



Fall Update 2013: Endocrine Surgical Oncology

Thyroid Cytopathology: Weighing In The Bethesda System



In partnership with:

BC Cancer Agency
UBC Department of Surgery
The Royal College of Physicians
and Surgeons of Canada

Saturday, November 2, 2013
Four Seasons Hotel
791 West Georgia, Vancouver, BC

Conflicts

- No financial consideration

Bias

- Work in the Canadian environment where litigation is less
- Thyroid cytology is often referred in by small group of well trained endocrinologist or radiologists
- Thyroid pathology is acted on by a small number of thyroid surgeons

The Problem

Fine Needle Aspiration Biopsy of right thyroid showing groups of thyroid follicles and colloid.

Hyperplasia vs. thyroid neoplasm.

Can not rule out a low grade thyroid malignancy.

Clinical correlation recommended.

The Problem

Fine Needle Aspiration Biopsy of right thyroid showing groups of thyroid follicles and colloid.

No Surgery

No Surgery

Hyperplasia vs. thyroid neoplasm.

Surgery

Can not rule out a low grade thyroid malignancy.

Clinical correlation recommended. ?

Surgery

Pathologists don't understand
clinicians and they don't
understand us



Bethesda system

- National Cancer Institute (NCI) Thyroid Fine Needle Aspiration State of the Science Conference
- October 22 and 23, 2007 in Bethesda, Maryland
- Co-hosted by Susan J. Mandel and Edmund S. Cibas

Bethesda system

The National Cancer Institute Thyroid fine needle aspiration state of the science conference : A summation. *CytoJournal* [serial online] 2008 [cited 2013 Oct 17];5:6.

Baloch ZW, Cibas ES, Clark DP, Layfield LJ, Ljung BM, Pitman MB, Abati A. Available from: <http://www.cytojournal.com/text.asp?2008/5/1/6/41200>

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 (pages 425–437)

Zubair W. Baloch, Virginia A. LiVolsi, Syl L. Asa, Juan Rosai, Maria J. Merino, Gregory Randolph, Philippe Vielh, Richard M. DeMay, Mary K. Sidawy and William J. Frable

The Bethesda System For Reporting Thyroid Cytopathology.

Cibas ES, Ali SZ;

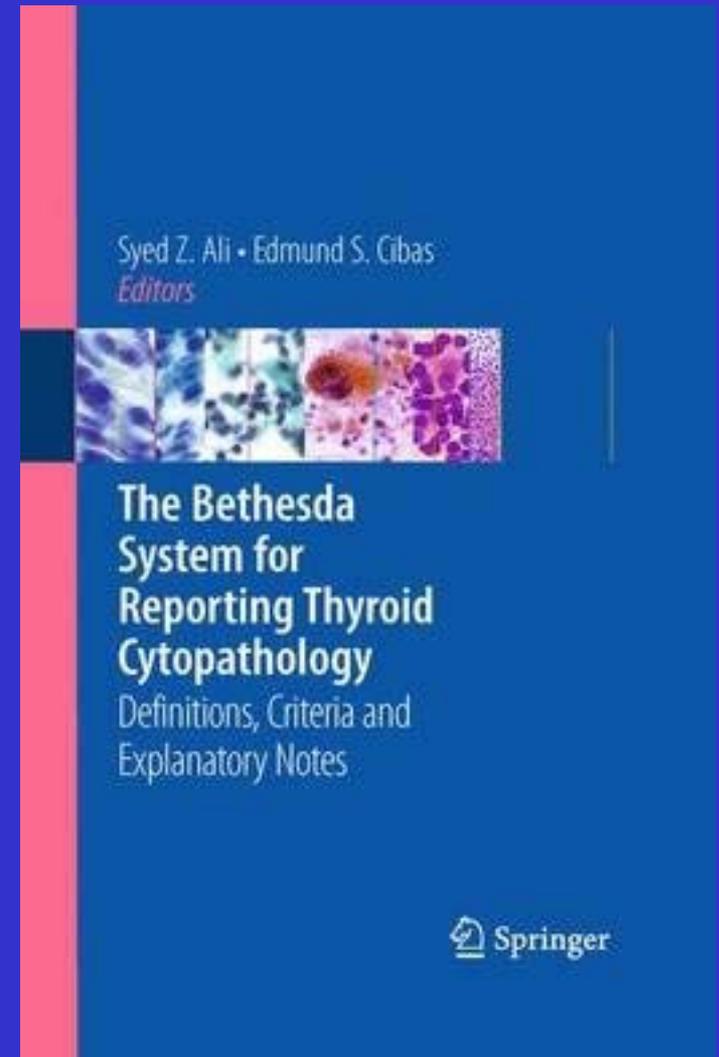
Am J Clin Pathol. 2009 Nov;132(5):658-65.

