My personal experience at University of Toronto and recent updates of Endocrine Pathology

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[2]Laboratory Medicine & Pathobiology, University of Toronto, Faculty of Medicine, Canada

Date of Presentation: Oct 5th 2015


Dr.神野
高松赤十字病院病理部

FOCUS ON NEUROENDOCRINE TUMORS

Recent update of endocrine pathology

Presentation Overview

Participants should have an understanding of:

I) Brief report and feed back of my personal experience at University of Toronto

II) Recent update of endocrine pathology (pituitary, thyroid, parathyroid, adrenal gland, neuroendocrine tumors)

III) Application to the routine practice and clinical-pathological correlation

UHN Laboratory Medicine Program

Sylvia L. Asa, MD, PhD, FRCPC, FCAP
Medical Director
Laboratory Medicine Program
Senior Scientist, Ontario Cancer Institute
Professor
Department of Laboratory Medicine & Pathobiology
University of Toronto

Preparatory steps

November 6, 2013

Toshitetsu Hayashi
Department of Diagnostic Pathology
Faculty of Medicine, Kagawa University
1750-1 Ikenobe, Miki-cho, Kita-gun,
Kagawa prefecture, Japan

Dear Dr. Hayashi

It is a pleasure to offer you a position as a Post-doctoral Fellow and Observer again in the Endocrine Pathology section of the Department of Pathology at the University Health Network beginning February 1, 2014. This position is offered for three months with an opportunity for renewal for a second three month period to be completed on July 31, 2014.

During this training period we expect you to focus on the pathology of thyroid with the goal of expanding understanding of thyroid tumors, increasing your diagnostic skills in the diagnosis of thyroid lesions, and learning new molecular genetic techniques, insights and possible application to surgical and biopsy material to achieve a correct diagnosis of thyroid tumors. During your visit, you will observe and review the slides of our consultation cases and study sets, and discuss issues that arise for a better comprehension and understanding of endocrine diseases.

The Endocrine Pathology group consists of three consultants, Dr. Ozgur Mete, Dr. Daniel Winer and myself. We also have at least one fellow and one or two residents working on the diagnostic service at all times. In my research lab, there is a team of up to 12 individuals, including my collaborator Dr. Shereen Ezzat. You will have many resources to work with during your stay.

We have not been able to obtain any financial support for your stay, and we hope that you could keep your scholarship in Japan.

I am confident that you will have a productive experience that will be successful for you. We look forward to seeing you continuing your study and research in Toronto.

Yours sincerely,

Sylvia L. Asa, M.D., Ph.D.

The adventure begins at this way

The Pathology Report

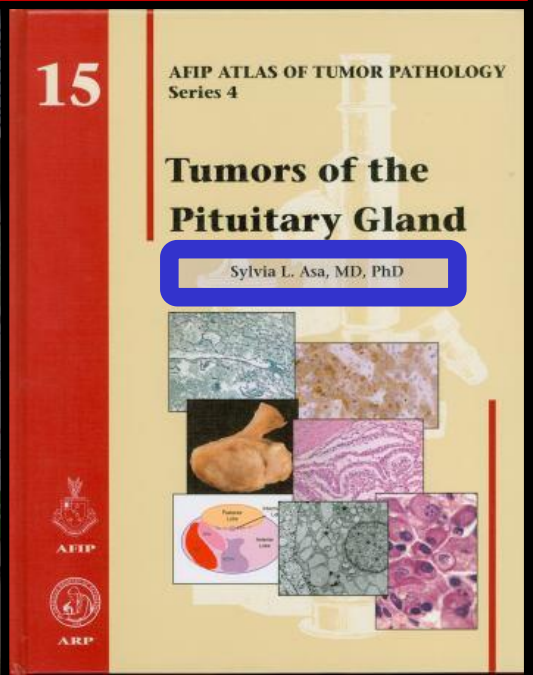
Beyond the microscope @ UHN

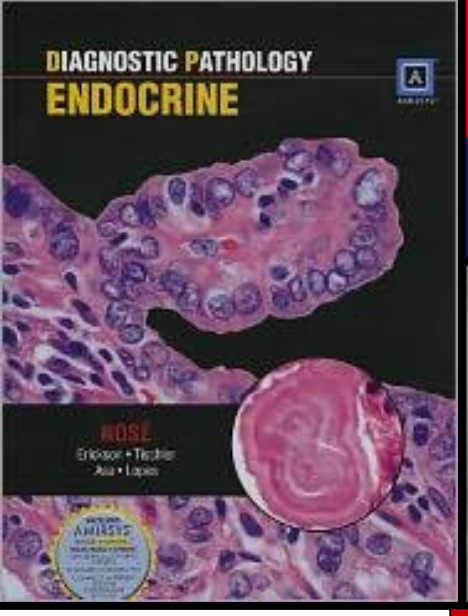
Everything you always wanted to ask but were afraid to know!

About Pathology at UHN

The pathology department is part of the larger Laboratory Medicine Program (LMP) at the University Health Network (UHN) that includes Toronto General Hospital, Princess Margaret Hospital, Toronto Western Hospital and Toronto Rehab.

With over 425 staff, including 60 medical and scientific staff, we are the largest diagnostic lab in Canada and one of the largest academic labs in the world. Every patient at UHN is impacted by the tests performed within LMP and we provide detailed, knowledgable and comprehensive consultations as integrated members of the healthcare team.





