Classificazioni citologiche: verso uno schema internazionale unificato?

A. Crescenzi

Diagnostic categories

AACE-AME (2006)
ATA (2006)

- Non diagnostic
- Benign
- Suspicious/indeterminate
- Malignant

PSC (2007)

- Unsatisfactory
- Benign
- Cellular lesion, can not rule out follicular neoplasm
- Follicular Neoplasm
- Suspicious
- Malignant

Categorie Diagnostiche

Roma,
9-11 novembre 2012

SIAPEC-SIE (2007)

- Tir 1. Non diagnostico
- Tir 2. Negativo per cellule maligne
- Tir 3. Indeterminato (Proliferazione follicolare)
- Tir 4. Sospetto per malignità
- Tir 5. Positivo per cellule maligne

BTA (2002/7)

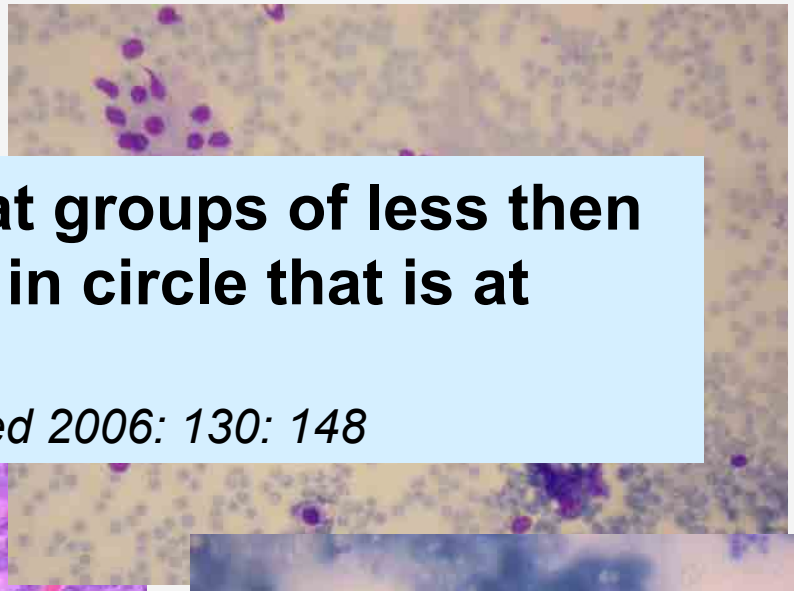
- Thy 1. Non diagnostic
- Thy 2. Non neoplastic
- Thy 3. Follicular lesion
- Thy 4. Suspicious of malignancy
- Thy 5. Diagnostic of malignancy

TIR3: Inconclusive/indeterminated (follicular proliferation) Siapec 2007

- Adenomatoid hyperplasia
- Follicular adenoma
- Follicular carcinoma
- Hurthle cell neoplasm
- Follicular variant of papillary carcinoma
- *Worrisome follicular alterations that cannot be placed in Tir2 but are not sufficient for a Tir4 categorization.*

