Thyroid master class

Thyroid Fine needle aspiration cytology and liquid-based techniques: Hologic and Becton Dickinson

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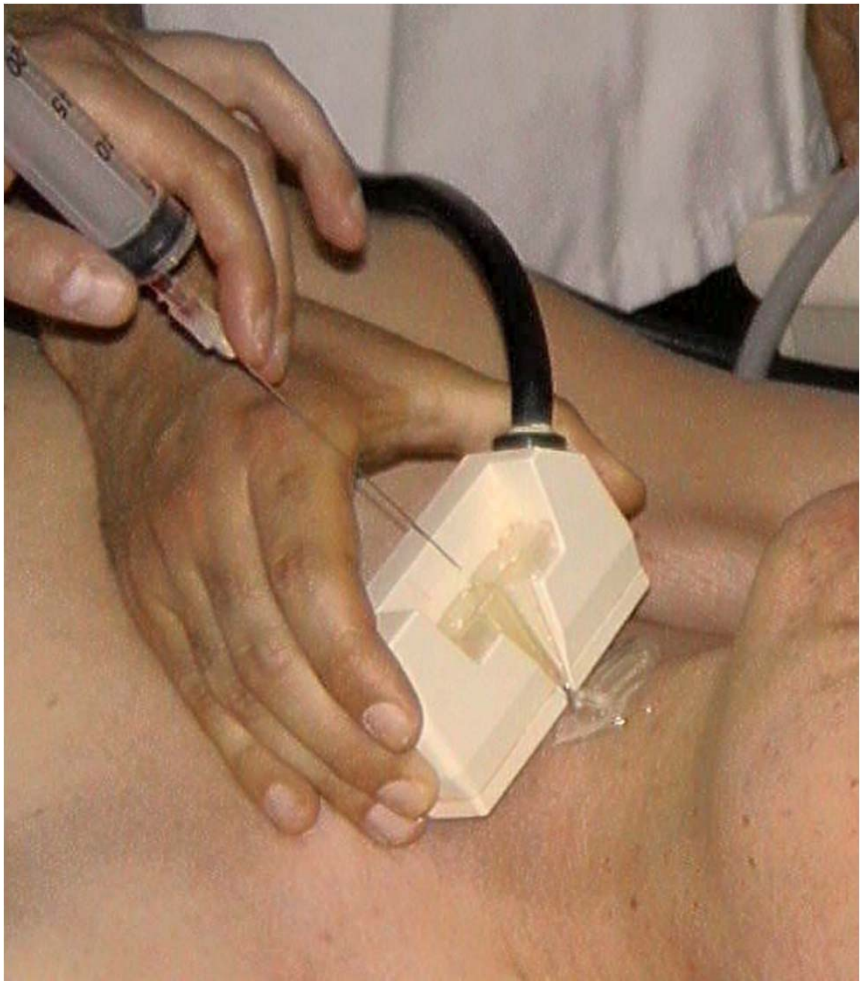
Principle of LBC

- Collection of cells in liquid medium
- Immediate fixation
- Processor-prepared slide
- Standardization