Toronto General Hospital

Section of Endocrine Pathology

Prof. Dr. Asa

Dr. METE

Dr. Winer

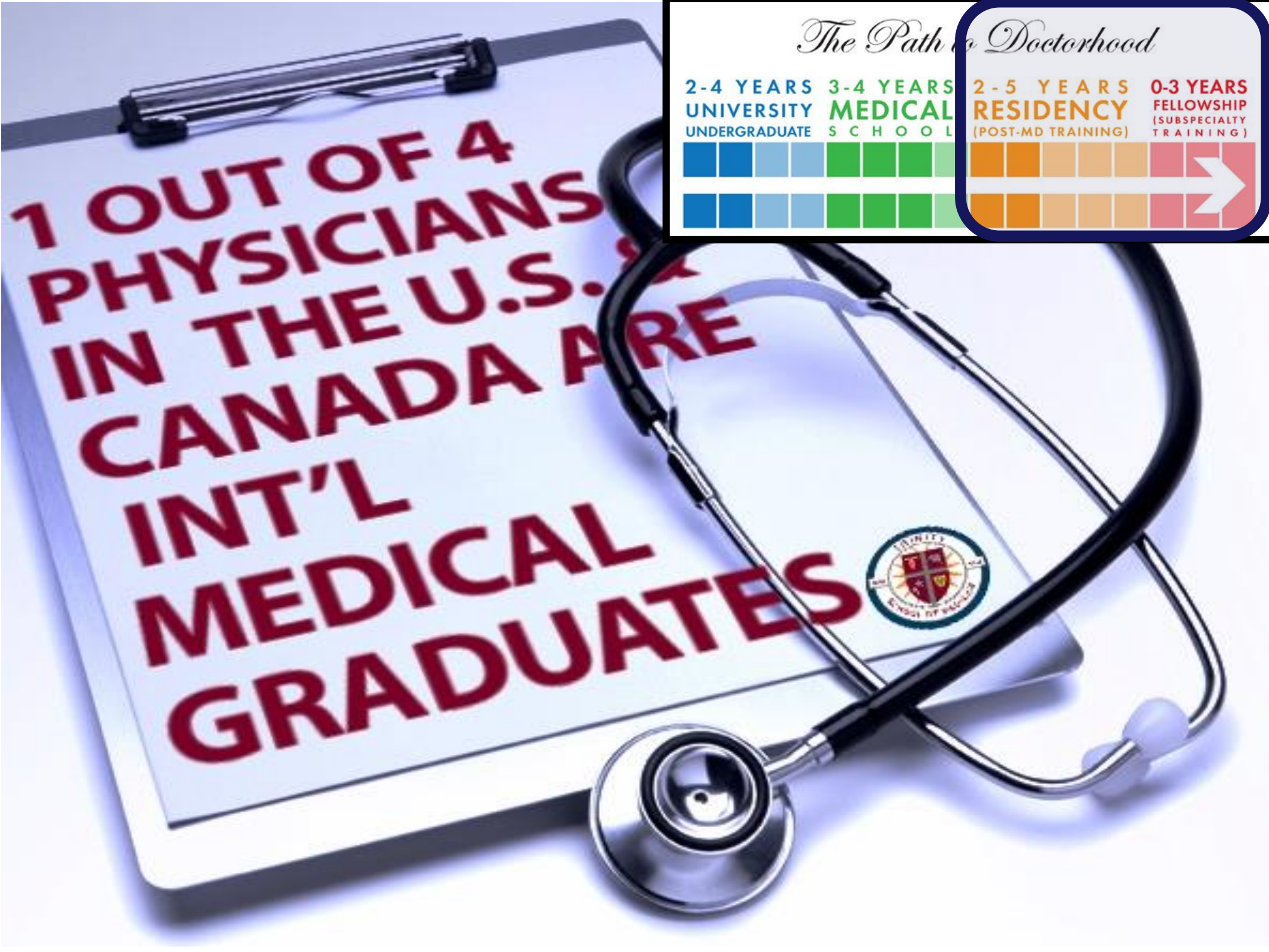
Members of the section of Endocrine Pathology:

* 3 consultants (board certified pathologists)
* 1 clinical fellow, residents doing rotation or medical students

Research team:

*Laboratory: 12 scientists or research fellows


INSULIN:
Toronto's Gift
to the World
A burst of inspiration in the middle of the night led to one of the greatest discoveries of the 20th century. With a legacy that still resonates today, insulin has saved the lives of millions of people and paved the way for unprecedented progress in medical science.
Before insulin, the life of a person with diabetes – especially type 1 – was inevitably tragic and short. Racked by unquenchable thirst, excessive urination and rapid weight loss, a person with diabetes would suffer emaciation, coma and, eventually, death.
Studies as far back as the 1800s led scientists to speculate that the pancreas was the critical gland for regulating sugar in the body. This theory launched experiments by researchers for decades. None would yield promising results until October 1920, when a young Canadian surgeon, Dr. Frederick G. Banting, was struck by a compelling idea for an experiment to isolate an internal secretion of the pancreas.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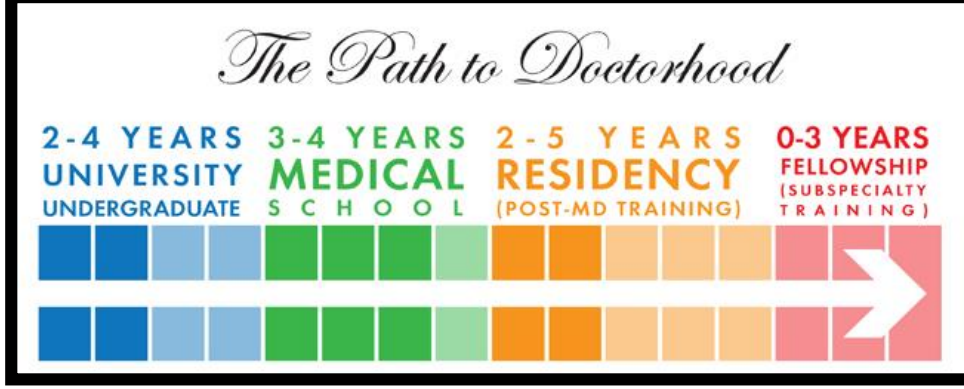
PHYSICIANS
IN THE U.S.
CANADA ARE
INT'L
MEDICAL
GRADUATES
The Path to Doctorhood
2-4 YEARS
UNIVERSITY
UNDERGRADUATE
3-4 YEARS
MEDICAL
SCHOOL
2-5 YEARS
RESIDENCY
(POST-MD TRAINING)
0-3 YEARS
FELLOWSHIP
(SUBSPECIALTY
TRAINING)



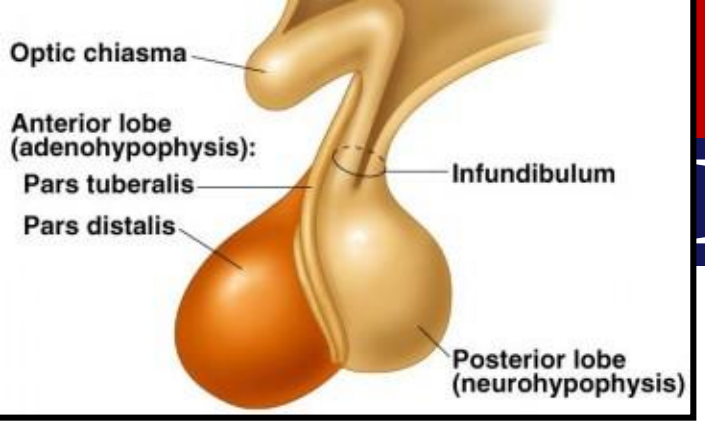
International medical graduates

With specialist (board) license of home-country: Academic license (restricted license): University Hospital