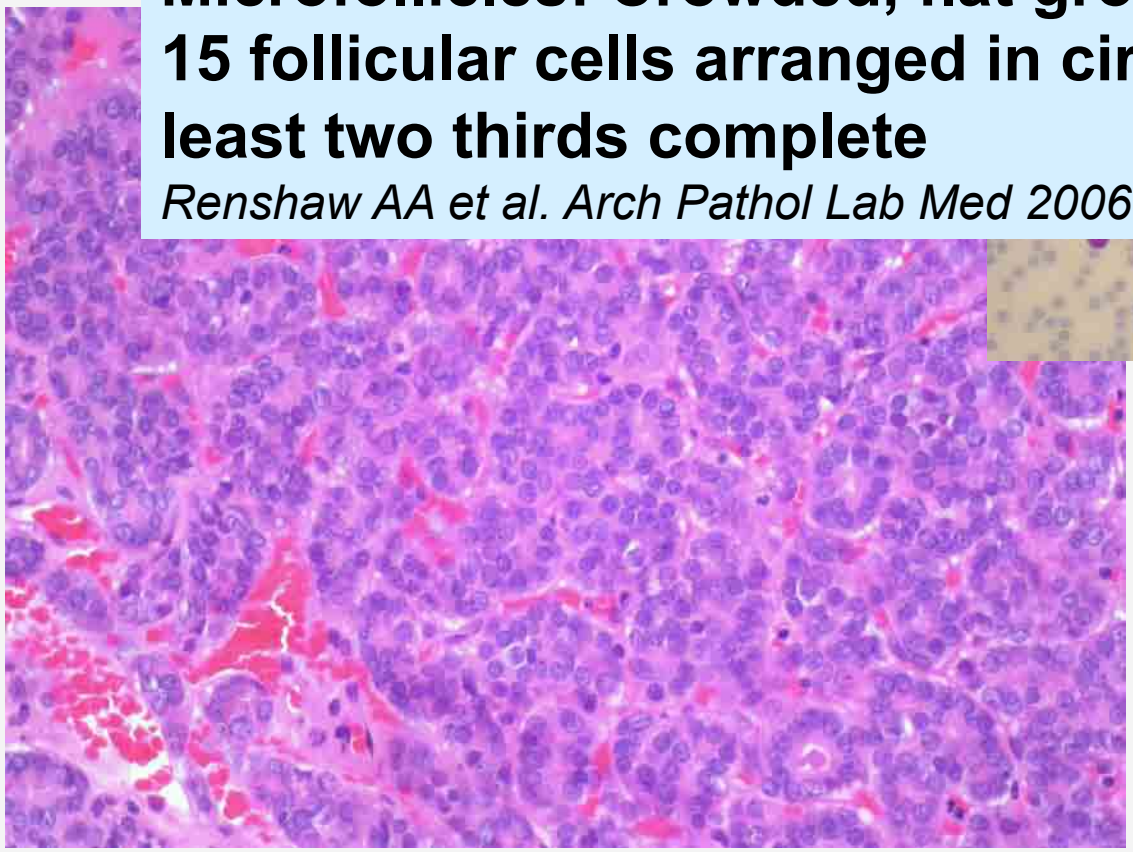
Follicular proliferation

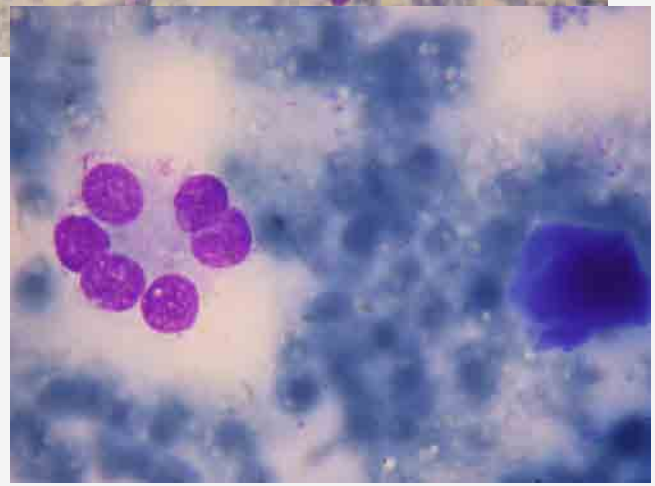
Needle diameter 300 microns
normal follicles 50-500
macrofollicles > 500
mic



