FNA is the most reliable and cost effective diagnostic modality in the pre-operative assessment of the thyroid nodule in euthyroid patients. The key to the success of the FNA consists of an adequate and representative cell sample and expertise in cytology.

Fine Needle Aspiration (FNA) has become the cornerstone of thyroid nodule management. It is the most reliable and cost effective diagnostic modality in the pre-operative assessment of the thyroid nodule in euthyroid patients, reliably triaging patients for either surgical excision or clinical follow up, reducing unnecessary surgery in benign nodules and allowing appropriate and timely surgical intervention for malignant nodules.

The prevalence of thyroid nodules is high, but fewer than five percent are malignant. Every palpable thyroid nodule is a candidate for FNA which can be guided either by palpation or ultrasound. Although there are benefits of reduced cost and logistical efficiency with palpation guidance, the FNA performed with ultrasound guidance ensures precise needle placement and therefore reduces unsatisfactory samples and improves diagnostic accuracy. However, many nodules are impalpable, with an increasing number of these detected incidentally by imaging studies of the neck, and it is not practical to perform an FNA on all of these. Therefore nodules less than 1cm in diameter by ultrasound are not usually biopsied unless they have sonographically suspicious features. FNA is not advised for hyperfunctioning or “hot” nodules because these are rarely malignant, but frequently show cytological features which may mimic thyroid neoplasia.

It is crucial that the interpretation and results of thyroid cytology are clearly, succinctly and unambiguously conveyed to the referring clinicians in a clinically useful manner. However, thyroid cytology reporting varies considerably from one laboratory to another, and is often confusing, hindering universal comparison of clinically meaningful data. Similar to standardised cervical cytology reporting, a uniform, synoptic reporting system for thyroid FNA has been developed by the National Cancer Institute, Bethesda MD, in order to facilitate effective communication among pathologists, clinicians and radiologists, allow research into epidemiology, molecular biology and pathology and enable reliable national and international comparison of data. In line with this trend, Melbourne Pathology has adopted the Australian Modified Bethesda System for reporting thyroid cytology. There are six diagnostic reporting categories and for each, there is an implied risk of malignancy and recommended clinical management.

### Diagnostic category | Risk of malignancy (%) | Usual management (a)
--- | --- | ---
Non-diagnostic | 0 – 3 | Repeat FNA with ultrasound guidance
Benign | 0 – 3 | Clinical follow up
Indeterminate | ~5 – 15 | Repeat FNA in 6 – 8 weeks or refer to specialist
Suspect for follicular patterned neoplasm | 15 – 30(b) | Surgical lobectomy
Suspicious for malignancy | 60 – 75 | Near-total thyroidectomy or surgical lobectomy
Malignant | 97 – 99 | Near-total thyroidectomy

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(a) Actual management may depend on other factors (eg clinical, sonographic) besides the FNA interpretation.
1. Non-diagnostic
This category accounts for approximately 10 – 30 percent of thyroid FNAs. Adequate samples are necessary to prevent false negative reports. For a thyroid FNA specimen to be adequate and satisfactory for evaluation, at least six groups of benign follicular cells, each consisting of at least ten cells, are required. This is partly dependent on the nature of the lesion, namely whether it is solid or cystic. For simple cysts, this category applies to “cyst fluid only” (CFO) specimens, containing only macrophages, as the cystic variant of papillary thyroid carcinoma cannot be excluded in the absence of follicular cells.

Correlation of cyst size and complexity on ultrasound may assist with further management. Insufficient cellular material obtained from FNA of a solid nodule will be reported as non-diagnostic or unsatisfactory for diagnosis and a repeat FNA is advised if clinically indicated. Poor or inadequate fixation and preservation, obscuring blood and overly thick smears are other causes of a result in this category and again, repeat FNA is advised.

The risk of malignancy for a CFO on a non-diagnostic sample is up to 4% and a repeat FNA with ultrasound guidance proves to be diagnostic in 50 – 88% of cases. Some nodules remain persistently non-diagnostic and for these cases, surgical excision is recommended as 10% prove to be malignant.