Medical license

BOARD EXAM

Clinical fellow/ Staff pathologist



Recent update of endocrine pathology

I) Pituitary gland

New concepts and approach for pituitary tumors

I) Adequate use of immunohistochemistry (panel of transcription factors and hormones for accurate classification)

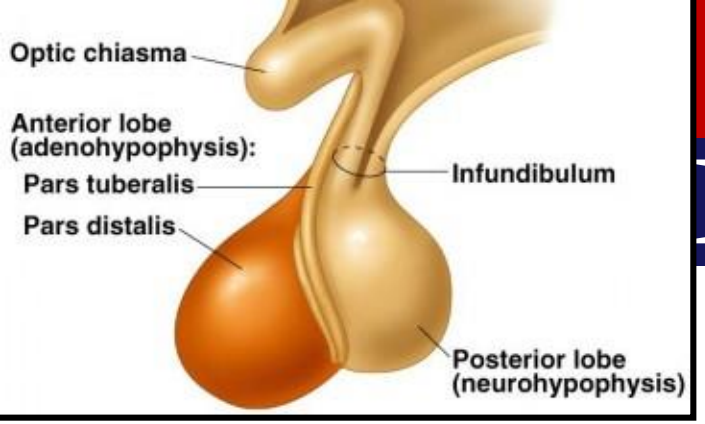
II) New classification scheme for pituitary adenomas

III) Spindle cell oncocytomas and granular cell tumors of the pituitary are variants of pituicytoma

Table 2. Classification of pituitary adenomas. Abbreviations: Pit-1 = pituitary specific transcription factor 1; GH = growth hormone; PRL = prolactin; TSH = thyroid stimulating hormone; ACTH = adrenocorticotropic hormone; SF-1 = steroidogenic factor 1; α-SU = alpha subunit; ER-α = estrogen receptor alpha; GATA-2 = GATA binding protein 2; Tpit = T-box transcription factor; β-FSH = follicle stimulating hormone; β-LH = luteinizing hormone.

Adenoma subtypes	Immunoreactivities	CAM 5.2
Pit-1 (GH/PRL/TSH) family tumors		
GH-producing adenomas		
Densely granulated somatotroph adenoma	Pit-1, GH (diffuse), α-SU	Perinuclear
Intermediate type somatotroph adenoma*	Pit-1, GH (diffuse), α-SU	Few fibrous bodies
Sparsely granulated somatotroph adenoma	Pit-1, GH (weak)	Fibrous bodies (>90%)
Mammosomatotroph adenoma	Pit-1, ER-α†, α-SU	
Mixed somatotroph and lactotroph adenomas	Pit-1, ER-α†, α-SU	
GH-producing plurihormonal adenoma	Pit-1, (ER-α†), (GATA-2)	
PRL-producing adenomas		
Sparsely granulated lactotroph adenoma	Pit-1, ER-α†, PRL (Golgi)	
Densely granulated lactotroph adenoma	Pit-1, ER-α†, PRL (Diffuse)	
Acidophil stem cell adenomas	Pit-1, ER-α†, PRL (Diffuse), GH (variable)	Few fibrous bodies
TSH-producing adenomas		
Thyrotroph adenoma	Pit-1, GATA-2	
Monomorphous Pit-1 lineage plurihormonal adenoma		
Silent subtype 3 adenoma	Pit-1, (ER-α†, α-SU), GH/PRL/TSH (variable)	
T pit (ACTH) family tumors		
Densely granulated corticotroph adenoma	Tpit, ACTH (strong, diffuse)	Strong diffuse
Sparsely granulated corticotroph adenoma	Tpit, ACTH (weak, variable)	Strong diffuse
Crooke cell adenoma	Tpit, ACTH (juxtanuclear and peripheral)	Ring-like pattern
SF-1 (Gonadotroph) family tumors		
Hormone active gonadotroph adenoma	SF-1, ER-α†, GATA-2, α-SU, β-FSH, β-LH	Usually negative
Hormone-inactive gonadotroph adenoma	SF-1, ER-α†, GATA-2, α-SU (variable)	Usually negative
Transcription factor and hormone negative adenoma		
Null cell adenoma	Negative for all transcription factors and hormones	Variable positive
Polymorphous plurihormonal adenoma		
Plurihormonal adenoma, NOS	Multiple	

*This tumor is usually classified as densely granulated somatotroph adenoma as their biology is similar to densely granulated somatotroph adenomas.
†ER-α is sensitive to fixation and can be very focally and weakly positive.



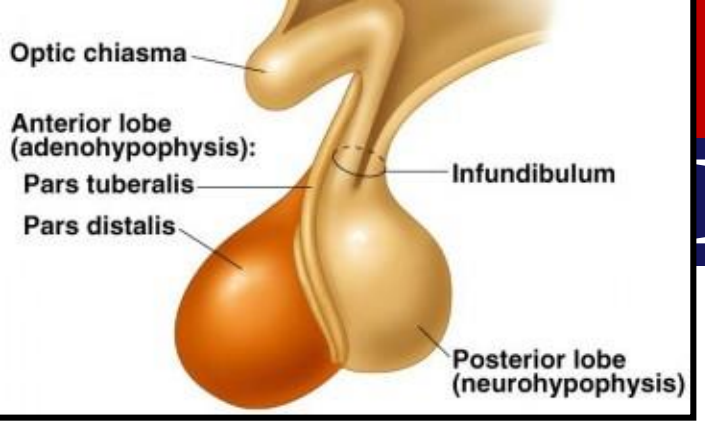
Recent update of endocrine pathology

I) Pituitary gland

* Reticulin and PAS stains

Immunohistochemistry panel for pituitary adenomas

* Transcription factors: PIT-1, T-PIT-1 (N/A), SF-1
* GH, TSH, FSH, LH, TSH, ER, ACTH, Alpha-HCG
* FGFR-4
* MIB-1
* CAM 5.2 (LMWCK)



Recent update of endocrine pathology

I) Pituitary gland

New concepts and approach for pituitary tumors

I) Adequate use of immunohistochemistry (transcription factors and h… …ation)