Microfollicles: Crowded, flat groups of less then 15 follicular cells arranged in circle that is at least two thirds complete

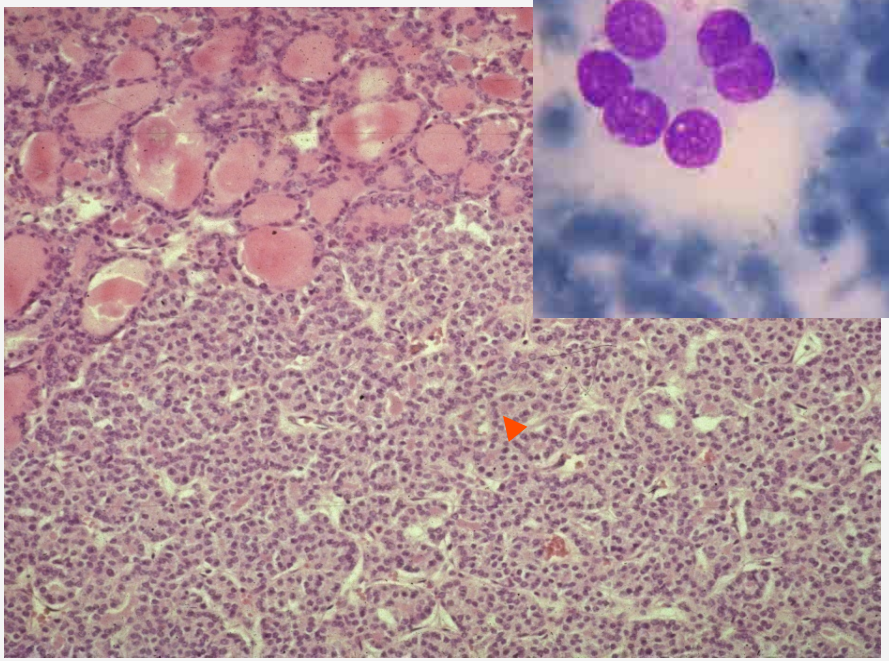
Renshaw AA et al. Arch Pathol Lab Med 2006: 130: 148