2. Benign
Most thyroid nodules are benign and therefore approximately 65% of FNAs will fall into this category. A benign diagnosis implies an adequate sample and encompasses nodules in nodular goitre, hyperplastic (adenomatoid) nodules, colloid nodules, nodules in Grave’s disease and follicular adenomas of macrofollicular type. Differentiation of these entities is not possible on cytology but this is of little importance as all of these entities are essentially managed in a similar, conservative manner, generally with clinical follow up and in some cases, with ultrasound, at 6 – 18 month intervals for 3 – 5 years. Repeat FNA is performed for nodules which show significant growth or which develop various ultrasound abnormalities such as hypervascularity, irregular outlines, calcification and hypoechogenicity. Surgery is recommended for the subset which include large, symptomatic nodules, worrisome clinical or ultrasound features and those nodules associated with a contralateral malignancy. The reported false negative rate is 1 – 3% with this category carrying a very low risk of malignancy.

3. Indeterminate
This is used for FNAs where the cytomorphological features are not convincingly benign but where the degree of cytological and/or architectural atypia or sample cellularity is not sufficient for a definite diagnosis of a follicular neoplasm or malignancy. This category should only account for approximately 10% of all thyroid FNAs.

This heterogeneous category carries a low risk of malignancy and surgery is therefore not recommended. Rather, a repeat FNA in 3 – 6 months, which yields a definitive cytologic diagnosis in up to 80% of cases, with surgery if the FNA is repeatedly atypical recommended.

4. Suspect for a follicular patterned neoplasm
Here, cytology is regarded as a screening test, selecting for surgery those nodules with a greater probability of malignancy. A diagnosis of “suspect for a follicular patterned neoplasm” is preferable over follicular neoplasm (FN) as up to 35% prove not to be neoplasms, but benign or hyperplastic nodules in nodular goitre. This term also recognises that it is impossible to distinguish a follicular adenoma from a follicular carcinoma on cytology alone, as the defining features of capsular and vascular invasion cannot be evaluated cytologically. The Hurthle cell variant is incorporated in this category and is differentiated from the follicular neoplasm because of its striking morphological differences. Management is surgical, either with hemithyroidectomy or lobectomy.

5. Suspicious for malignancy
This is a heterogeneous category which incorporates a variety of malignancies, excluding follicular and Hurthle cell neoplasms, where the features may be quantitatively or qualitatively insufficient for a definite diagnosis of malignancy. This category is comprised mostly of lesions which are suspect for papillary carcinoma (SPTC) and its variants, in addition to lesions which are suspect for medullary carcinoma and lymphoma. The positive predictive value of this category should be greater than 50%, ideally ranging between 65 – 85%. Management is surgical, but because this diagnosis is a degree less than definitive, it allows for a variety of management options such as lobectomy, total thyroidectomy or lobectomy with subsequent completion thyroidectomy.

6. Malignant
A malignant diagnosis accounts for 4 – 8% of all thyroid FNAs, most being papillary thyroid carcinomas. Specificity of a cytdiagnosis of papillary carcinoma is high, and 95 –100% prove to be so histologically. Management is surgical, the extent depending on patient age and status and radiological features.

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Dr Obers completed a Bachelor of Medicine and Bachelor of Surgery in 1985 at the University of Witwatersrand, Johannesburg, South Africa. She went on to complete her Pathology Fellowship Examination at the College of Medicine of South Africa in 1991 and in 1995, completed her fellowship Examination of the International Academy of Cytopathology. During this time, Dr Obers held several appointments at a number of medical institutions.

From 1986 – 87, she was a Registrar in the Cytopathology Unit at the Department of Anatomical Pathology, School of Pathology of the South African Institute of Medical Research (SAIMR) and the University of Witwatersrand. She went on to become Head of the Cytopathology Unit at Baragwanath Branch Laboratory, School of Pathology, SAIMR and the University of Witwatersrand. Dr Obers was appointed Practising Pathologist in 1994 at Lancel Laboratories in Johannesburg where she remained until 2009, heading up the Cytopathology Unit.

Dr Obers moved to Australia in February 2009 and joined Melbourne Pathology as a full time Histo and Cytopathologist. She became a fellow of the Royal Australasian College of Pathologists in 2010.

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