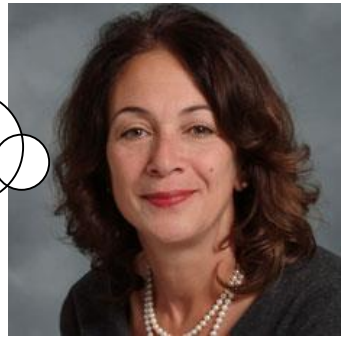
II) New c… …enomas

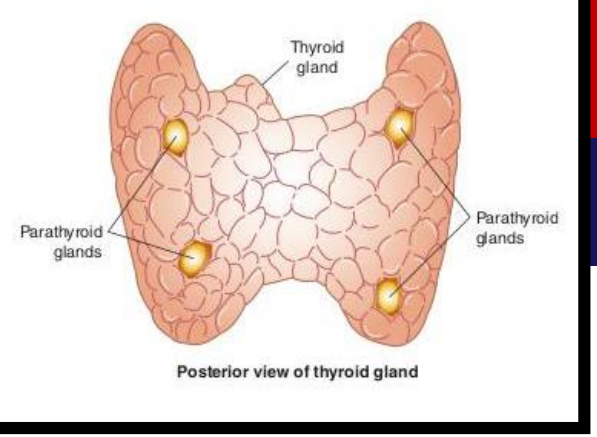
III) Spi… …l tumors of the…

Feed-back for Kagawa University

I) Acquisition of CAM 5.2 antibody and other hormones (SF-1)

II) Beware of aggressive variants, corticotroph adenomas and Crooke- hyaline change in non-tumoral part





Recent update of endocrine pathology

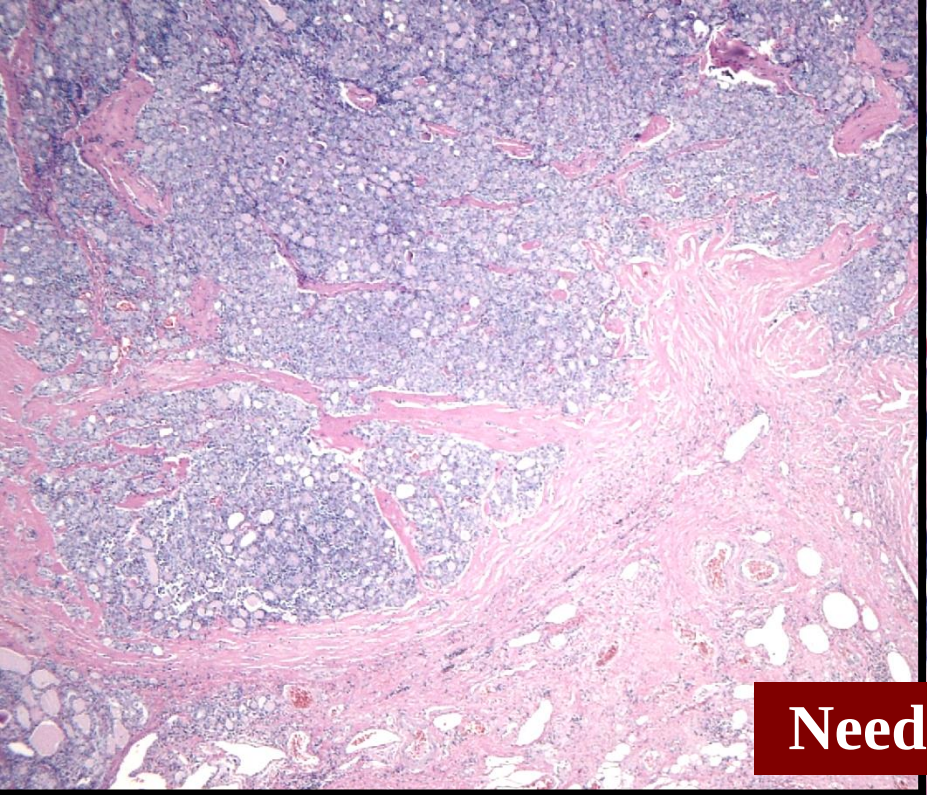
II) Thyroid and parathyroid gland

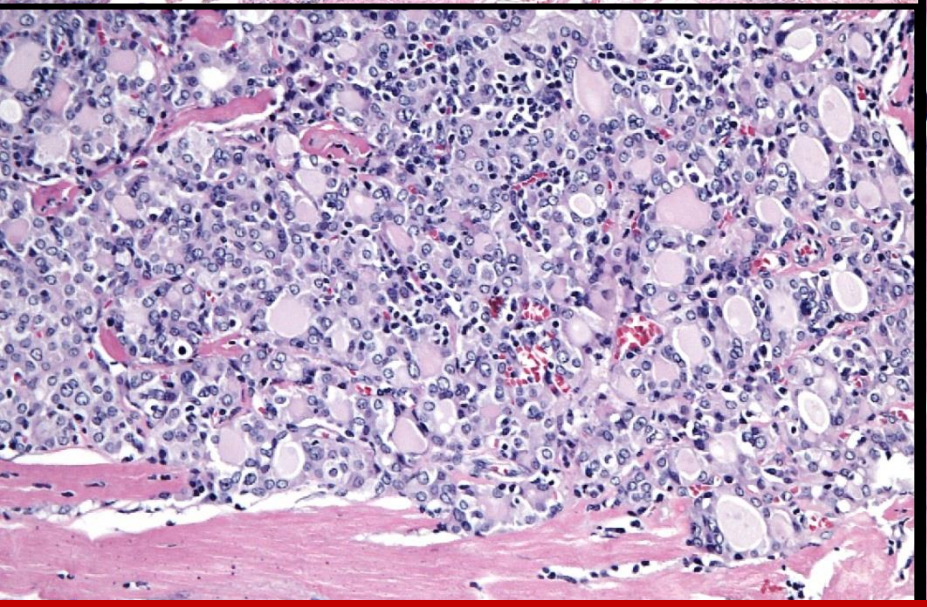
A) New concepts and approach for thyroid tumors