Procedure for LBC FNAC

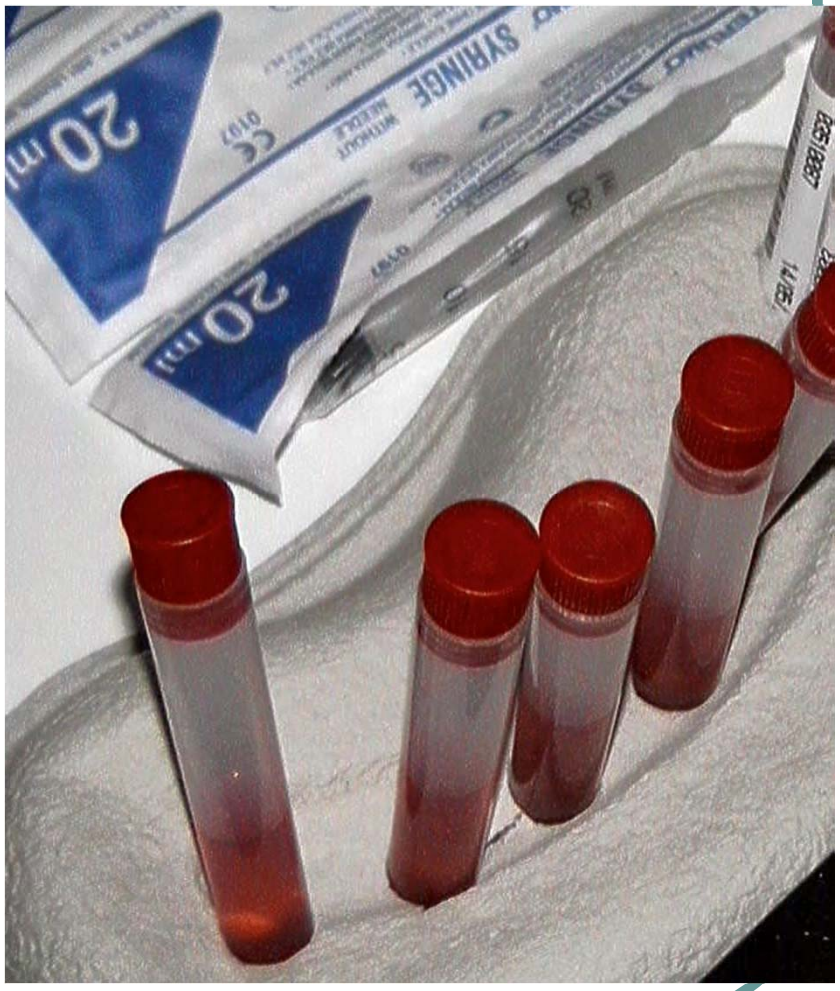
- Fixation
  - CytoLyt solution (Hologic)
  - Cytorich red (BD)
- Concentration by centrifugation
- Wash step
  - PreservCyt
  - H2O
- Process

