

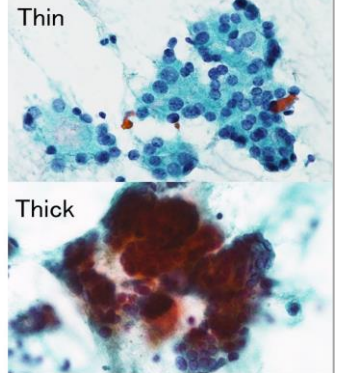
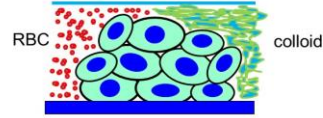
甲状腺細胞診 観察のポイント

隈病院 病理診断科
 廣川 満良

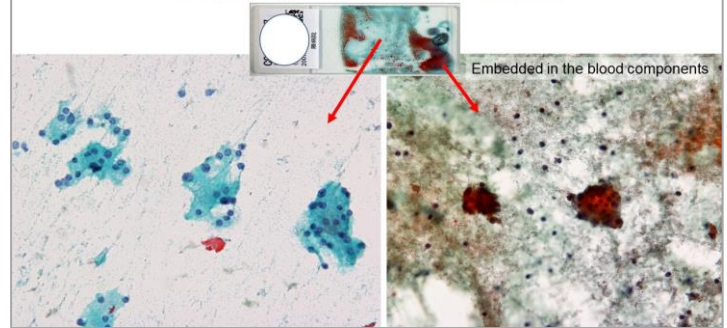
No potential COI to disclose



Optimal thyroid FNA specimens



Oncocytic follicular tumor

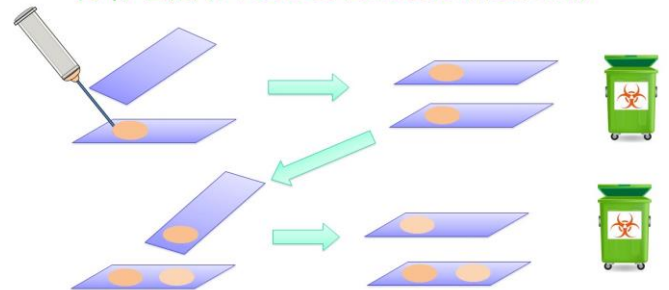


細胞量が多い

適正: 細胞診断ができる標本: 下記の4項目のいずれかの場合

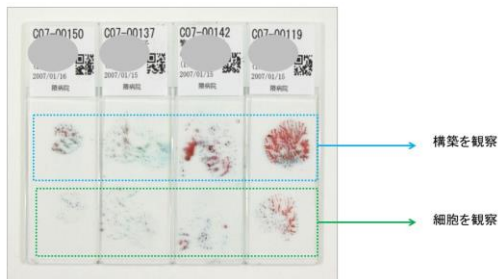
- 1) 10個程度の濾胞上皮細胞からなる集塊が6個以上
- 2) 豊富なコロイド
- 3) 異型細胞の存在(細胞数は問わない)
- 4) リンパ球、形質細胞、組織球などの炎症細胞

合わせ法(Press & release method)



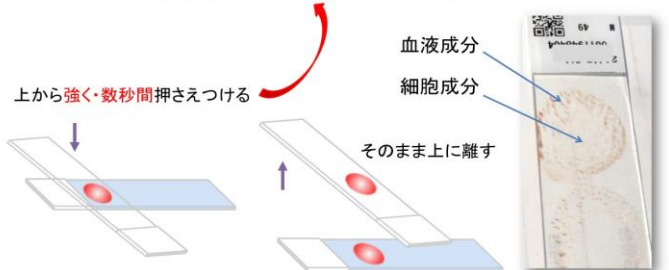
Hirokawa M, et al. VideoEndocrinology.2018.

合わせ法で作成したプレパラート



合わせ法(Press & release method)

薄く塗抹、血液を除去、組織構築を保持



血性検体は血液成分を落とす

プレパラートを垂直に立てる

プレパラートを台に叩きつけて、血液を落とす

細胞成分は残る

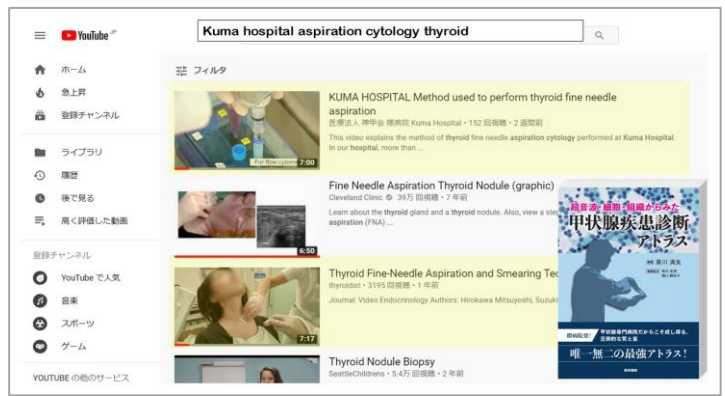
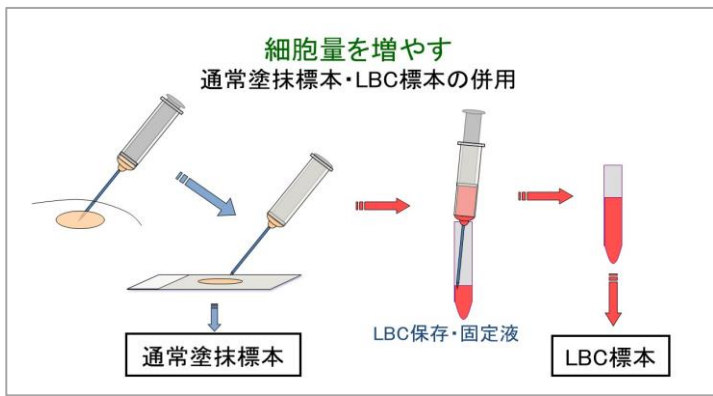
血液成分はティッシュで拭き取る

血性検体は溶血させる

穿刺

LBC固定・保存液 溶血作用

LBC標本



WHO classification of tumours of the thyroid gland (5th)

Developmental abnormalities
Thyroglossal duct cyst
Other congenital thyroid abnormalities

Follicular cell-derived neoplasms
Benign tumours
Thyroid follicular nodular disease
Follicular thyroid adenoma
Follicular thyroid adenoma with papillary architecture
Oncocytic adenoma of the thyroid
Low risk neoplasms
NIFTP
Thyroid tumours of uncertain malignant potential
Hyalinizing trabecular tumour of thyroid

Malignant neoplasms
Follicular thyroid carcinoma
Invasive encapsulated follicular variant papillary carcinoma
Papillary thyroid carcinoma
Oncocytic carcinoma of the thyroid
Follicular-derived carcinomas, high-grade
Anaplastic follicular cell derived thyroid carcinoma

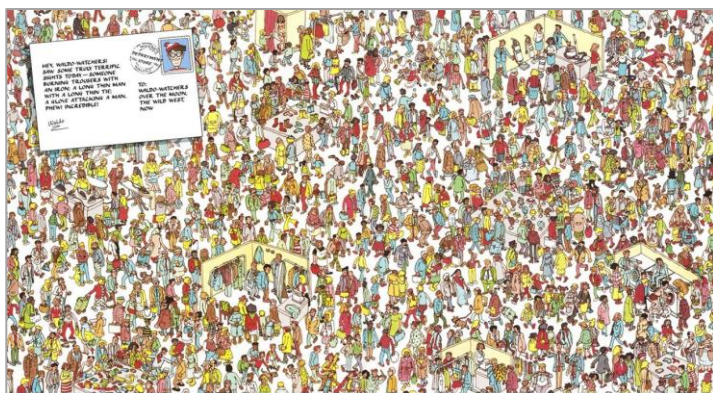
Thyroid C-cell derived carcinoma
Medullary thyroid carcinoma
Mixed medullary and follicular-cell derived carcinomas
Mixed medullary and follicular cell-derived thyroid carcinoma
Salivary gland-type carcinomas of the thyroid
Mucoepidermoid carcinoma of the thyroid
Secretory carcinoma of salivary gland type
Thyroid tumours of uncertain histogenesis
Sclerosing mucoepidermoid carcinoma with eosinophilia
Cribriform morular thyroid carcinoma
Thymoma family
Thymoma family
Spindle epithelial tumour with thymus-like elements
Thymic carcinoma family
Embryonal thyroid neoplasms
Thyroidblastoma