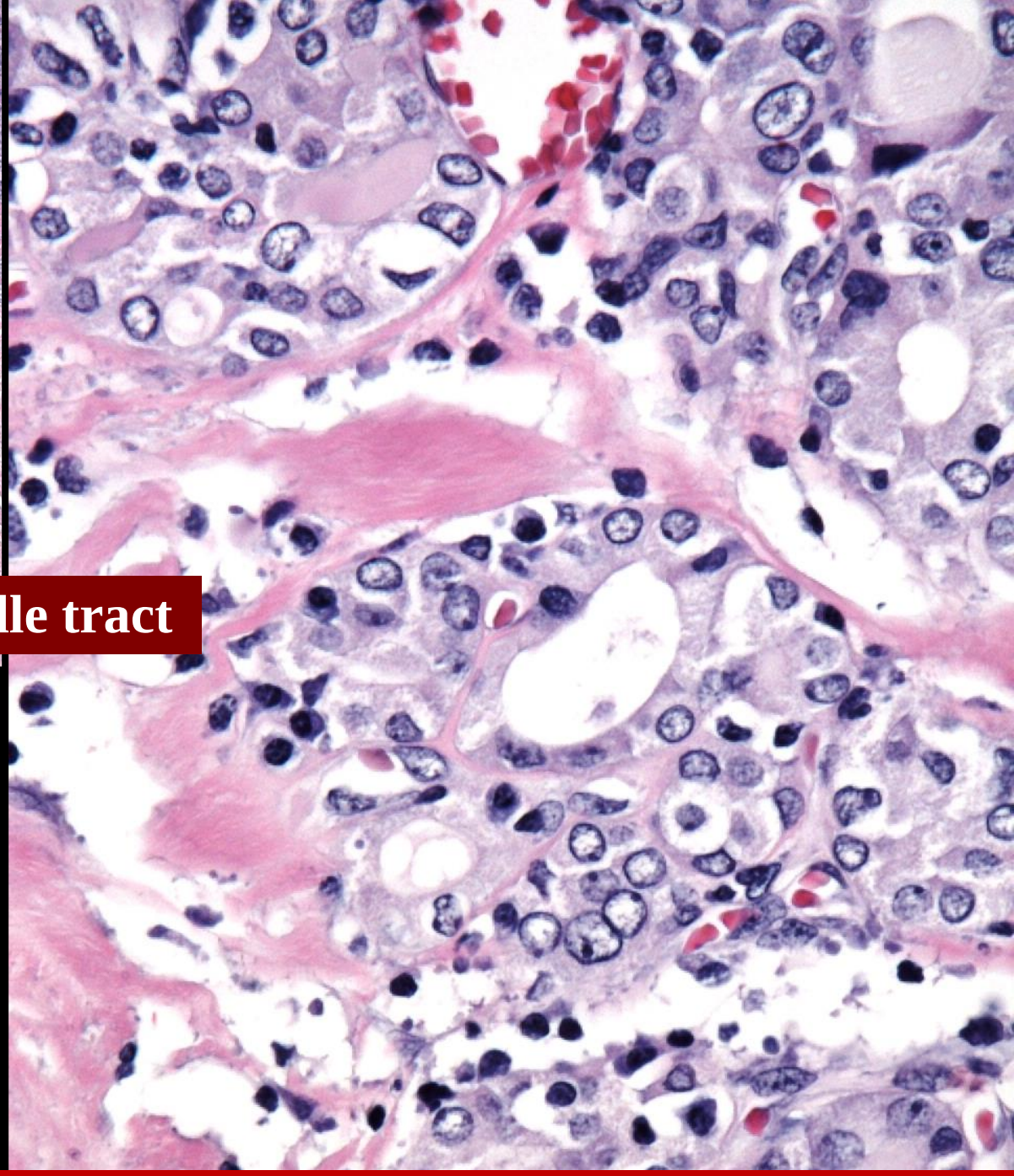
I) WHAFFT

II) Papillary thyroid carcinoma (PTC): new definition

III) Controversial thyroid capsule: Extrathyroidal extension (ETE; pT3)