Available from: <http://ajcp.ascpjournals.org/content/132/5/658.full.pdf>

Bethesda system

The Bethesda System For
Reporting Thyroid
Cytopathology.
Definitions, Criteria and
Explanatory Notes

Ali SZ, Cibas ES



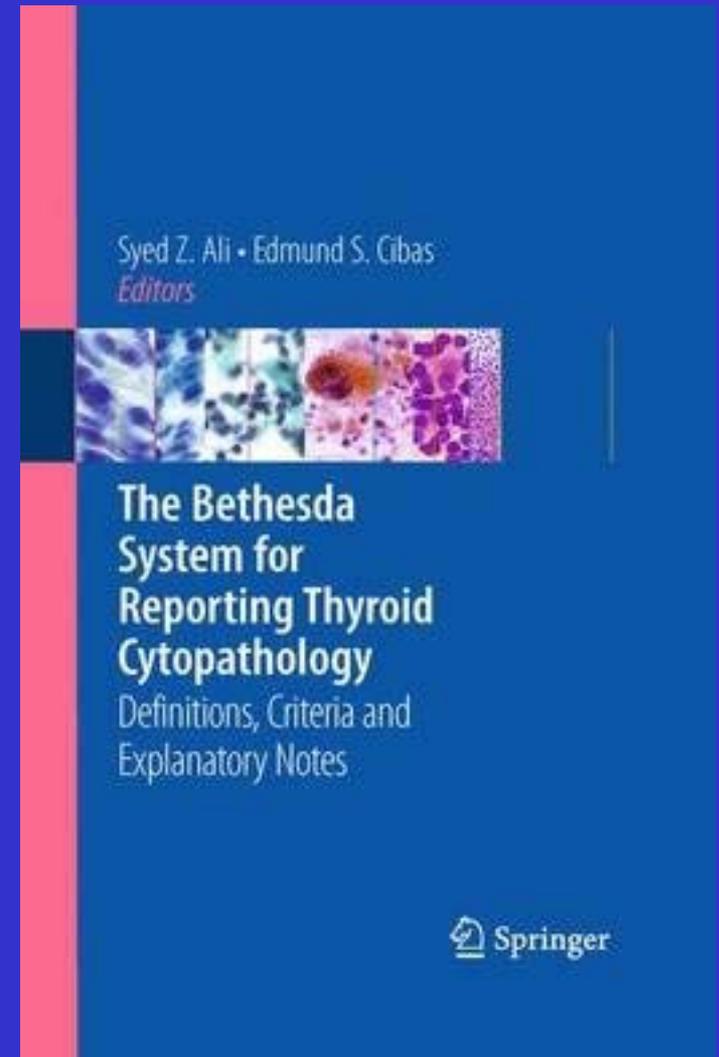
Bethesda system

Background

Definition

Criteria

Explanatory notes



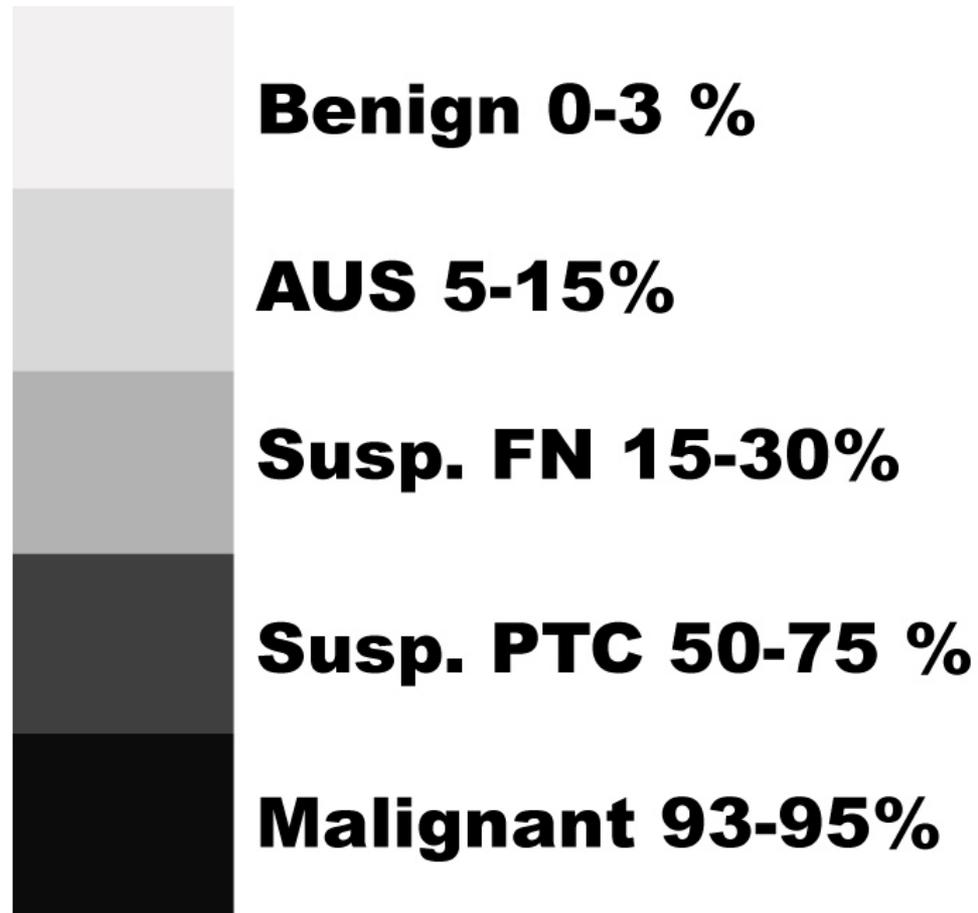
Bethesda system

1. Nondiagnostic / Unsatisfactory
2. Benign
3. Atypia of Undetermined significance / Follicular Lesion of Undetermined Significance
4. Follicular neoplasm / Suspicious for follicular neoplasm +/- Hurthle cell
5. Suspicious for Malignancy
6. Malignant

Bethesda system

1. Unsatisfactory
2. Benign
3. Atypia of Undetermined Significance
4. Suspicious for Follicular Neoplasm
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6. Malignant

Stratification of the risk of malignancy



Bethesda system

1. Unsatisfactory (Risk 1-4%)
2. Benign (0-3%)
3. Atypia of Undetermined Significance
(5 to 15%)
4. Suspicious for Follicular Neoplasm (15-30%)
5. Suspicious for Malignancy (50-75%)
6. Malignant (97-99%)

Table 2
The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management

Diagnostic Category	Risk of Malignancy (%)	Usual Management†
Nondiagnostic or Unsatisfactory	1-4	Repeat FNA with ultrasound guidance
Benign	0-3	Clinical follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	~5-15‡	Repeat FNA
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	15-30	Surgical lobectomy