The Bethesda System for Reporting Thyroid Cytopathology (3rd edition)

Diagnostic category	Risk of malignancy Avg% (% range)	Usual management
Nondiagnostic or Unsatisfactory	13 (2-20)	Repeat FNA with ultrasound guidance
Benign	4 (0-6)	Clinical and sonographic follow-up
Atypia of Undetermined Significance	22 (20-32)	Repeat FNA, molecular testing , diagnostic lobectomy, or surveillance
Follicular Neoplasm	30 (25-50)	Molecular testing , diagnostic lobectomy
Suspicious for Malignancy	74 (50-80)	Molecular testing , lobectomy or near-total thyroidectomy
Malignant	97 (85-100)	Lobectomy or near-total thyroidectomy

甲状腺癌取扱い規約 (第8版) の細胞診報告判定区分

検体不適正 (Unsatisfactory)
嚢胞液 (Cyst Fluid)
良性 (Benign)
意義不明 (Undetermined Significance)
濾胞性腫瘍 (Follicular Neoplasm)
悪性の疑い (Suspicious for Malignancy)
悪性 (Malignant)



How to observe exfoliative cytology

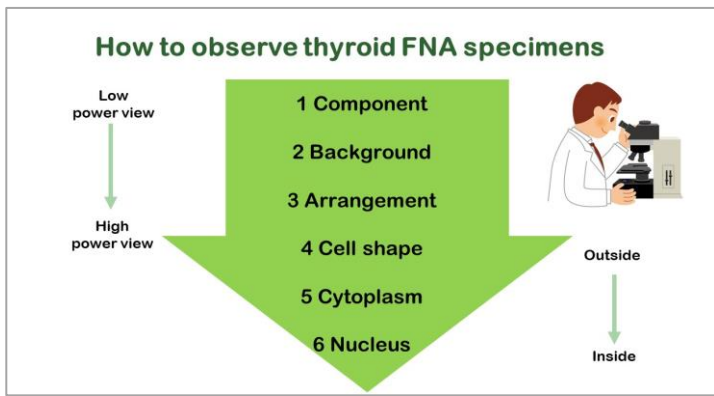
Detection of atypical cells by
Screening ⇒ Diagnosis

ラベル ↑



穿刺吸引細胞診の見方

- 1) 肉眼的観察: 塗抹方法、塗抹部位
- 2) 弱拡大 (x4): 成分、背景、細胞配列
- 3) 中拡大 (x10): 細胞形、細胞質、核
- 4) 診断: 鑑別診断、診断カテゴリー、推定診断
- 5) **スクリーニング**: 診断の確定、逆鑑別診断、副病変・見逃し所見の抽出



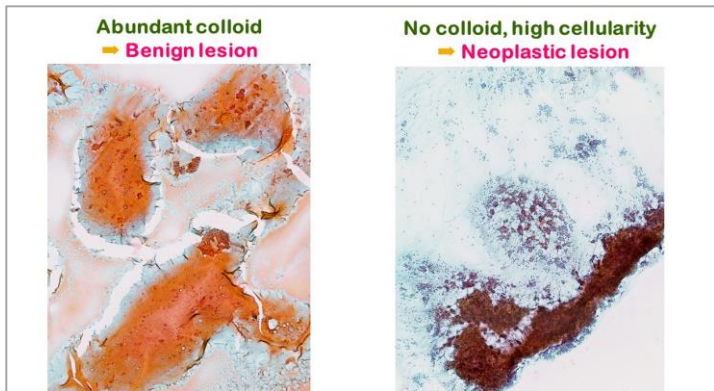
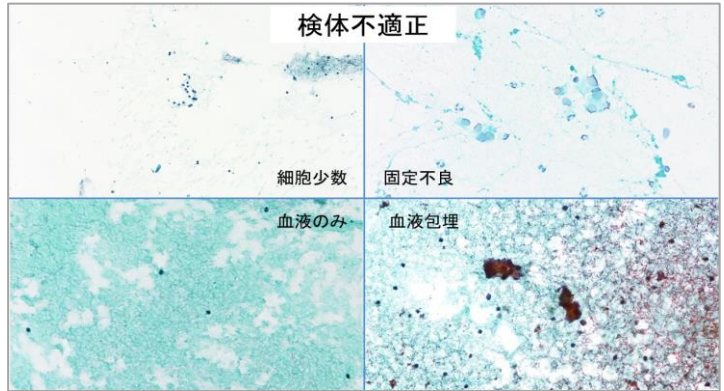
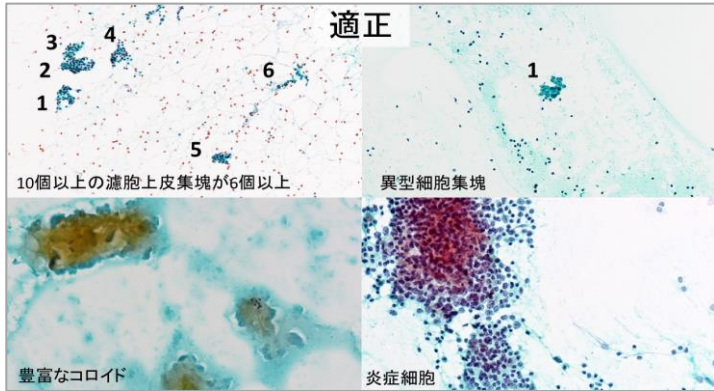
検体の適正・不適正の基準

適正: 細胞診断ができる標本: 下記の4項目のいずれかの場合

- 1) 10個程度の濾胞上皮細胞からなる集塊が6個以上
- 2) 豊富なコロイド
- 3) 異型細胞の存在(細胞数は問わない)
- 4) リンパ球、形質細胞、組織球などの炎症細胞