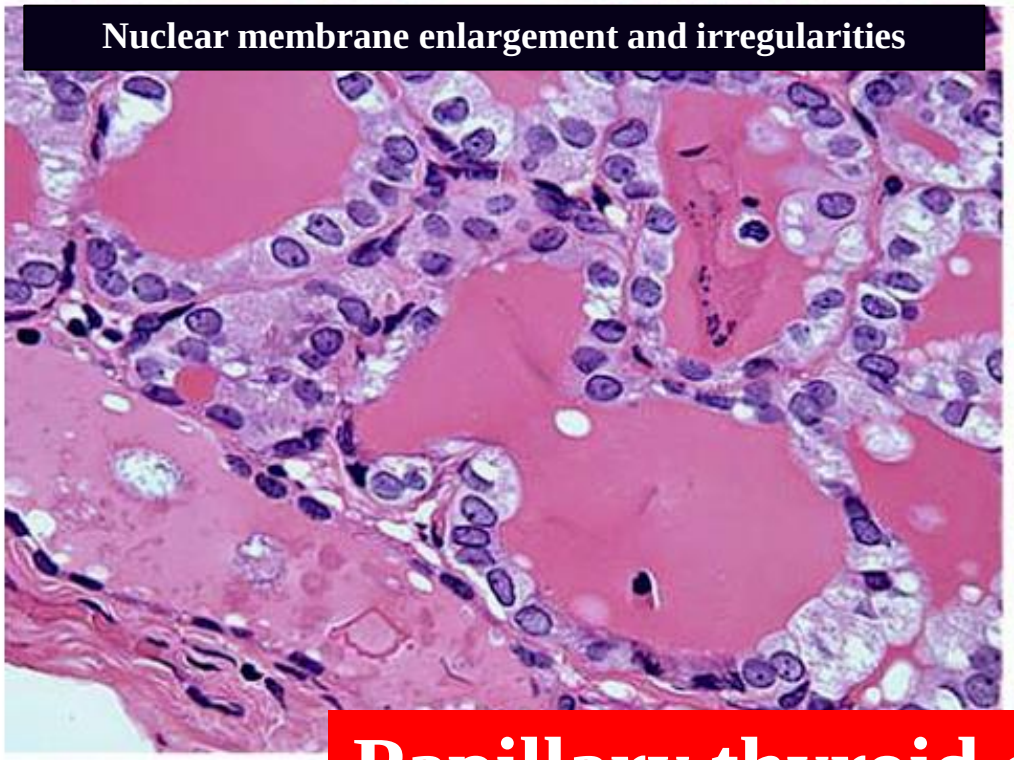


Needle tract

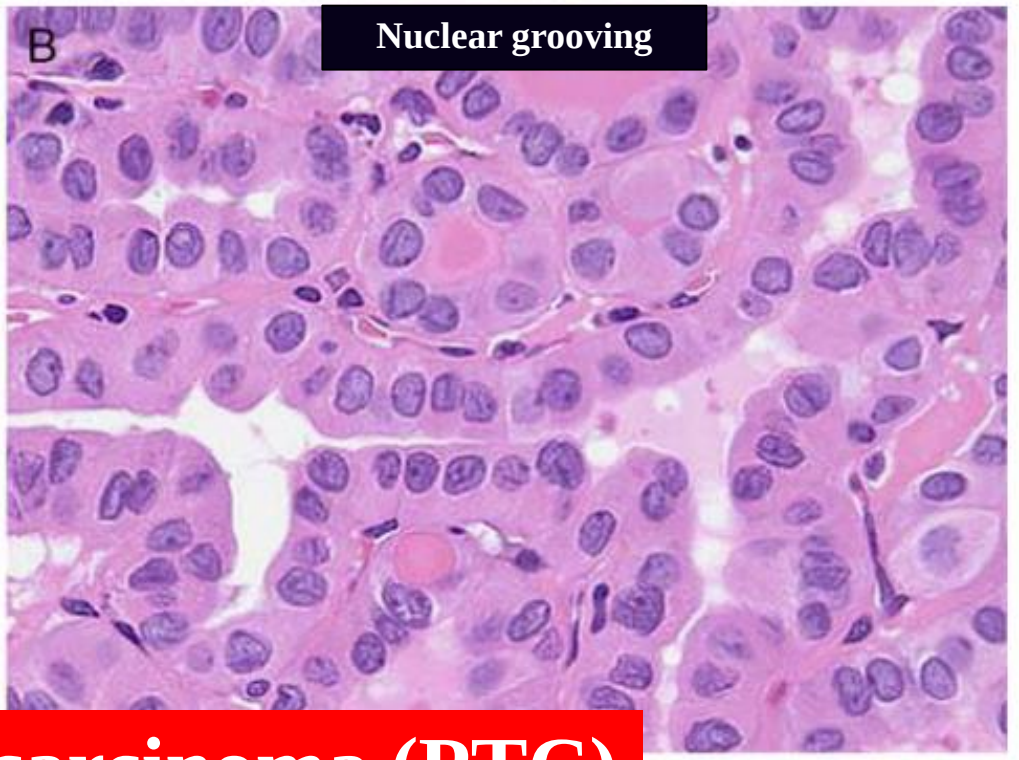
I) WHAFFT? WHAT????????

(**W**orrisome **H**istologic **A**lterations **F**ollowing **F**ine needle aspiration of the **T**hyroid)

Papillary thyroid carcinoma (PTC)

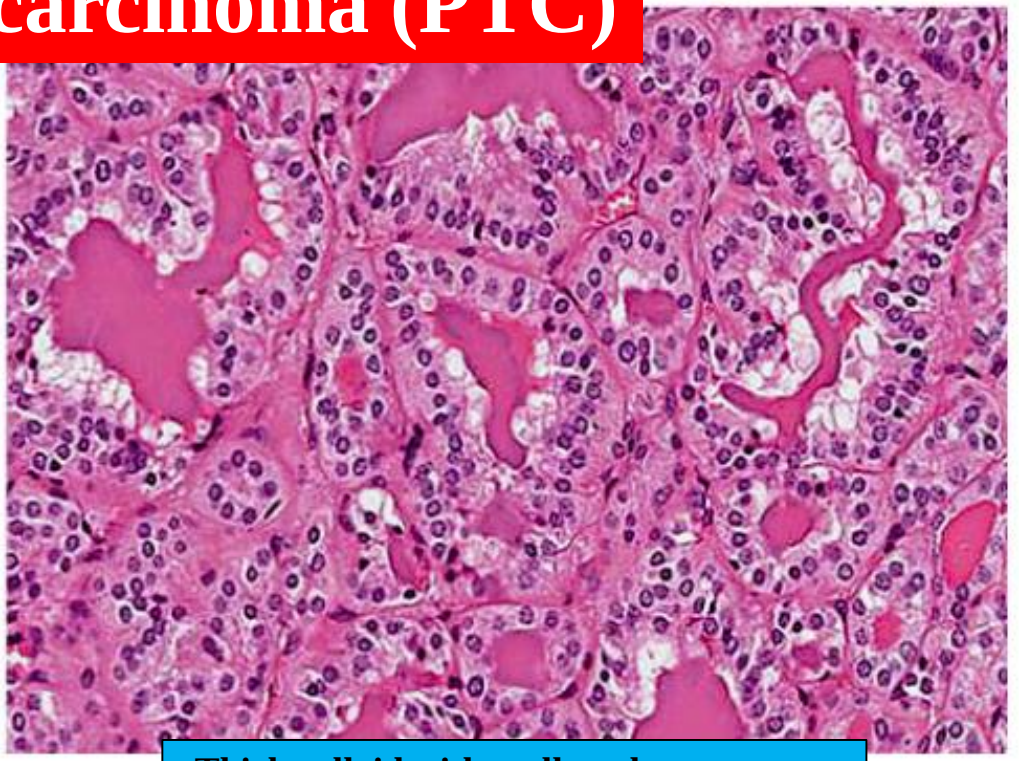


Nuclear membrane enlargement and irregularities



Nuclear grooving

Intranuclear pseudoinclusion



Thick colloid with scalloped appearance

How to make diagnosis of PTC?

First of all: nuclear enlargement and irregularities

Dr. METE

Adv Anat Pathol • Volume 19, Number 6, November 2012 *Diagnosis of Thyroid Follicular Neoplasms*