Suspicious for Malignancy	60-75	Near-total thyroidectomy or surgical lobectomy§
Malignant	97-99	Near-total thyroidectomy§

FNA, fine-needle aspiration.

* Adapted with permission from Ali and Cibas.²

† Actual management.

‡ Estimate extra.

§ In the case of a follicular neoplasm, if a follicular neoplasm is confirmed on pathology, surgery may not be indicated.

interpretation.

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Risk of Malignancy (%)

1-4

0-3

~5-15‡

15-30

60-75

97-99

Cibas ES and Ali SZ (2009)
 Am J Clin Path 132:658-65

Bethesda system

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Nondiagnostic / Unsatisfactory

Adequacy

- 5-6 groups, each with 10 or more cells (1)
- 10 groups, each with 20 or more cells (2)
- 6 groups on at least 2 of six aspirates (3)
- 8 groups, on at least 2 slides (4)

1. Goellner et al Acta Cytol (1987) 31:587

2. Nguyen GK et al (1991) Path Annu 26:63

3. Hamburger H and Hsain M Diagn Cytopathol (1988) 4:14

4. Kini SR in guidels to clinical aspiration biopsy: Thyroid, Igaku-Shoin, second edition, New York, 1996,521p.

As cited by Auger M from CSC “Practice guidelines for fine Needle Aspiration Cytology of the thyroid http://cap-acp.org/guidelines_fine_needle_aspiration.cfm

Adequacy

...if the pathologist needs to count the number of cells present in the smears, then I believe the specimen is unsatisfactory.

Oertel YC J (2002) Clin Endocrin Met 87(4)1459-61

Adequacy

“How can I tell if the specimen is adequate unless it is diagnostic of the lesion being aspirated?”