不適正: 細胞診断ができない(してはいけない)標本: 下記の2項目のいずれかの場合

- 1) 標本作製不良
乾燥、変性、固定不良、末梢血混入、塗抹不良など
- 2) 上記適正の項目のいずれにも該当しない



Background

Colloid materials

- Amyloid
- Psammoma bodies
- Inflammatory cells
- Necrosis

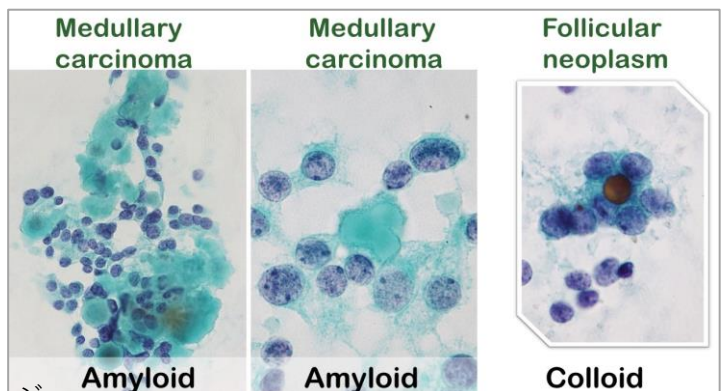
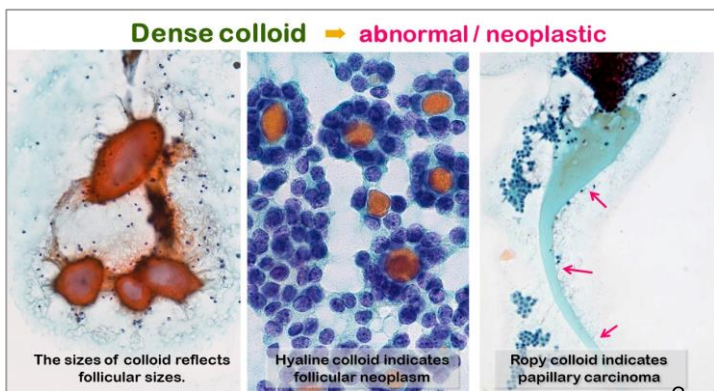
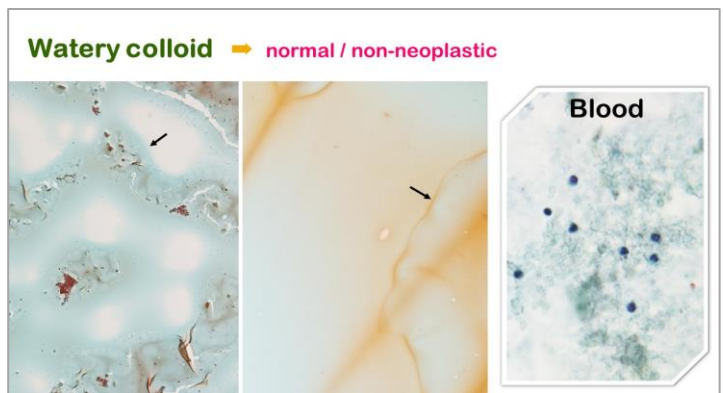
Colloid materials

Watery colloid => normal / non-neoplastic

- Thin, acellular, homogeneous, film-like materials
- Look like plastic wrap or parched earth with cracks (Pap stain)
- Stained glass appearance, spider-web-like appearance (Giemsa stain)

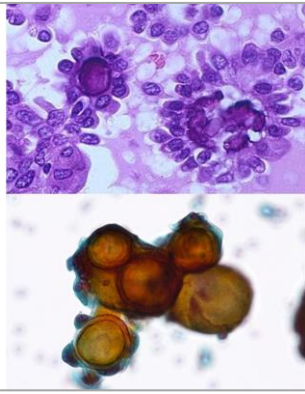
Dense colloid => abnormal / neoplastic

- Hyaline colloid : follicular neoplasm
- Ropy colloid : papillary carcinoma



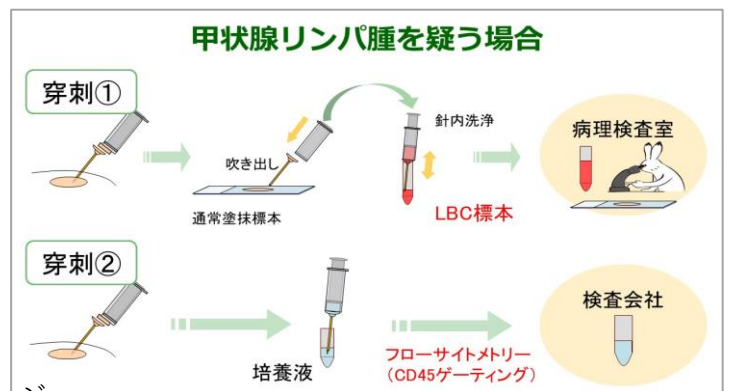
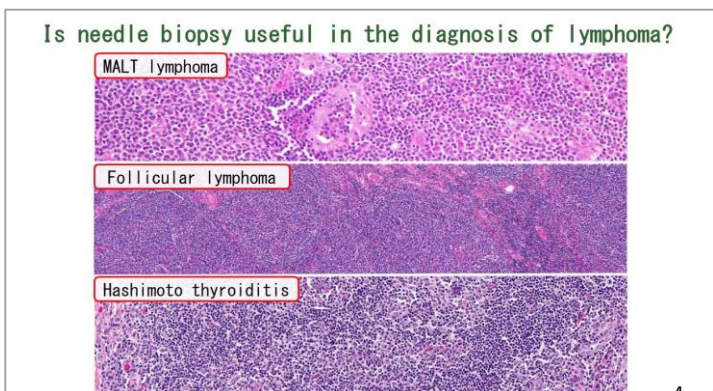
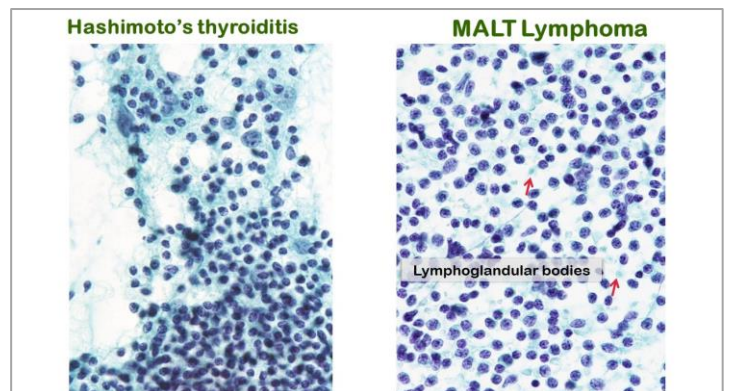
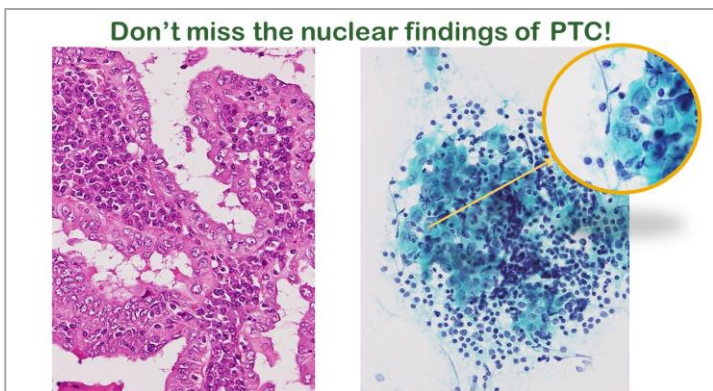
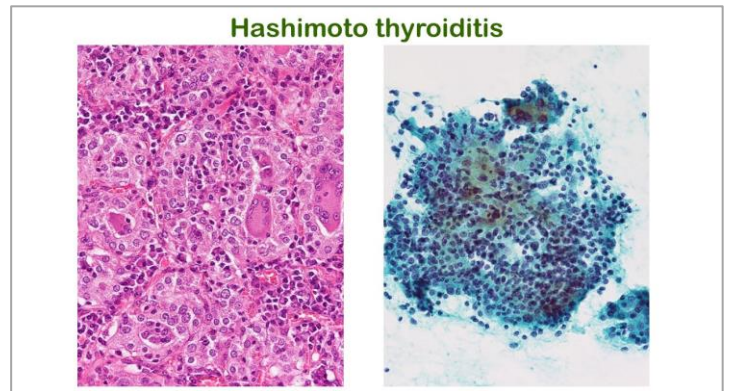
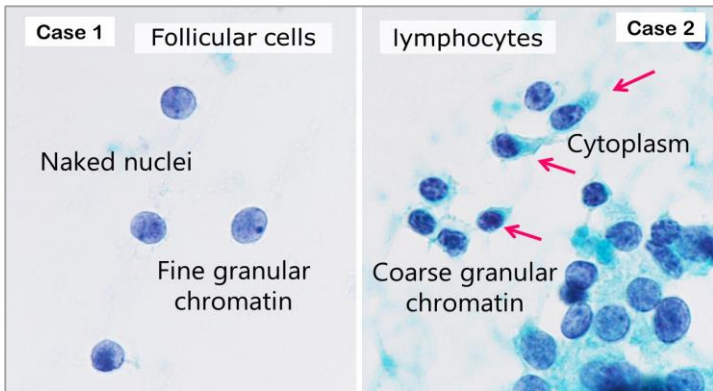
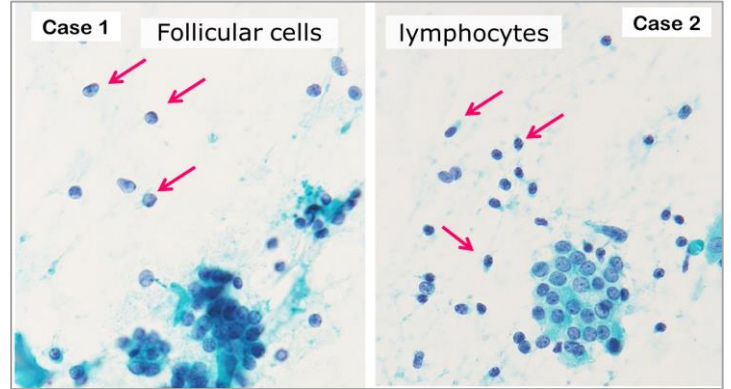
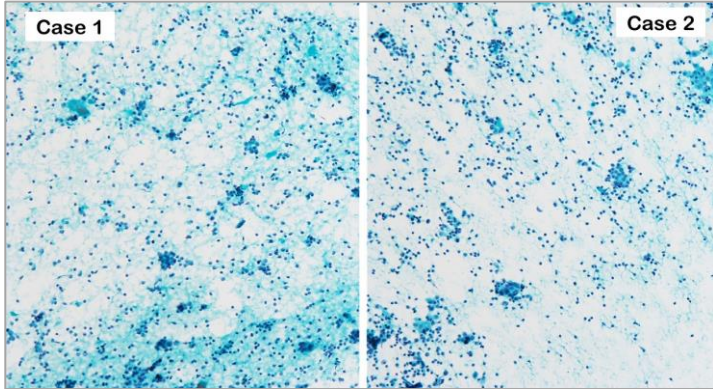
Psammoma bodies