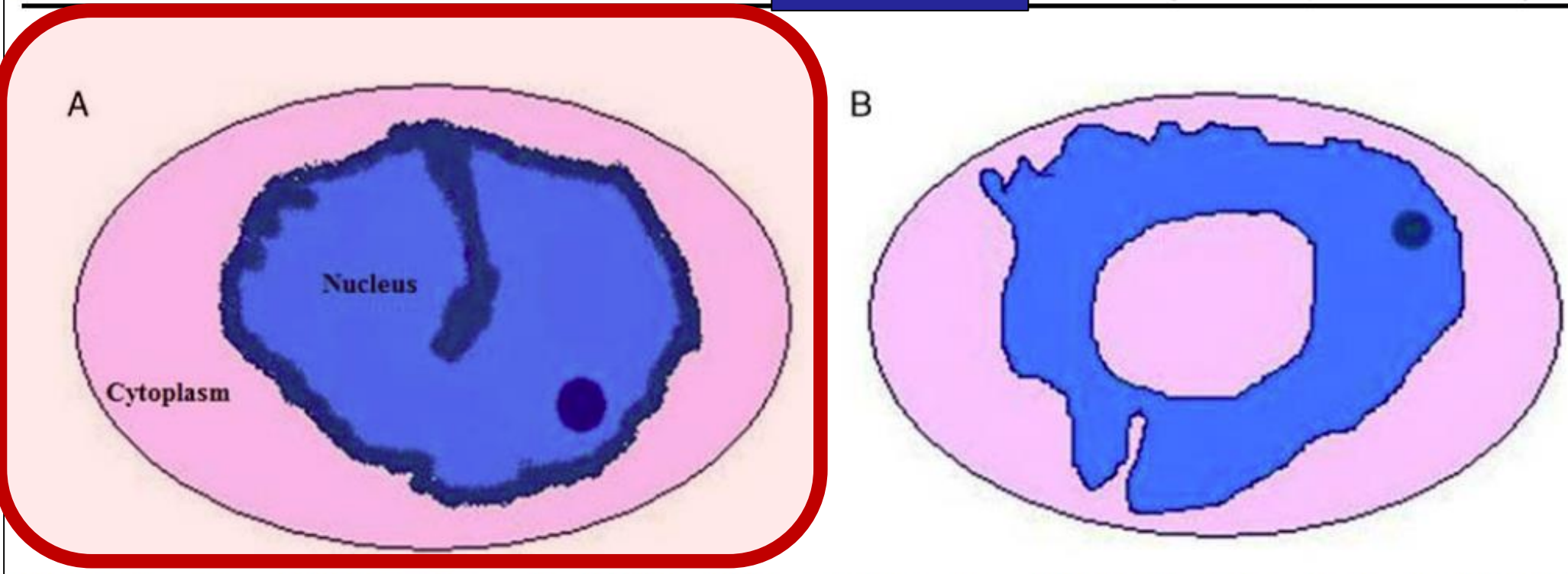
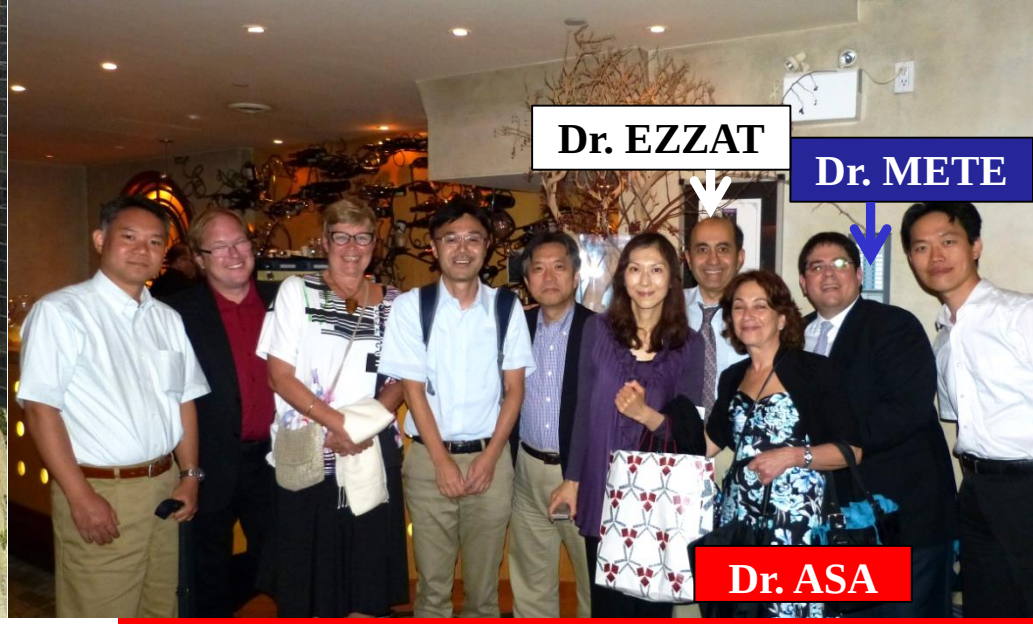


FIGURE 4. Schematic illustration of the nuclear changes seen in papillary thyroid carcinoma (PTC). The nuclear membrane exhibits irregularities that result in loss of nuclear roundness. Peripheral chromatin margination and prominent micronucleoli are also characteristic features. The more nuclear membranes fold into themselves, the more florid nuclear features such as "grooves" (A) or "intranuclear pseudoinclusions" (B) are formed. The most florid feature, intranuclear cytoplasmic pseudoinclusions (B), result from deep invaginations of the cytoplasm. The nuclear pseudoinclusion must contain material similar to the cell cytoplasm, and it must have sharpely defined edges. Intranuclear pseudoinclusions are not required to make a diagnoss of PTC.

Princess Margaret Hospital (Cancer Center)



ROUNDS @ UHN

(this is a general overview only - confirm times and location with staff)
* mandatory for pathology residents

Endocrine rounds: 4/month

GENERAL

*Autopsy rounds	weekly	Thurs @ 8:30 am	TGH, 11th floor autopsy suite
*Unknown rounds	weekly	Thurs @ 4 pm	TGH, multiheader (for residents)
*Gross rounds	weekly	Fri @ 9 am	TGH, 2nd floor SurgPath lab
Case-based rounds	monthly	4th Mon @ noon	TGH, 11th floor conference room

BREAST

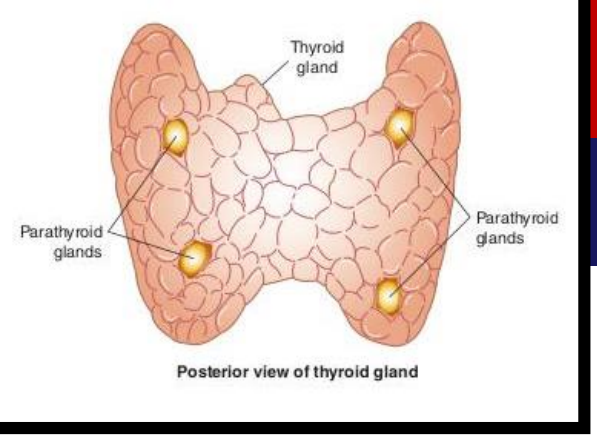
Tumour Board	weekly	Tues @ 12:30 pm	PMH, 6th floor auditorium
Surgery/RadOnc	weekly	Thurs @ 8 am	PMH, 2nd floor

DERMPATH

Skin multidis. Rds	biweekly	Wed @ 5:30 pm	PMH, 6th floor auditorium
Dermpath rounds	monthly	4th Tues @ 1:30 pm	TGH, multiheader

ENDOCRINE

H&N endocrine rds	monthly	last Mon @ 5:30 pm	PMH, 6th foor auditorium
NE tumour board	monthly	3rd Tues @ 5:00 pm	PMH, 6th foor auditorium
Pituitary tumour board	monthly	last Wed @ 5:30 pm	PMH, RadOnc department
Provincial inter-hosp	monthly	3rd Wed @ 5:30 pm	PMH, 7th floor