Thyroid FNAC



US-guided punction

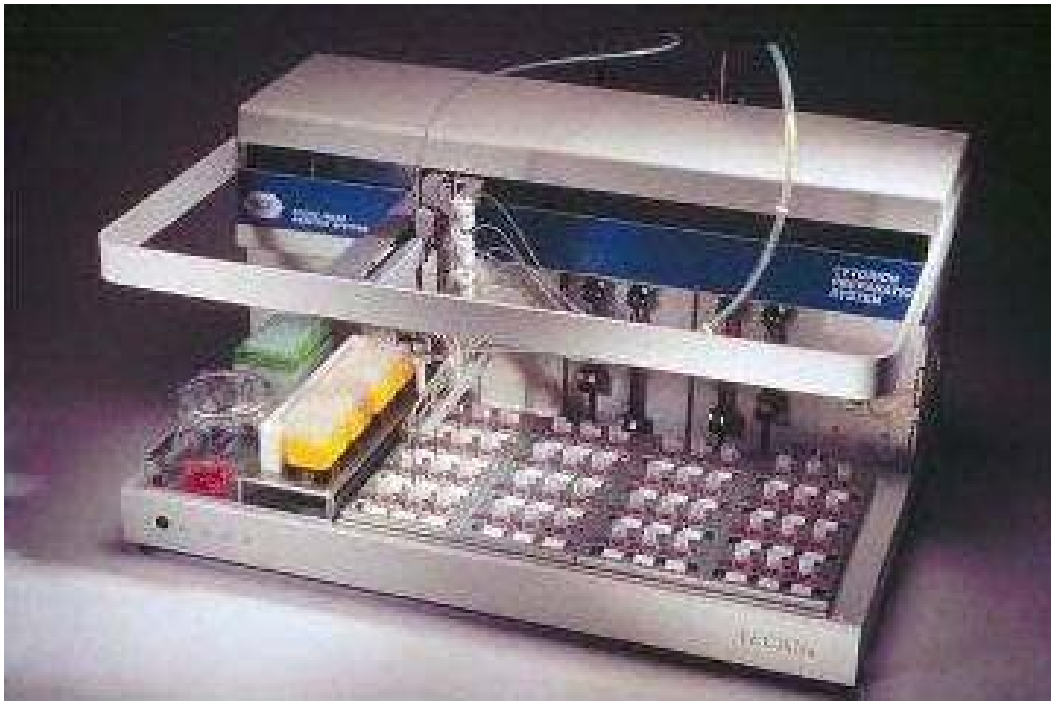
Cell collection



Cytolyt™ fixation

Cytorich Red™ fixation

Sample processing



Processor

Thinprep

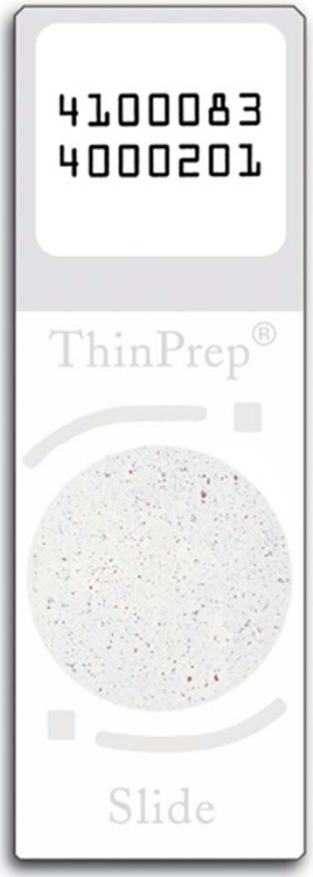
- **Filter system**
- **One slide**
- **No staining**

SurePath

- **Pipet system**
- **4 slides**
- **PAP staining or**
- **Unstained**

LBC slides

- **ThinPrep**



- **Surepath**

LBC general features

- Cell size is reduced
- Cells are rounded up
- Colloid appears different
- Nuclear details are well preserved
- Less RBC and inflammatory cells
- Possibility for ancillary techniques

Thyroid Bethesda Terminology

Terminology 2009	Risk of Malignancy (%)	Usual Management
Non Diagnostic or Unsatisfactory	**	Repeat FNA with US
Benign	0-3	Clinical Follow-up 6-18 months
AUS or Foll lesion of US	5-15	Repeat FNA
Foll Neoplasm or suspicious for a foll neoplasm (*specify if Hürthle cell (oncocytic) type)*	15-30	Surgical lobectomy
Suspicious for malignancy	60-75	Near-total thyroidectomy or surgical lobectomy
Malignant	97-99	Near-total thyroidectomy

Methodology

- **Black colour : general comments or same criteria on CS and LBC**
- **Blue colour: different on LBC compared with CS**
- **Green color: different on Hologic compared to Surepath**
- **Brown colour: title or some specific comments or cases not shown during the master class**

Benign category

- **Includes all the benign nodules (colloid nodules, nodular goiter, hyperplastic nodules, Graves' disease nodules)**
- **Follicular adenoma**
- **All thyroiditis**
- **Lack of cytological or architectural changes**

Report : benign (follicular nodule or hyperplastic nodule or lymphocytic thyroiditis)

Recommendations: Ultrasonographic control 6-18 months later

Risk of cancer: 0-3%

Benign category

- **Nodular goiter**
- **Some monolayered or three-dimensional sheets of follicular cells**
- **Some balls**
- **Abundant colloid**
  - **not obvious when watery colloid**
  - **amphophilic, watery or dense**
- **Histiocytes with granular hemosiderin**
- **Spindle-shaped cells with enlarged, elongated nuclei**

- **Follicular adenoma**
- **More monolayered than three-dimensional sheets of follicular cells**
- **Abundant, dense colloid**

Benign category

- **Hyperplastic nodule**

- **Large sheets of numerous cells**
- **Folded sheets ‘on top’**
- **Few microfollicular patterns**
- **Histiocytes with granular hemosiderin**
- **Sometimes nuclear atypia or grooved nuclei**
- **Some oncocytes**

- **Graves’ disease**

- **High cellularity**
- **Follicular cells in large sheets like in adenomatous nodules.**
- **Some microfollicles**
- **Nuclei often enlarged, vesicular and grooved.**
- **Prominent nucleoli have been described**