- Calcified, concentrically laminated, spherical bodies
- 5-100 μm in diameter
- Hematoxyphilic (HE stain)
- Lavender, golden brown, or amphophilic (Pap stain)
- Specific to PTC (40-60%)
 - Numerous (diffuse sclerosing PTC)
- Mimicking calcified colloid

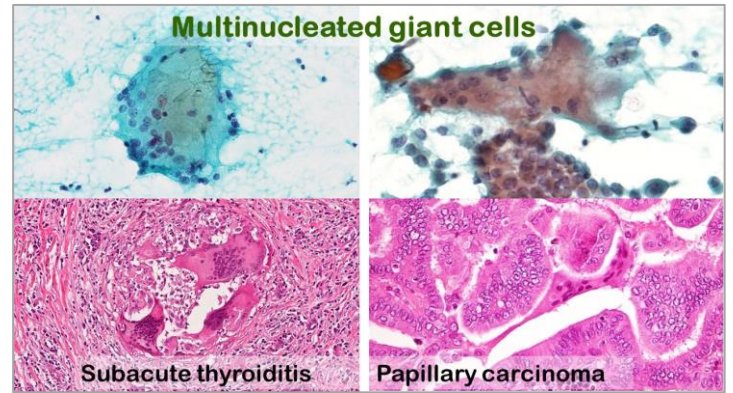
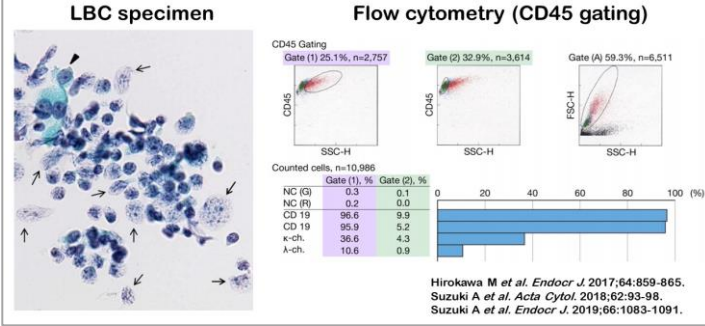


Inflammatory cells

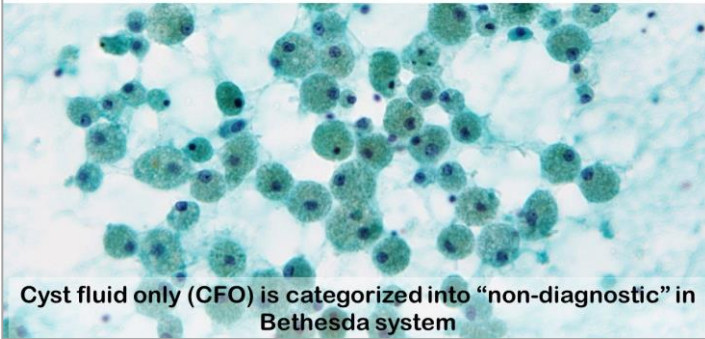
Lymphocytes	Hashimoto / subacute thyroiditis PTC, Lymphoma
Neutrophils	Acute / subacute thyroiditis Anaplastic carcinoma
Multinucleated giant cells	Subacute thyroiditis, Suture granuloma, Sarcoidosis, Tuberculosis, PTC Medullary carcinoma, Anaplastic carcinoma
Foamy cells	Cyst, Follicular nodular disease, PTC
No inflammatory cells	Follicular neoplasm (excluding oncocytic)



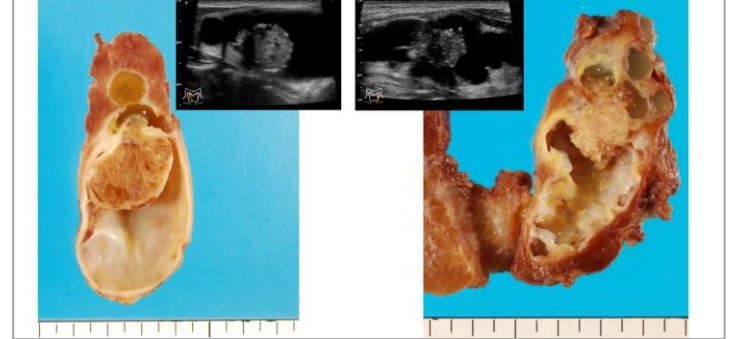
Thyroid lymphoma



Foamy histiocytes indicate cystic lesion



Follicular nodular disease Papillary carcinoma



ROM of ND/UNS excluding cyst fluid only (CFO), CFO, and Benign Nodules in Kuma Hospital

	ND/UNS Excluding CFO	CFO	Benign
Incidence (/all FNA)	7.6% (766/10,036)	4.8% (469/9,767)	67.8% (7,007/10,333)
ROM (/resected nodules)	41.7% (43/103)	7.1% (1/14)	13.9% (79/577)
ROM	5.6% (43/766)	0.2% (1/469)	1.1% (79/7007)
	Takada <i>et al.</i> (2017)	Kanematsu <i>et al.</i> (2018)	Suzuki <i>et al.</i> (2014)

p<0.001

Takada N *et al. Endocr J*, 2017;64:759-765.
 Kanematsu R *et al. Diagn Cytopathol.* 2020 48:30-34.