Unidentified Pathologist SPH (2009)

“It is my responsibility to determine whether the specimen is adequate for diagnosis”

Blair Walker (2013)

Bethesda system

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Benign

- Benign nodules have:
 - Macro follicles, colloid, cystic change

American Thyroid Ass. Guidelines	NCI	NCI Malignancy risk	Literature Malignancy risk	Treatment
Inadequate	Nondiagnostic		2-9% or 37-54%	Repeat
Benign	Benign	< 1%	0.8-3.4%	Follow-up 6-18 m, repeat FNA if growing
Indeterminate,	Follicular lesion			

%	Malignant	Total	Reference
3.4%	2	70	Flanagan MB et al (2006) Am J Clin Path 125:698-702
2.4%	6	246	Hamburger JL (1987) Arch Intern Med 147:97-9
1.7%	4	196	Dwarankanathan AA et al (1993) Am J Surg 166:350-2
0.8%	2	235	Chehade JM (2001) 7:237-43

omy

omy

omy +/- frozen section or FNA & total thyroidectomy

thyroidectomy

aspiration, surgery if ed or solid component

Suspicious for follicular neoplasm

- Or Follicular neoplasm +/- Hurthle cell

Neoplastic nodules have:

- Microfollicules
- *No colloid, not cystic,*
- Follicular carcinomas are **ONLY** diagnosed on histology
 - *Never “malignant”*

St. Paul's data

Suspicious for Follicular Neoplasm

Final Diagnosis	N	
Benign	236	78%
Carcinoma	67	22%

Follicular Carcinoma 7%

PTC 6%

Medullary Carcinoma <1%

Micro PTC 8%

Bethesda system

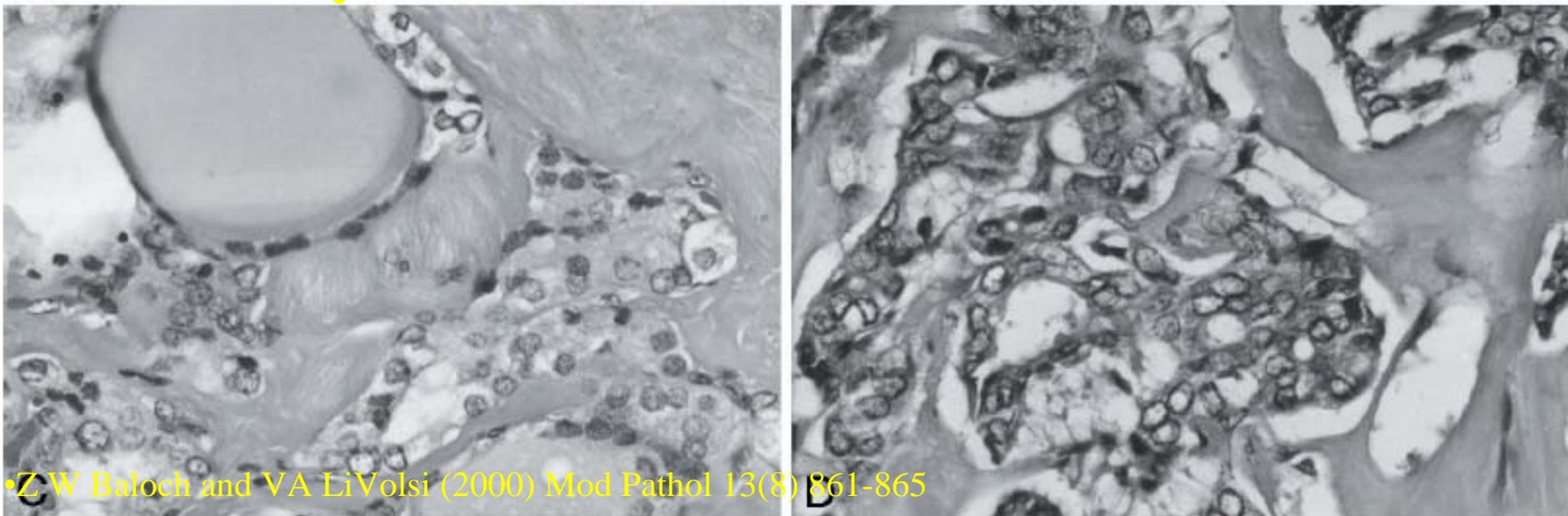
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Malignant

- Papillary thyroid carcinoma
- Medullary, Anaplastic, Lymphoma, ect

Malignant- Papillary thyroid carcinoma

- Classic papillary thyroid carcinomas are easy
- Follicular variants are subtle and arbitrary



• Z W Baloch and VA LiVolsi (2000) Mod Pathol 13(8) 861-865

FIGURE 1. Case 3. Low-power view showing a encapsulated follicular patterned lesion (A). B, high-power view showing follicles of varying sizes and areas of sclerosis. C, D, high-power views showing follicles with and without nuclear features of papillary carcinoma.