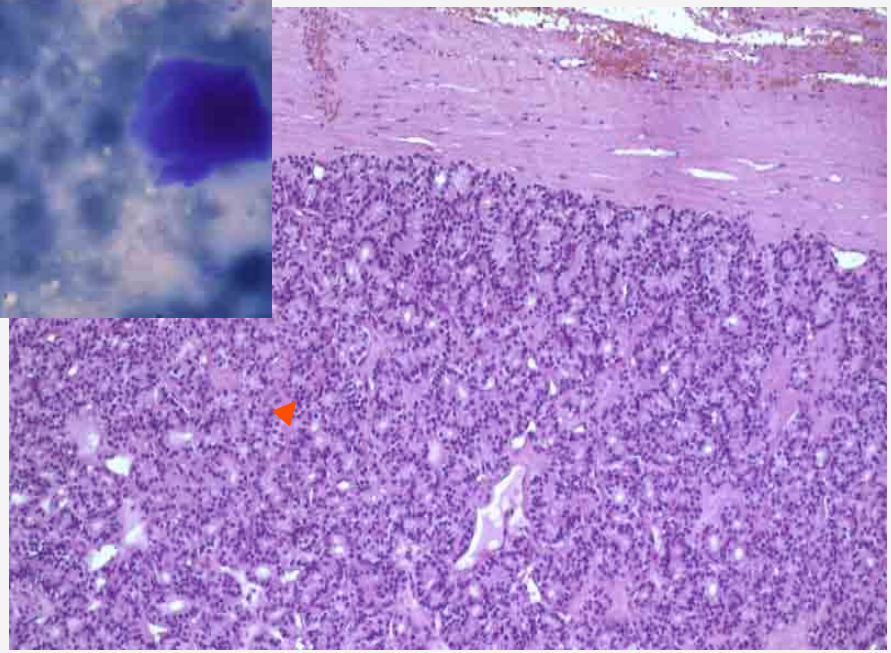




Follicular lesion TIR3

Adenomatoid h ar neoplasm



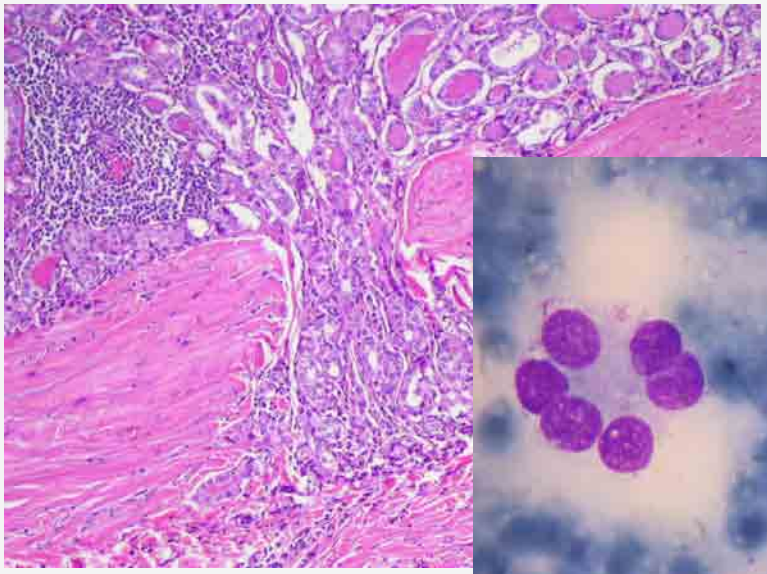


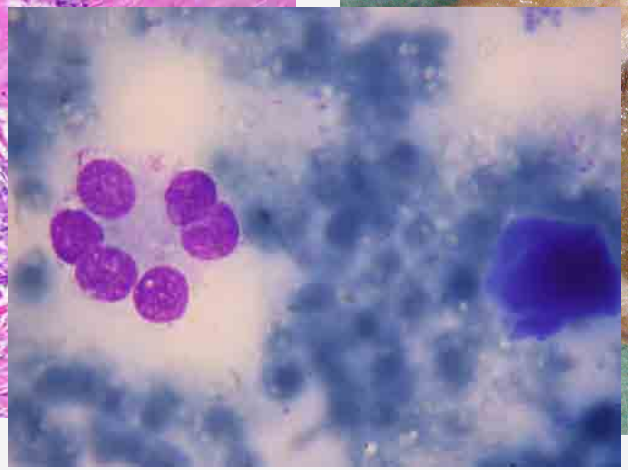
FNA

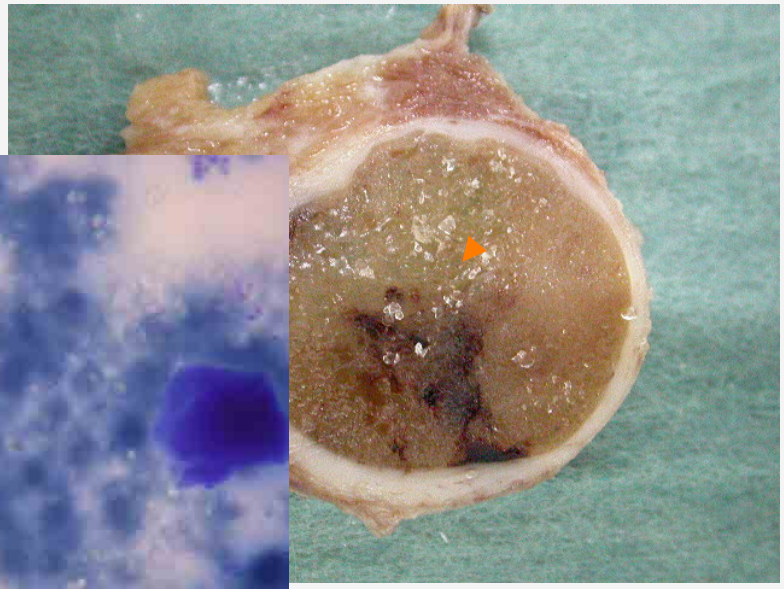
Follicular lesion TIR3

Follicular carcinoma: the diagnosis of malignancy depends primarily on the demonstration of unequivocal capsular and/or vascular invasion.