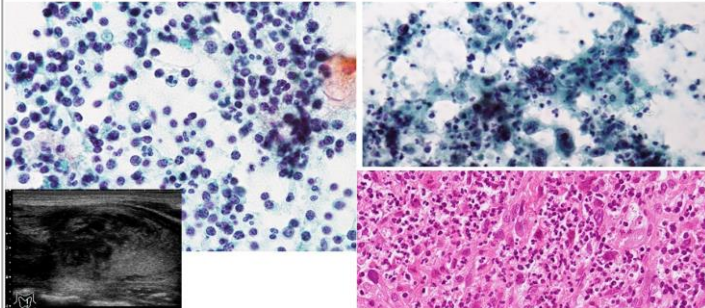
Comparison between the Japanese and the Western system in the non-diagnostic/unsatisfactory category

	United States and Canada (TBSRTC)	United Kingdom	Italy	Japan
Insufficient for cytologic diagnosis	Nondiagnostic	Thy 1 (Non-diagnostic for cytological diagnosis)	TIR 1 (Non-diagnostic)	Unsatisfactory
Cyst fluid only	Nondiagnostic: Cyst fluid only	Thy 1c (Non-diagnostic for cytological diagnosis - cystic lesion)	TIR 1c (Non-diagnostic for cystic)	Cyst fluid (satisfactory specimen)

TBSRTC, The Bethesda System for Reporting Thyroid Cytopathology

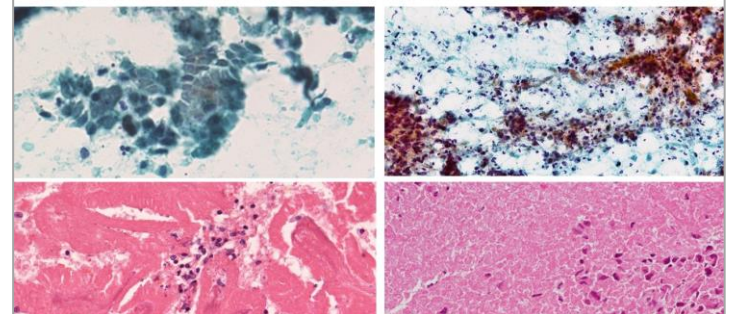
Neutrophilic background

Pyriiform sinus fistula **Anaplastic carcinoma**



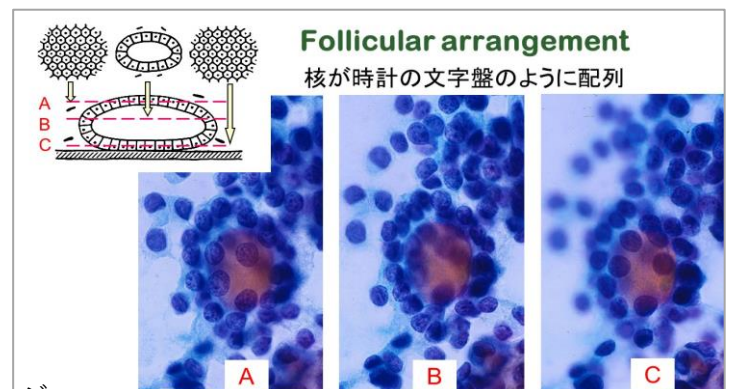
Necrotic background

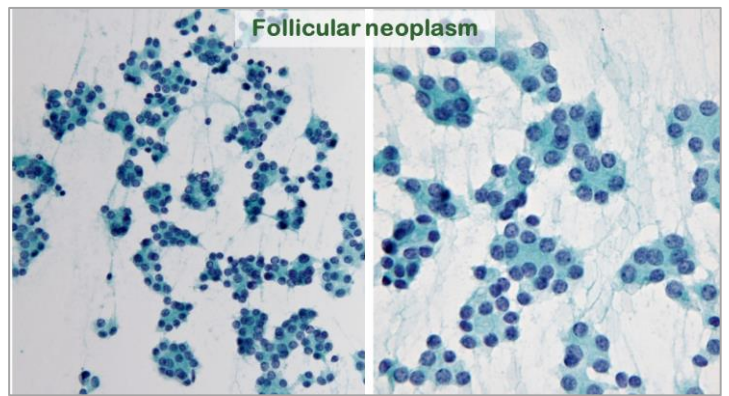
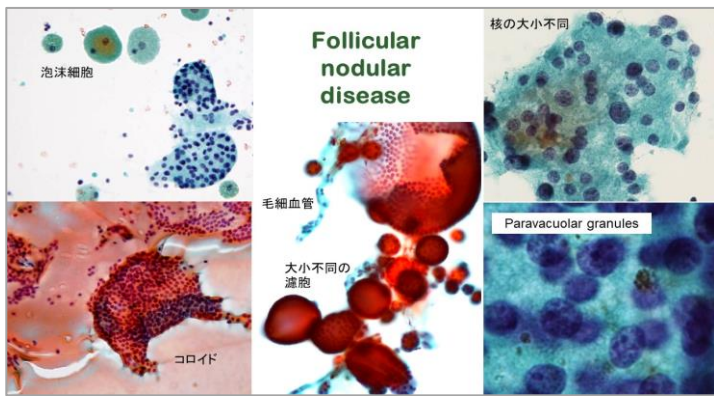
Coagulation (Papillary carcinoma) **Liquefaction (Anaplastic carcinoma)**



Arrangements

Follicular	Follicular neoplasm, NIFTP, FT-UMP Follicular nodular disease Infiltrative follicular PTC
Papillary	PTC, Follicular tumor with papillary architecture Follicular nodular disease
Trabecular	Poorly differentiated carcinoma PTC Follicular neoplasm
Solid	Poorly differentiated carcinoma Solid/trabecular PTC Intrathyroid thymic carcinoma
Isolated cells	Lymphoma Medullary carcinoma Anaplastic carcinoma





Follicular adenoma vs. Follicular carcinoma

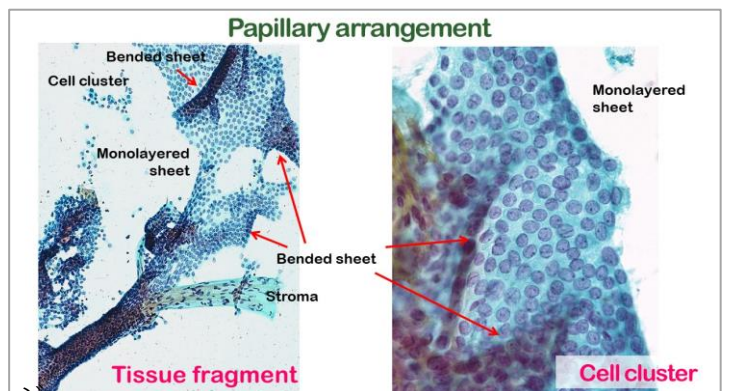
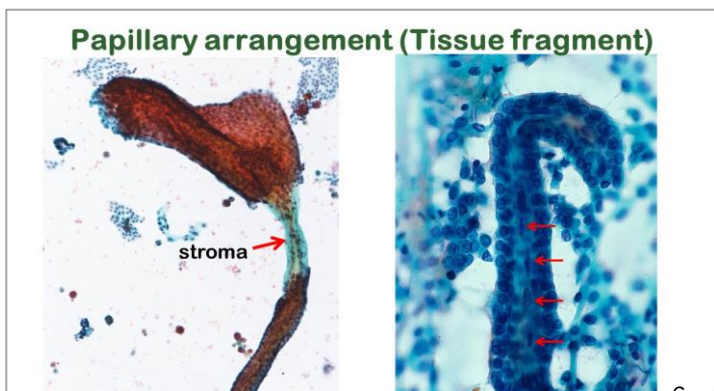
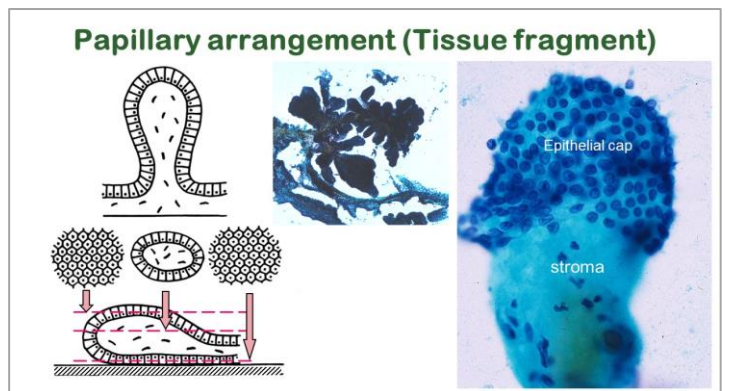
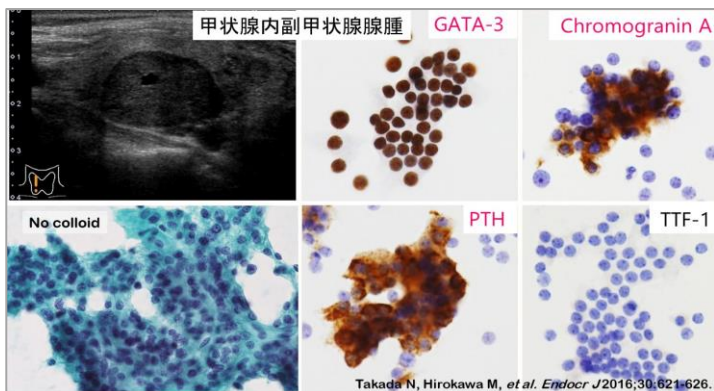
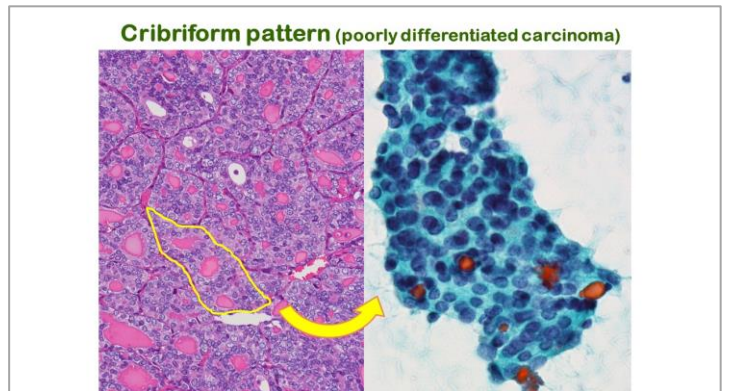
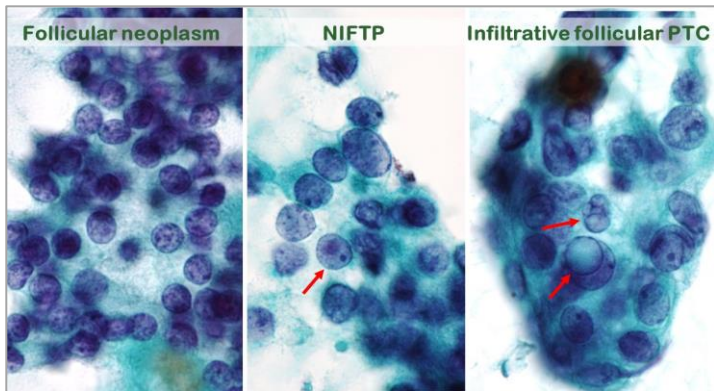
- Capsular invasion
- Vascular invasion
- Metastasis