Benign category

Hashimoto's disease

- **Polymorphic lymphocytic background in variable quantity, mixed with neutrophils**
- **Hürthle cells**
- **More or less nuclear atypia (FLUS)**

De Quervain thyroiditis

- **Hypocellularity**
- **Giant histiocytic cells**
- **Epithelioid cells**

Non diagnostic category

- **FNA with less than 6 well-preserved follicular cells groups with ten cells each**
- **Poorly prepared or stained cells (less frequent in LBC)**
- **Cyst fluid with or without histiocytes and with less than six groups of ten benign cells**

Report : Non diagnostic

Recommendation: 2nd FNA at least in 3 months under US

Risk of cancer : ?

Non diagnostic category

- **Colloid nodules are excluded from this category (benign category)**
- **As well as nodules with inflammation (lymphocytic thyroiditis) (benign category)**
- **Or nodules with atypical cells even if the required number of cells is not available (AUS or LSM or FN or FN Hürthle cells type)**

Malignant category

- **Papillary carcinomas**
- **Medullary carcinoma**
- **Poorly differentiated carcinoma**
- **Anaplastic carcinoma**
- **Lymphoma**
- **Metastases**

- **Hürthle cell carcinoma**
- **Well-differentiated follicular carcinomas**

are excluded from this category

Recommendations: surgery
except for metastases

Report :

Malignant nodule (medullary carcinoma)

Risk of malignancy: 97-99%

Papillary carcinoma/Criteria

- Syncitial-like monolayers
- Papillae
- Cell size reduced
- Ground glass nuclei (rare)
- Irregular shaped nuclei
- Enlarged nuclei
- Nuclear inclusions (rare)
- Grooved nuclei
- Psammoma bodies
- Giant histiocytic cells
- Lack of colloid
- Cellularity+++

- **PC follicular variant**

see follicular neoplasm

Papillary carcinoma/variants

- **PC/ oncocytic variant**

-oncocytes
-NA suggestive for PC
-pseudoinclusions

-Risk to be classified as FN/HC type

- **PC tall cell variant**

-isolated cells
-cylindric elongated cells
-high cellularity
-monotonous features and few NA suggestive for PC

- **Risk : low cellularity and classified as benign**

Papillary carcinoma/variants

- **PC/ Warthin-like variant**
  -oncocytes, lymphocytes
  -DD Hashimoto

- **PC/ Cystic variant**
  - macrophages, few cells
  - AUS/FLUS

- **PC/ Columnar cell variant**
  - dark nuclei
  - DD benign

- **Hyalinizing trabecular tumor**

Papillary carcinoma/ Immunohistochemistry

- **Immunohistochemical panel**
  - **On extra LBC preparation**
  - **On cell block**

    Always try to obtain a cell block!
- **HBME-1**
- **CK19**
- **(Galectin)**

Medullary Carcinoma/criteria

- Cellularity
- Many isolated cells
- Small cells
- Polymorphic features with polygonal, cuboïdal and elongated cells
- Nuclear inclusions
- Bi or multinucleation

- Fragile isolated dyscohesive cells
- Intracytoplasmic granules are rare
- Very little cells
- Plasmocytoid chromatin less obviously observed
- Small nucleoli may be present
- Amyloid deposits difficult to recognize without Congo red
- ICC with thyrocalcitonine positivity

ICC with thyrocalcitonine positivity

Risk of mistake with oncocytes

Poorly differentiated carcinoma

- **High cellularity**
- **Dyscohesive cells**
- **Trabecular arrangment**
- **Some microfollicules**
- **Small, intermediate sized cells**
- **Bland nuclei**
- **Fine chromatin ; small nucleoli**