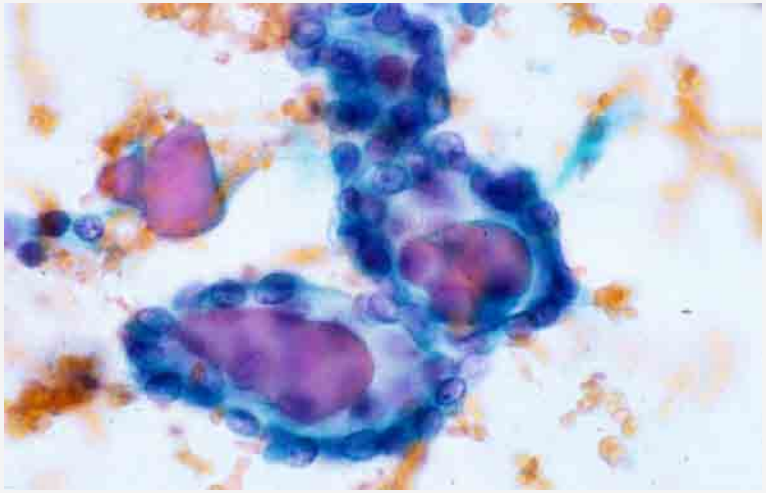
FNA

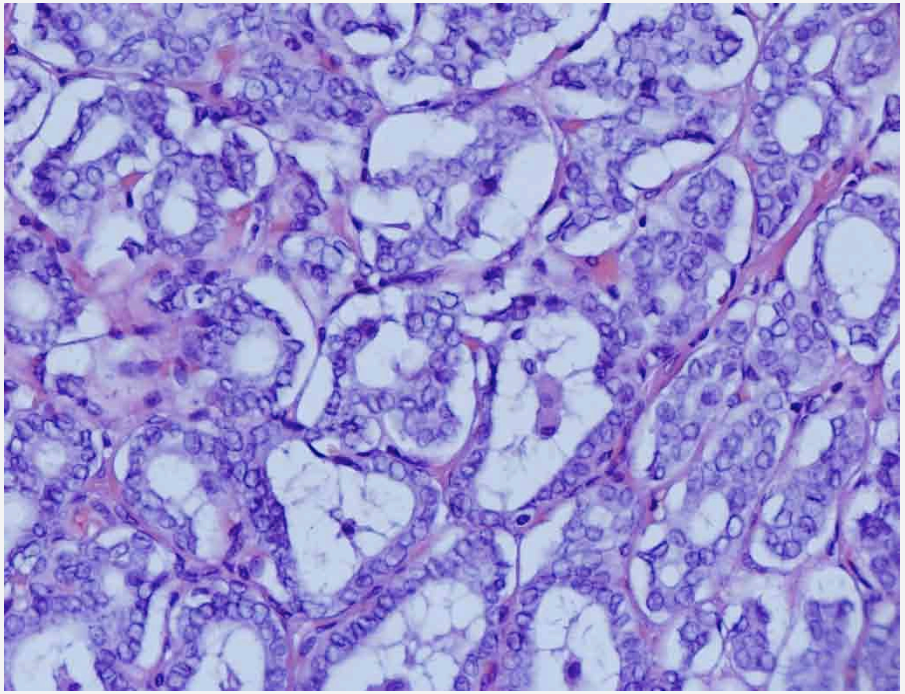






Follicular lesion TIR3 (Follicular variant of papillary carcinoma)





Cytologic diagnoses should be organized into 5 classes:

- **Class 1. Nondiagnostic** (inadequate or insufficient): samples with processing errors or an insufficient number of follicular cells
- **Class 2. Benign** (or negative for malignancy): includes colloid or hyperplastic nodules, Hashimoto or granulomatous thyroiditis, and cysts
- **Class 3. Follicular lesions:** all follicular-patterned lesions, including follicular neoplasms, Hürthle cell lesions, and the follicular variant of PTC.

In centers with specific experience in thyroid cytology, follicular cytology may be further subdivided into “follicular lesion/atypia of undetermined significance” and “follicular neoplasm.” This distinction separates 2 cytologic groups at different risk for thyroid malignancy but with the same operative Indications.

- **Class 4. Suspicious:** samples that suggest a malignant lesion but do not completely fulfill the criteria for a definite diagnosis
- **Class 5. Malignant (or positive):** samples characterized by malignant cytologic features that are reliably identified by the cytopathologist and are diagnostic of primary or metastatic tumors

7.3. Follicular Lesions

Treatment

- Surgical excision is recommended for most follicular thyroid lesions
- Intraoperative frozen section is not recommended as a routine procedure
- Consider clinical follow-up in the minority of cases with favorable clinical, US, cytologic, and immunocytochemical features

Diagnostic categories

The Bethesda System for Reporting Thyroid Cytopathology

Edmund S. Cibas, MD,[1] and Syed Z. Ali, MD[2]

- Unsatisfactory
- Benign
- Atypia of undetermined significance or follicular lesion of undetermined significance
- Follicular Neoplasm
- Suspicious for malignancy
- Malignant

Am J Clin Pathol 2009;132:658-665

Follicular Neoplasm or Suspicious for a Follicular Neoplasm

- The hallmark of this diagnostic category is a disturbed cytoarchitecture: follicular cells are arranged **predominantly** in microfollicular or trabecular arrangements

- Benign follicular nodules often have a small population of microfollicles and crowded groups. If these constitute **the minority** of the follicular cells, they have little significance and the FNA can be interpreted as benign.

- A suspicious interpretation is rendered only when **the majority** of the follicular cells are arranged in abnormal architectural groupings (microfollicles, crowded trabeculae).