Cytological specimens cannot identify the findings

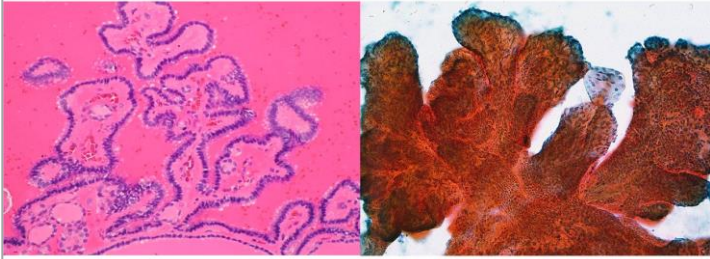
Thyroid Bethesda System for Reporting Thyroid Cytology (TBSRTC)



- Nondiagnostic or Unsatisfactory
- Benign
- Atypia of Undetermined
- Follicular Neoplasm
- Suspicious for Malignancy
- Malignant

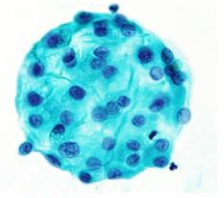


Follicular nodular disease with papillary structure



Strongly cohesive tissue fragment

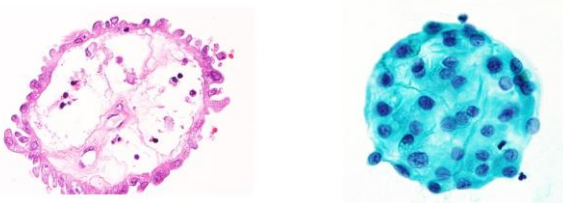
Mirror ball-like cluster



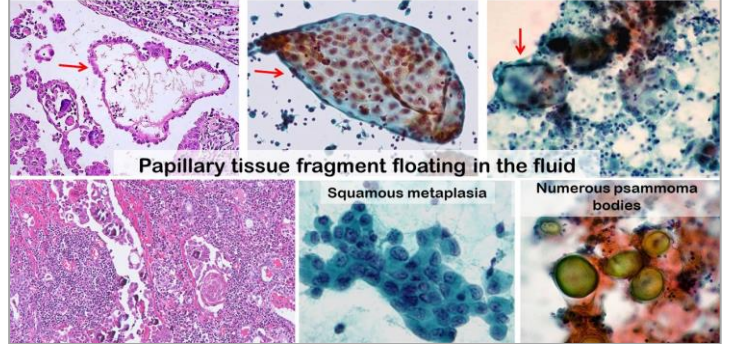
Means floating in the fluid

Variant of Papillary Arrangement

Edematous stroma covered with monolayered epithelial cells



Diffuse sclerosing Papillary carcinoma



Papillary tissue fragment floating in the fluid

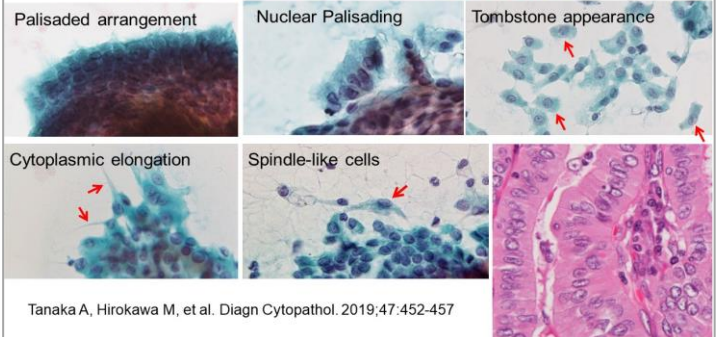
Squamous metaplasia

Numerous psammoma bodies

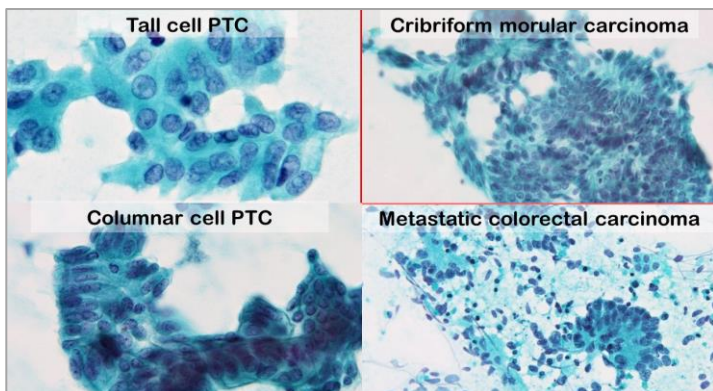
Cell shape

Tall columnar 高細胞	Tall cell PTC, Columnar cell PTC Cribriform morular carcinoma Metastatic colorectal carcinoma
Polygonal	Anaplastic carcinoma, Medullary carcinoma
Spindle	Medullary carcinoma, Cribriform morular carcinoma
Plasma cell-like	Medullary carcinoma, Oncocytic tumor
Tail-like	Medullary carcinoma, Tall cell PTC Hyalinizing trabecular tumor
Giant cells with bizarre nuclei	Anaplastic carcinoma, Medullary carcinoma Follicular adenoma with bizarre nuclei