		%	False +ve	Total	Reference
American Thyroid Ass. Guidelines	Benign	0.9%	5	583	Bakhos R et al (2000) Diagn Cytopathol 23:233-237
Inadequate	Nondiagnostic	3.1%	1	32	Baloch et al (2001) 25:231-4
Benign	Benign	2.1%	>1	47	Cap J et al (1999) Clin Endocrin 51:509-15
Indeterminate, suspect for neoplasm	Follicular of undetermined significance	0%	0	11	B Kuru (2008) surgery 143:835-6
Indeterminate, suspect for neoplasm	Follicular neoplasm	3.7%	1	27	Renshaw A (2001) Am J Clin Path 116:477-82
Indeterminate, suspect for neoplasm	Suspicious for malignancy	50-75%			Lobectomy +/- frozen section or repeat FNA & total thyroidectomy
Malignant	Malignant	100%		96-99%	Total thyroidectomy
Cyst	Cyst			10-15%	Repeat aspiration, surgery if undefined or solid component

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Atypia of Undetermined Significance

- Or Follicular lesion of Undetermined Significance (FLUS)

Atypia of Undetermined Significance

1. Some microfollicles but not enough for “Suspicious for follicular neoplasm”
2. Cellular Hurthle cell lesion
3. Artifacts resulting in follicular cell atypia, cyst atypia and treatment effect
4. PTC-like features in benign lesions (Hashimoto’s, hurthle cells)
5. Too many lymphocytes

Suspicious for Malignancy

- Likely papillary thyroid carcinoma but not enough
 - Arbitrary threshold for PTC in follicular variants
 - Atypical cysts
 - Hashimoto's clear cell change

The Problem

- Why be wrong?
 - Favor *Atypia of undermined significance*
 - Favor *Suspicious for PTC over Malignant*

Bethesda system

- Can it be done?
- Need
 - Buy in
 - Department wide usage
 - Recognition of the “stratification of risk” concept
 - Application of criteria

St. Paul's data

Distribution

<i>Diagnosis</i>	<i>Number</i>	<i>Distribution percentage</i>	<i>Literature incidence</i>
Nondiagnostic	513	23%	10%
Benign	1355	61%	60%
AUS	167	8%	8%
FN	89	4%	9%
Susp. M	44	2%	4%
Malignant	60	3%	7%
Total	2228	100%	

St. Paul's data

Cancer risk

<i>Diagnosis</i>	<i>Cases with follow-up</i>	<i>Cases with malignant histology on follow-up</i>	<i>Cancer risk</i>	<i>NCI published cancer risk</i>
Nondiagnostic	50	7	4%*	1-4%
Benign	80	5	6%	0-3%
AUS	49	11	22%	5-15%
Susp.FN	38	12	31%	15-30%
Susp. M	18	17	84%*	60-75%
Malignant	41	40	98%*	97-99%
Total	286	104	36%	

St. Paul's data

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Benign	80	5	6%	0-3%
AUS	49	11	22%	5-15%
Susp.FN	38	12	31%	15-30%
Class	Risk of Malignancy		10%*	60-75%
AUS- PTC	30%		98%*	97-99%
AUS- FL or AUS-FH	12%		36%	
AUS-NOS	14%			

“Not papillary thyroid carcinoma” St. Paul’s data

“Not papillary thyroid carcinoma”

Benign

AUS (AUS-FL, AUS-NOS)

Suspicious for follicular neoplasm

No mention of nuclear grooves, nuclear clearing, intra nuclear inclusions, papillary architecture, psammoma bodies

“Not papillary thyroid carcinoma”

St. Paul’s data

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Benign	80	5	6%	0-3%
AUS	49	11	22%	5-15%
Susp. FN	38	12	31%	15-30%
Diagnosis			10%*	60-75%
Benign	90%		98%*	97-99%
Follicular carcinoma	2%			
Papillary Thyroid Carcinoma	7%		36%	