Diagnostic Terminology and Morphologic Criteria for Cytologic Diagnosis of Thyroid Lesions:

A Synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference

Zubair W. Baloch, M.D., Ph.D.,[1*] Virginia A. LiVolsi, M.D.,[1,2] Syl L. Asa, M.D., Ph.D.,[3] Juan Rosai, M.D.,[4] Maria J. Merino, M.D.,[5] Gregory Randolph, M.D.,[6] Philippe Vielh, M.D., Ph.D.,[7] Richard M. DeMay, M.D.,[8] Mary K. Sidawy, M.D.,[9] and William J. Frable, M.D.[10]

	R/O neoplasm Atypical follicular lesion Cellular follicular lesion	
Neoplasm • Follicular neoplasm • Hurthle cell neoplasm	Suspicious for neoplasm • Suspicious for follicular neoplasm • Suspicious for Hurthle cell neoplasm	20–30%
Suspicious for malignancy		50–75%
Malignant		100%
Nondiagnostic	Unsatisfactory	

[a]Based on NCI Thyroid FNA website responses/discussions.
[b]Data collected from literature.[29,32,48,55,56]

UK RCPath

Diagnostic category

Thy1/Thy1c

Non-diagnostic for cytological diagnosis
Unsatisfactory, consistent with cyst

Thy2/Thy2c

Non-neoplastic

Thy 3a

Neoplasm possible – atypia/non-diagnostic

Thy 3f

Neoplasm possible - suggesting follicular neoplasm

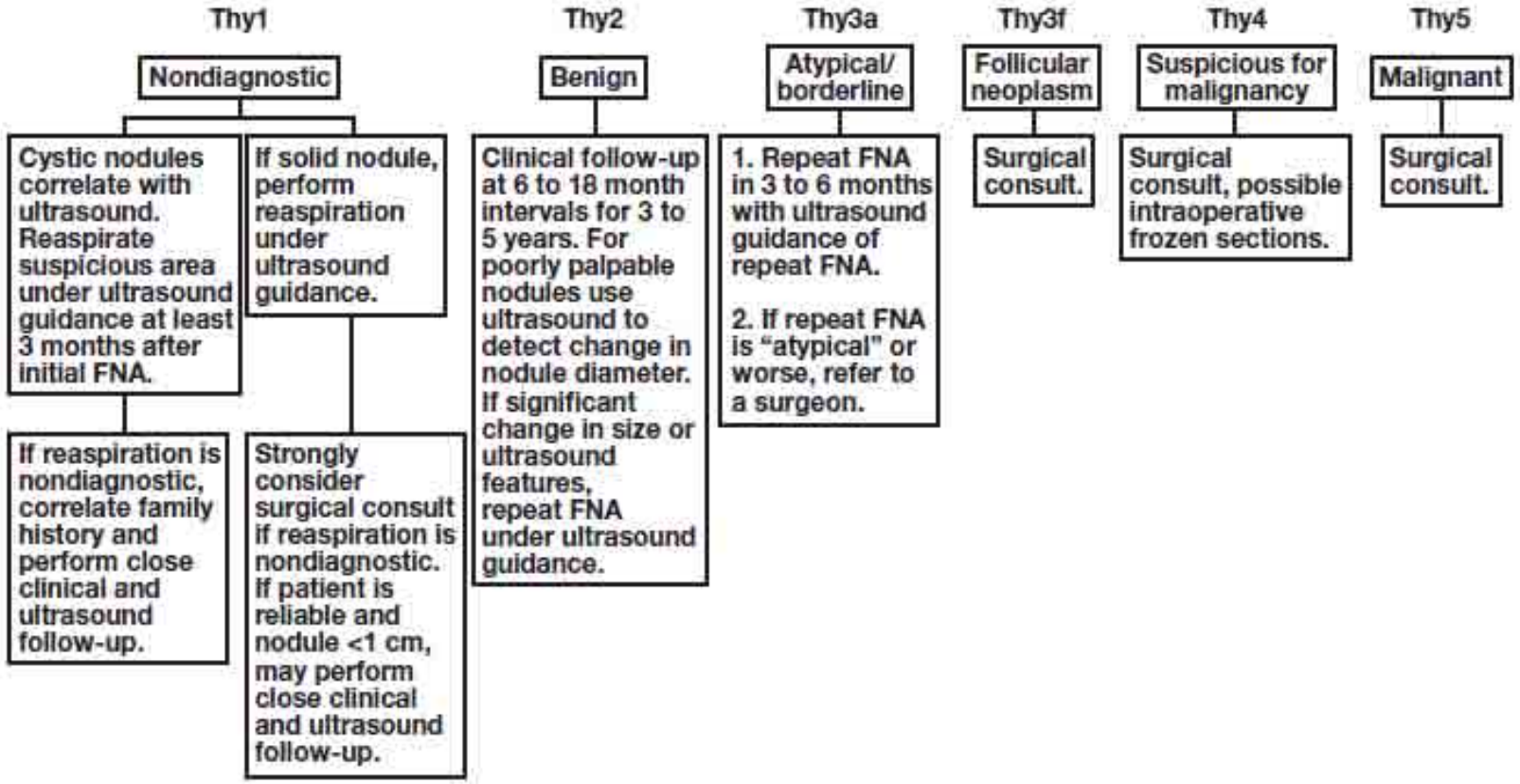
Thy 4

Suspicious of malignancy

Thy5 Malignant

The Interobserver Reproducibility of Thyroid Fine-Needle Aspiration Using the UK Royal College of Pathologists' Classification System

Figure 2 Clinical management implications following from the 6 main categories of thyroid cytology reporting as described by The Bethesda System for Reporting Thyroid Cytology and adapted to the UK Royal College of Pathologists classification. Modified from Layfield et al.[24] FNA, fine-needle aspiration.



Am J Clin Pathol 2011;135:852-869

Gabrijela Kocjan et al.

NCCN® Practice Guidelines in Oncology – v.1.2010

Thyroid Carcinoma

Nodule Evaluation

Guidelines Index
Thyroid Carcinoma TOC
Staging, Discussion, References

FNA RESULTS → **TREATMENT**

- **Carcinoma**
  - Papillary or suspicious for papillary → See Primary Treatment (PAP-1)
  - Medullary or suspicious for medullary → See Primary Treatment (MEDU-1)