Cytological findings indicating Tall cell PTC

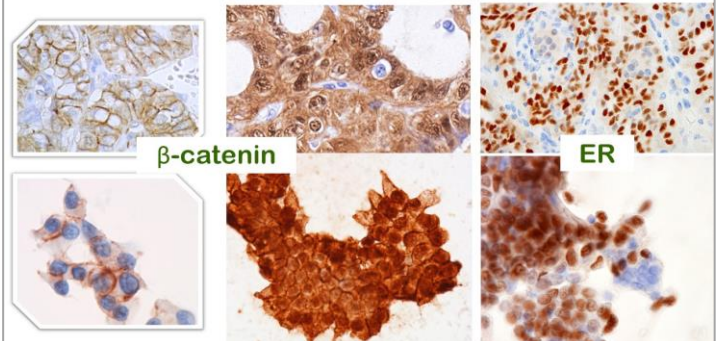


Tanaka A, Hirokawa M, et al. Diagn Cytopathol. 2019;47:452-457



Conventional

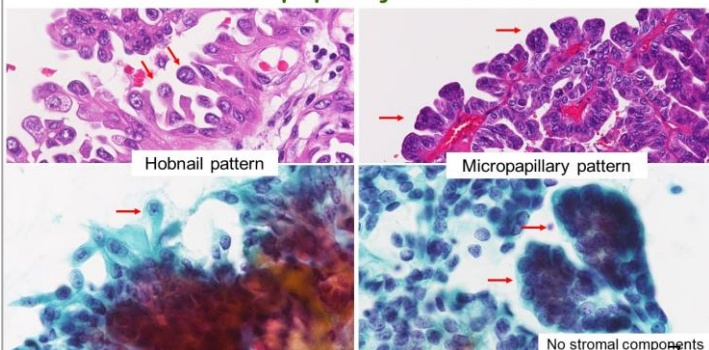
Cribriform morular carcinoma



β -catenin

ER

Hobnail papillary carcinoma



Hobnail pattern

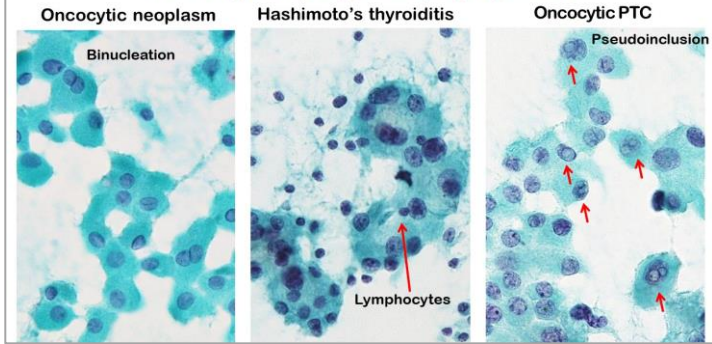
Micropapillary pattern

No stromal components

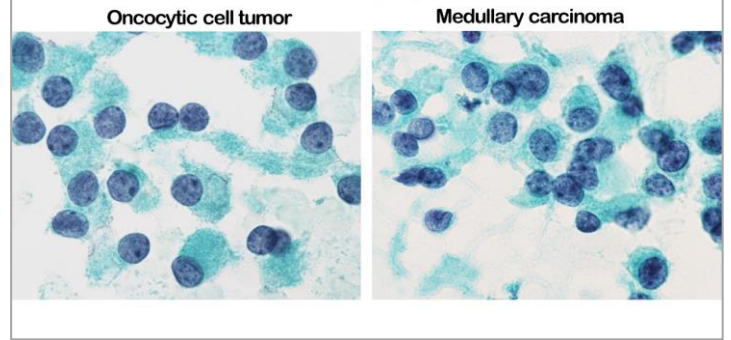
Cytoplasmic findings

Oncocytic	Oncocytic cell tumor, Follicular nodular disease Hashimoto's thyroiditis, PTC
Granular	Oncocytic cell tumor Medullary carcinoma
Metachromatic granule	Medullary carcinoma
Metaplastic cell	PTC, Anaplastic carcinoma Cyst, Follicular nodular disease
Septated intracytoplasmic vacuole	PTC
Yellow bodies	Hyalinizing trabecular tumor
Paravacuolar granules	Follicular nodular disease

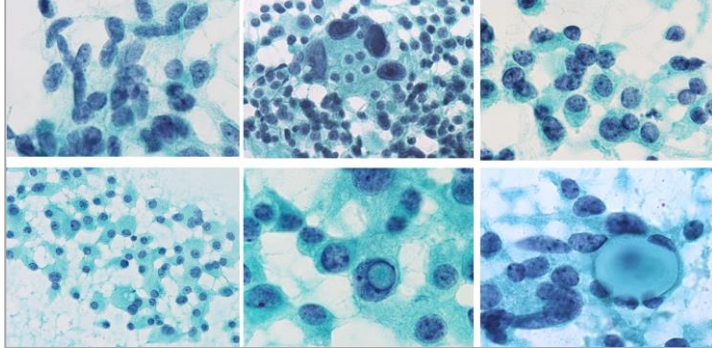
Oncocytic (Oxyphilic) cytoplasm



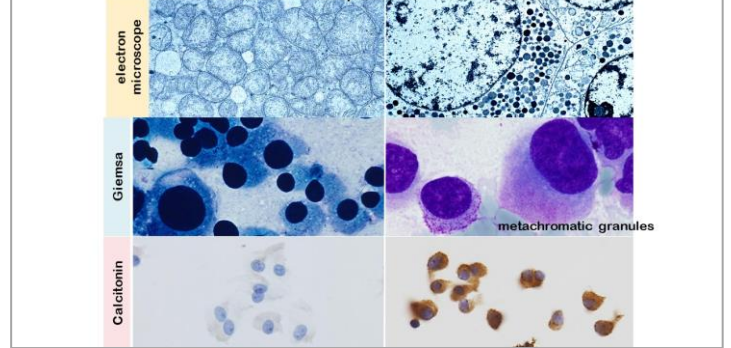
Granular cytoplasm



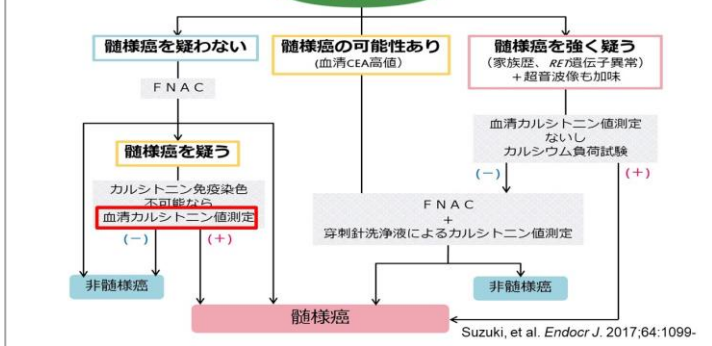
Various types of medullary carcinoma



Oncocytic cell tumor Medullary carcinoma

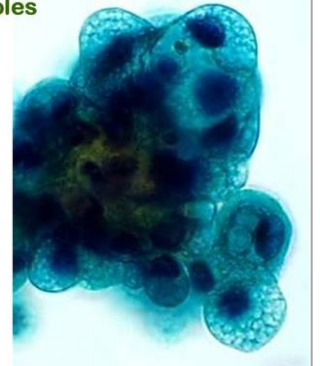
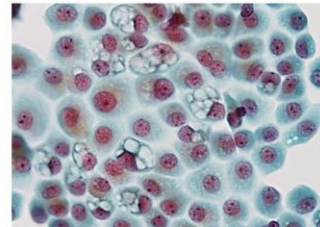


甲状腺結節



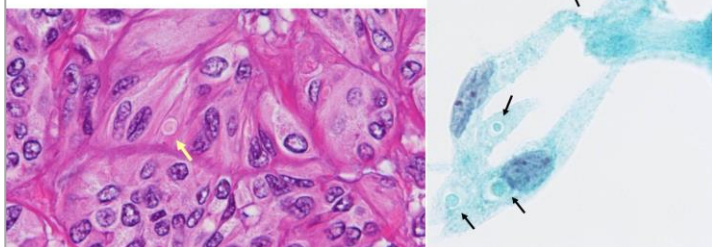
Septated intracytoplasmic vacuoles

- Small, uniform, and well-defined vacuoles separated by dense cytoplasm
- Observed in metaplastic cells
- Characteristic of PTC (52.6 to 64.0%)