Therefore there is a risk of false negative in case of low cellularity

CC/PDTC

AB	CK19	HBME1	TTF1	Tg	Ki67
Literature	+ focal	+ (33%) or neg	++	+ focal	+ or ++

Prasad ML Modern Pathol; 2005 18, 48-57

Choi; J Korean Med Sci; 2005; 5 :853-9

Anaplastic carcinoma

- Obvious malignant cells
- Isolated cells and clusters of cells
- Necrosis

Diferential diagnoses

- Metastases (lung, breast, kidney)
- Lymphoma
- Acute thyroïditis

Follicular neoplasm category

- ***Suspicious for a follicular neoplasm***
- **Includes all cases for which it is impossible to distinguish a benign follicular lesion (follicular adenoma, hyperplastic adenoma, benign nodule in a multinodular thyroid) from a follicular carcinoma**
- **Very specific category**
- **Should not but may include some follicular variant of papillary carcinoma**

Report : follicular neoplasm

Recommendations: surgical control (lobectomy)

Risk of cancer : 15-30%

Follicular neoplasm

Criteria on CS

- Numerous microfollicles
- Low amount of colloid
- More or less nuclear enlargment
- Higher cellularity

Criteria on LBC

- Numerous microfollicles
- More or less nuclear enlargment

ICC may be helpful to consider benign/malignant

Follicular neoplasm / Hürthle cell type category

- ***Suspicious for a follicular neoplasm/Hürthle cell type***
- **Includes all cases with exclusively or almost exclusively oncocytes**
- **Very specific category**

- **Papillary carcinoma oncocytic variant are excluded**
- **No ancillary techniques (No help from ICC)**

Report : follicular neoplasm/Hürthle cell type

Recommendations: surgical control (lobectomy)

Risk of cancer : 15-30%

Follicular neoplasm / Hürthle cell type category

Criteria on CS

- Large isolated cells
- Round eccentric nuclei
- One or more nuclei
- Granular cytoplasm
- Anisocaryosis

ICC is not helpful to consider benign/malignant

Criteria on LBC

- More or less isolated cells
- Eccentric nuclei
- One or more nuclei
- Homogeneous or vacuolated cytoplasm
- Irregular shaped nuclei
- Polygonal cells
- Sometimes small nuclei

Follicular neoplasm / Hürthle cell type category

Difficult diagnoses

1. **Small oncocytes**
2. **Cells mimicking medullary carcinoma**
3. **Cells mimicking histiocytes**

4. **Terminology when MNT (FLUS)**
5. **Terminology when sparse cellularity (FLUS)**
6. **Benign in cases of LT or association with normal follicular cells**

Follicular neoplasm / Hürthle cell type category

Criteria on CS

- Cells highly variable in size
- Enlarged eccentric round nuclei
- Prominent nucleoli
- Blue granular cytoplasm
- Bi/multinucleation

Criteria on LBC

- Cells variable in size
- Enlarged more or less eccentric nuclei
- Variable nuclei (size and irregular shaped)
- Bi/multinucleation
- Smooth nuclear membrane

Follicular lesion of undetermined significance or Atypia of undetermined significance

- **FLUS/ACUS**
- **Includes all cases that do not fulfill the diagnostic criteria of the previous described categories**
- **Therefore it includes many different situations**
- **Not a « waste-basket »**
- **Should not exceed 7%**

Report : FLUS or ACUS

Recommendations: 2nd FNA 6 months later under US

Risk of cancer : 5-15%

Follicular lesion of undetermined significance or Atypia of undetermined significance

1. Microfollicular architecture, but sparse cellularity
2. Predominant oncocytic cells and low celllularity
3. Predominant oncocytic cells and goiter or Hashimoto
4. Cytological atypias suggesting papillary carcinoma
5. Cytological atypias
6. Cytological atypias due to technical artifact
7. Atypical « cyst lining cells »
8. Abnormal lymphocytic population
9. Other

Lesions suspicious for malignancy

- **All cases previously described in the « Malignant category » for which the cytological criteria of malignancy are insufficient to assert the diagnosis**
- **All cases for which malignancy is considered more likely than not**
- **Same subcategories**

Report : LSM (suspicious for papillary carcinoma)

Recommendations : surgical control

Risk of malignancy: 60-75%

Cases shown

- Goiter
- Hyperplastic nodule
- Hashimoto thyroiditis
- Colloid nodule
- Non-diagnostic
- Papillary carcinoma
- Medulary carcinoma
- Anaplastic carcinoma
- FLUS
- Follicular neoplasm- hurtle cell type
- Metastasis