  - Anaplastic or suspicious for anaplastic → See Primary Treatment (ANAP-1)
- **Follicular or Hürthle cell neoplasm[d]**
  - TSH high or normal → Surgery[g] → See Primary Treatment for Follicular (FOLL-1) or Hürthle (HURT-1)
  - TSH low → Radioiodine imaging
    - Cold → Surgery[g] → See Primary Treatment for Follicular (FOLL-1) or Hürthle (HURT-1)
    - Hot → Evaluate and treat for thyrotoxicosis as indicated (malignancy is rare)
- **Follicular lesion of undetermined significance[e]**
  - TSH high or normal → Repeat FNA, consider surgery[g] based on clinical grounds, concerning growth, or suspicious sonographic findings → See Primary Treatment for Follicular (FOLL-1) or Hürthle (HURT-1)
  - TSH low → Radioiodine imaging
    - Cold → Repeat FNA, consider surgery[g] based on clinical grounds, concerning growth, or suspicious sonographic findings → See Primary Treatment for Follicular (FOLL-1) or Hürthle (HURT-1)
    - Hot → Evaluate and treat for thyrotoxicosis as indicated (malignancy is rare)
- **Thyroid lymphoma** → See NCCN Non-Hodgkin's Lymphoma Guideline
- **Insufficient biopsy, nondiagnostic**
  - Cystic → Correlate with ultrasound, re-aspirate suspicious areas
  - Solid → Repeat FNA, consider ultrasound guidance and immediate cytologic review or consider surgery
- **Benign[f]** → • Observe • If nodule growth, repeat FNA or consider surgery

Diagnostic categories for FNA results reflect NCI state of the science conference, available from http://www.cytojournal.com/content/5/1/6. Cytology reports should be interpreted in light of terminology used by local cytopathologists.

[d] Alternative term: Suspicious for follicular or Hürthle cell neoplasm. Estimated risk of malignancy is 20%-30%.

[e] Alternative terms include: Atypia of undetermined significance, rule out neoplasm, atypical follicular lesion, and cellular follicular lesion. Estimated risk of malignancy is 5%-10%.

[f] Includes nodular goiter, colloid nodule, hyperplastic/adenomatoid nodule, and Hashimoto's thyroiditis. Estimated risk of malignancy is < 1%.