St. Paul's- The warts

Bethesda leakage

A. FNA Thyroid Left - Dominant L thyroid lobe, mixed solid/cystic:

Cellularity limits interpretation

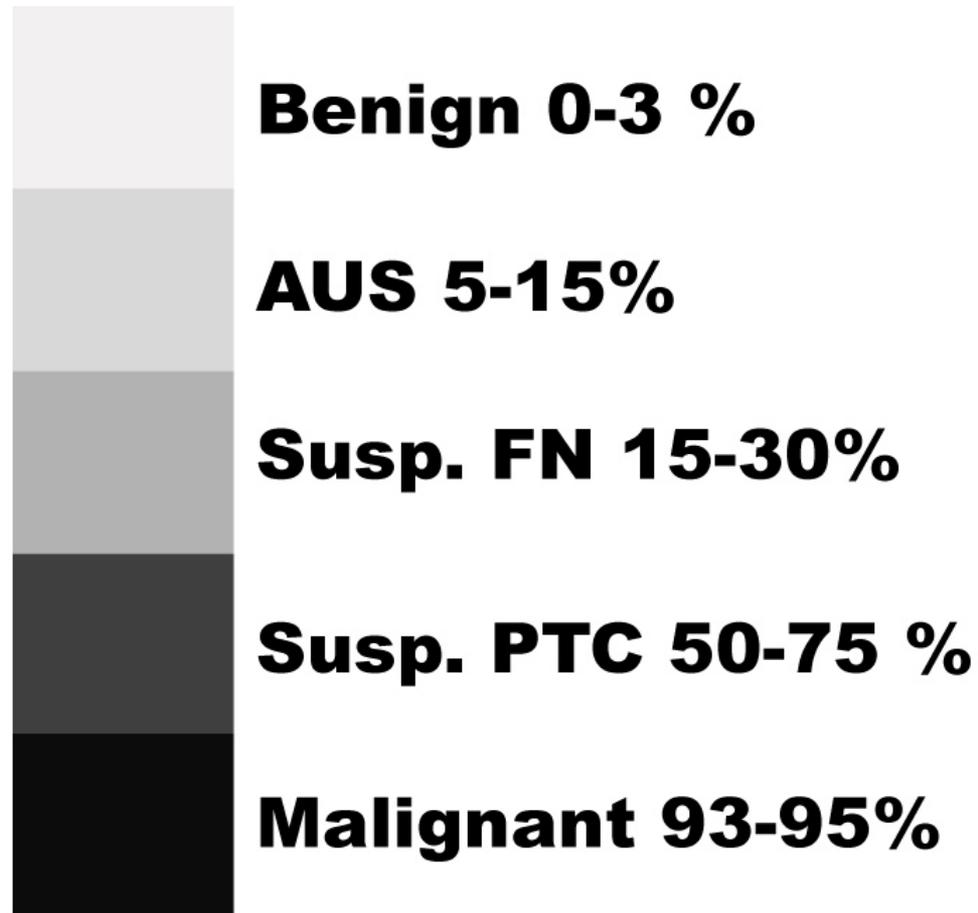
Bethesda terminology: Only a few small groups of benign appearing follicular cells present.

St. Paul's- The warts

In review 2013

5% use non-standard terminology

Bethesda System



Bethesda system

1. Unsatisfactory
2. Benign
3. Atypia of Undetermined Significance
4. Suspicious for Follicular Neoplasm
5. Suspicious for Malignancy
6. Malignant
7. **Cyst fluid Only**

Adequacy

- In my institution about one half of the aspirate the radiologist feel are reported “unsatisfactory” have cystic degeneration.
- Bethesda (NCI) consensus document:
Diagnosis “cyst fluid only”... “non diagnostic”
not “unsatisfactory”
- Canadian Society of Cytology:
cyst fluid “non diagnostic” with explanation

Balock ZW et al (2008) Cytojournal 5:6

Auger M from CSC “Practice guidelines for Fine Needle Aspiration Cytology of the thyroid”

Cyst fluid only

(Added to Bethesda terminology)

Risk on malignancy:

- 1- 4% in simple, non-complex cysts aspirates.
- 14% in mixed solid and cystic nodules, large cysts (>3cm) and recurring cysts.

Action generally recommended:

- if it recurs excision

Cyst fluid only

(Added to Bethesda terminology)

Entities included in this category:

- Cyst contents without adequate material to diagnose a solid component