FNA left thyroid lobe

CONCLUSION:
MALIGNANT (Category 6); an undifferentiated malignancy. Possibilities would include an anaplastic thyroid carcinoma of thyroid and metastatic malignancy.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist surgeon. A repeat FNA for ancillary studies may be helpful in further characterisation of malignant cells.

Comment: Suggest clinicopathological correlation.
Example 6

US FNA left thyroid lobe

CONCLUSION:
MALIGNANT (Category 6); consistent with metastatic renal cell carcinoma in the given clinical setting.

CYTOLOGICAL FINDINGS (MICROSCOPIC):
(as appropriate)

RECOMMENDATION:
Referral to specialist management.

Comment: Cytological features and are similar to those of the primary renal cell carcinoma (Ref XXXXXXXXX) and the immunohistochemical profile is consistent with a renal cell carcinoma.
References


10 RCPA (Royal College of Pathologists of Australasia) (2009 ). *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*. RCPA, Surry Hills NSW.


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<thead>
<tr>
<th>Reference</th>
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<tr>
<td>Baloch ZW, LiVolsi VA (2007).</td>
<td>Our approach to follicular-patterned lesions of the thyroid [J Clin Pathol 60:244-250.]</td>
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<tr>
<td>Nayar R, Ivanovic M (2009).</td>
<td>The indeterminate thyroid FNA: Experience from an academic center using terminology similar to that proposed in the 2007 NCI Thyroid [Cancer Cytopathology(117):195-202.]</td>
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<tr>
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Li C, Han PA, al LKe (2013). Does BRAF V600E Mutation Predict Aggressive Features in Papillary Thyroid Cancer? Results From Four Endocrine Surgery Centers. The Journal of Clinical Endocrinology & Metabolism 98(9):3702-3712.