[g] Surgery usually means a diagnostic lobectomy for these follicular lesions. Consider total thyroidectomy for bilateral disease, unilateral disease > 4cm (especially in men), or patient preference.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

2013 Italian Consensus
TIR 3: Indeterminate

Roma,
9-11 novembre 2012

TIR 3A

- Cellular microfollicular/Hurthle cell pattern in a background of sparse colloid amount with degenerative/regressive features
- Partially compromised specimens (blood contamination) with mild cytologic or architectural alterations
- *Expected lower risk of malignancy*

TIR 3B

- Monotonous, repetitive microfollicular pattern with scanty or absent colloid ("follicular proliferation")
- *More likely follicular neoplasm; expected higher risk of neoplasia.*

UK RCPath	SIAPEC-AIT 2013	USA BETHESDA
Diagnostic category		**Terminology**
Thy1/Thy1c Non-diagnostic for cytological diagnosis Unsatisfactory, consistent with cyst	**TIR 1** **TIR 1c** (cystic)	**I.** Non-diagnostic Cystic fluid only
Thy2/Thy2c Non-neoplastic	**TIR 2**	**II.** Benign
Thy 3a Neoplasm possible – atypia/non-diagnostic	**TIR 3A**	**III.** Atypia of undetermined significance or follicular lesion u.s. AUS/FLUS
Thy 3f Neoplasm possible - suggesting follicular neoplasm	**TIR 3B**	**IV.** Follicular neoplasm or suspicious for a follicular neoplasm
Thy 4 Suspicious of malignancy	**TIR 4**	**V.** Suspicious of malignancy
Thy5 Malignant	**TIR 5**	**VI.** Malignant

Eliminating the "Atypia of Undetermined Significance/ Follicular Lesion of Undetermined Significance" Category From the Bethesda System for Reporting Thyroid Cytopathology

Remmi S. Singh, MD, and Helen H. Wang, MD, DrPH

The Bethesda and Proposed Reporting Systems and Their Conversion*

Bethesda System	Proposed System
Malignant, including papillary thyroid carcinoma, poorly differentiated carcinoma, medullary thyroid carcinoma, and other specified malignancy	Positive for papillary carcinoma, medullary carcinoma, or other specified malignancy
"Suspicious" for malignancy, including papillary carcinoma, medullary carcinoma, and other specified malignancy	Suspicious for papillary carcinoma, medullary carcinoma, or other specified malignancy
	Indeterminate for malignancy, including
Follicular neoplasm or suspicious for a follicular neoplasm →	• Microfollicular or Hürthle cell neoplasm
Atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS)	
• Focal features suggestive of papillary carcinoma (whether cyst lining cells or not) in an otherwise predominantly benign-appearing sample →	• Follicular lesion with focal or some features suggestive of but not diagnostic for papillary carcinoma (report for a specimen suboptimal for any reason should be prefaced by "suboptimal due to ..." [see the following section])
• Sparsely cellular aspirate or interpretation hindered by sample preparation artifact	Suboptimal specimen due to ... but suggestive of
Prominent population of microfollicles →	• Papillary carcinoma
Predominance of Hürthle cells →	• Microfollicular lesion
• Cellular sample composed of exclusively Hürthle cells, yet clinical setting suggestive of benign Hürthle cell nodule†	• Hürthle cell nodule
Benign →	(Most probably)‡ benign follicular lesion, including mixed microfollicular and macrofollicular and macrofollicular lesions and thyroiditis
Nondiagnostic due to insufficient cellular materials	Nondiagnostic or unsatisfactory

* Arrows indicate the diagnostic equivalents.
† Established criteria should be applied to separate specimens in this category into neoplasm or (most probably) benign.[15-18] See the text for details.
‡ Because the false-negative rate for a benign category in thyroid cytology has been estimated to be 3%,[19] a modifier for the benign category may be considered to serve as a reminder.

Am J Clin Pathol 2011;136:896-902

	CONSERVATIVE		SURGERY		
RISK	VERY LOW	LOW	INTERMEDIATE	HIGH	VERY HIGH
CLASS	TIR 2 Thy2 Benign	TIR 3a Thy3a AUS FLUS	TIR 3b Thy3f FN	TIR 4 Thy4 Suspicious	TIR 5 Thy5 Malignant
ACTION	Control	Repeat FNA	Surgery/ rigoruos follow up	Surgery with intraoperative biopsy	Surgery, total resection