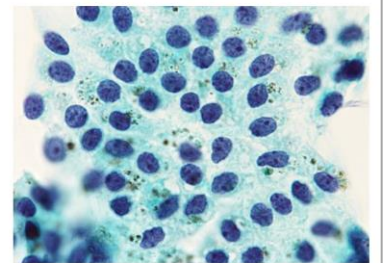
Yellow bodies

Small droplet with halo
Color in yellow in HE stain
Characteristic of HTT



Paravacuolar granules (PVG)

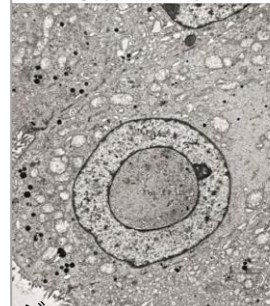
- Brown tiny granules in the small, clear cytoplasmic vacuoles
- Hallmark of benign lesions
- Lipofuscin or hemosiderin



Nuclear findings

Intranuclear cytoplasmic inclusions	PTC, Hyalinizing trabecular tumor Medullary carcinoma Anaplastic carcinoma
Nuclear grooves	PTC Graves' disease Hashimoto's thyroiditis Follicular nodular disease
Peculiar nuclear clearing	Cribriform morular carcinoma
Nuclear overlapping	PTC
Ground glass appearance	PTC
Salt & pepper chromatin	Medullary carcinoma

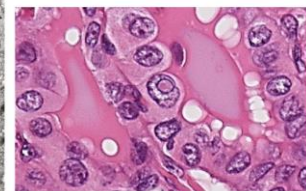
Invagination of nuclear membrane with cytoplasmic components



Intranuclear cytoplasmic inclusions (pseudoinclusion)

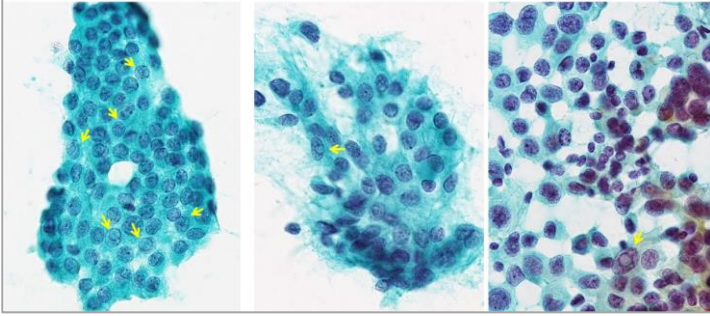
Diagnostic definition

- Sharp demarcation
- Chromatin clumping on the outer edge of membrane
- Color similar to cytoplasmic staining

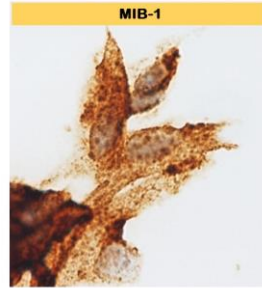


Intranuclear cytoplasmic inclusions

Papillary carcinoma Hyalinizing trabecular tumor Medullary carcinoma

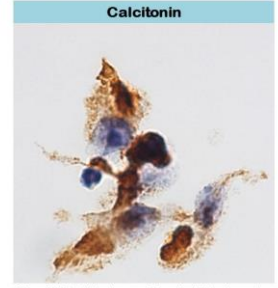


Hyalinizing trabecular tumor



Hirokawa M, Carney JA. Am J Surg Pathol. 2000 ;24:575-8.

Medullary carcinoma

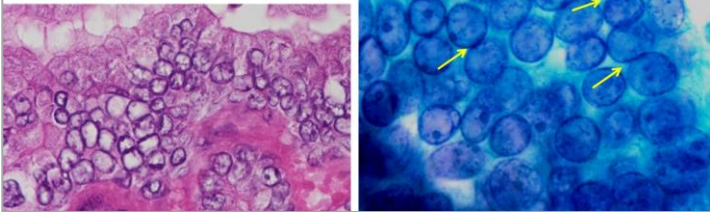


Suzuki A, Hirokawa M, et al. Endocr J. 2017;64:1099-1104.

Ground glass nuclei

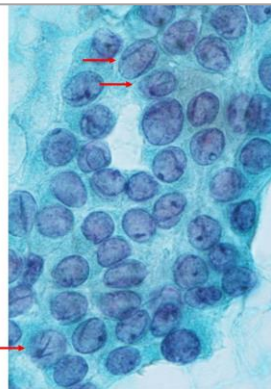
- Characteristic of PTC
- Orphan Annie eye nuclei on histological specimen

Nuclear overlapping



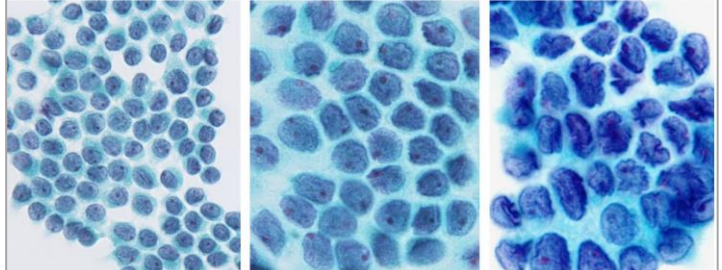
Nuclear grooves

- Longitudinal fold along the long axis of the nuclei
- Also seen in Graves' disease, Hashimoto's thyroiditis, or benign nodular disease
- Highly suggestive of PTC, when the presence is prominent or one nucleus has more than two folds



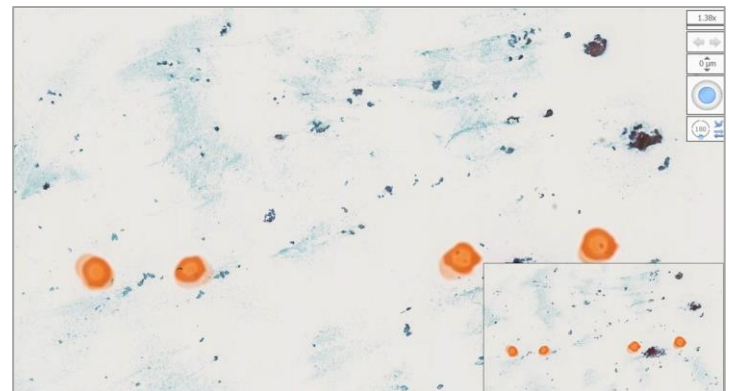
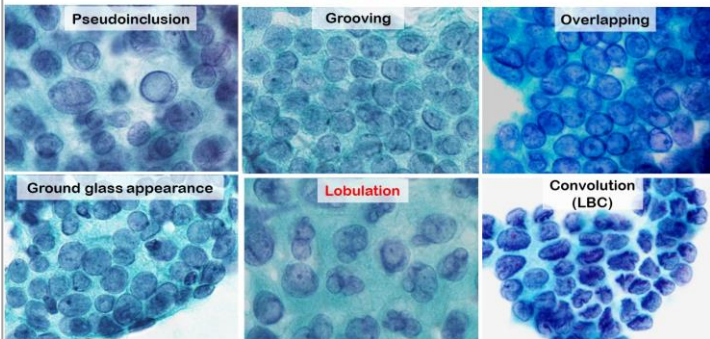
Nuclear findings of Papillary carcinoma in LBC

No overlapping & Windows No ground glass Convoluted nuclei



Suzuki A, Hirokawa H, et al. Diagn Cytopathol 43: 108-113, 2014

Characteristic nuclear findings of PTC



How to observe aspiration cytology

Low power → High power
Outside → Inside



- 1) Gross examination: Smearing method & state
- 2) Low-power view (x4): Components, Background, Cellular arrangement
- 3) Middle-power view (x10): Cell shape, Cytoplasm, Nucleus
- 4) Diagnosis: Differential diagnoses, Diagnostic category, Suspected diagnosis
- 5) Screening: Confirmation of diagnosis, Reversed differential diagnosis, Detection of associated or overlooked findings