Recent update of endocrine pathology

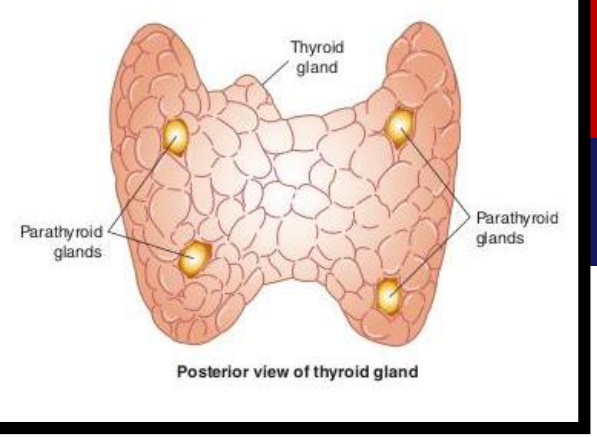
IIb) Parathyroid gland

Challenges of parathyroid pathology

I) Hyperplasia vs. adenoma

II) Adenoma (especially post-FNA) vs. atypical adenoma vs. parathyroid carcinoma

Staff of the Endocrine Pathology Service
Dr. METE and WINER (Holiday Party)



Recent update of endocrine pathology

IIb) Parathyroid gland

Challenges of parathyroid pathology

I) Hyperplasia vs. adenoma

II) Adenoma vs. atypical adenoma

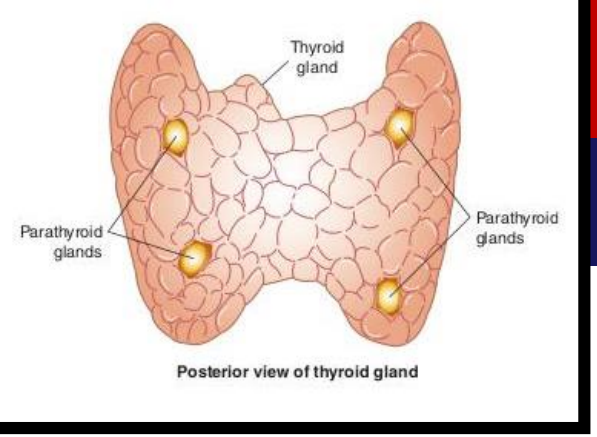
vs.

After the removal of an abnormal parathyroid gland

*Adenoma: a drop of intraoperative PTH >75%
*Hyperplasia: much lower

*Biochemical and morphological correlation is required.

Dr. METE



Recent update of endocrine pathology

IIb) Parathyroid gland

When can the diagnosis of parathyroid carcinoma be rendered?

I) Clinical diagnosis (distant metastasis or gross invasion at the moment of surgery)

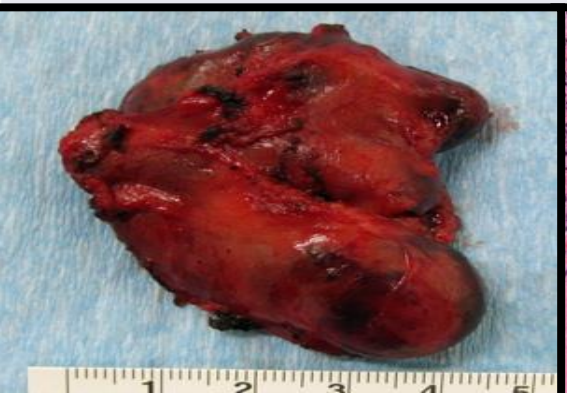
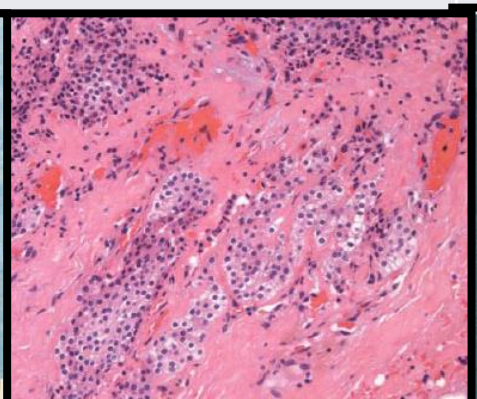
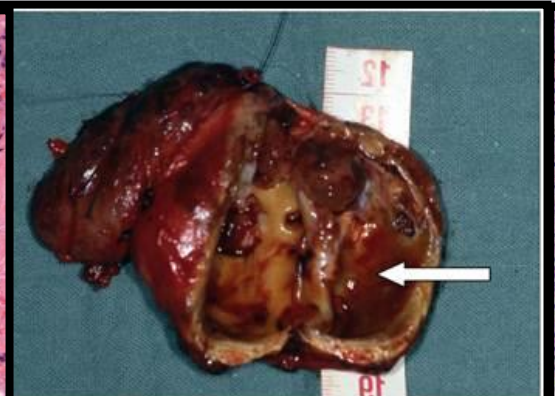
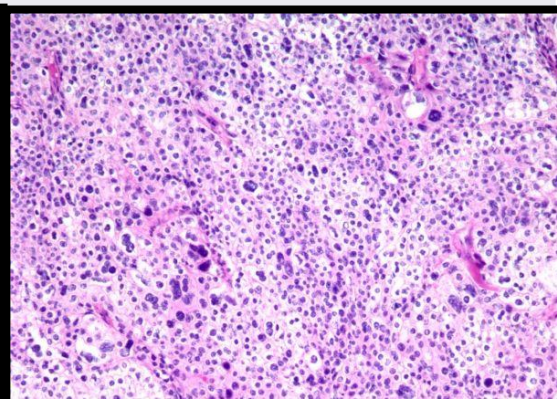
II) Morphological diagnosis: invasion of surrounding structure, vascular invasion, perineural invasion

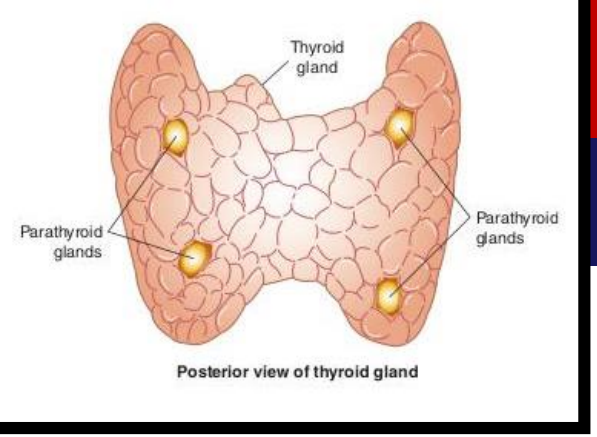
II) Immunohistochemical diagnosis

III) Molecular diagnosis: DNA methylation profile, HRPT2 gene mutation

Immunohistochemistry panel for parathyroid tumors

Atypical adenoma (adenoma with atypical features)	Parathyroid carcinoma
P27(+)	P27(-).
Bcl-2 (+)	Bcl-2(-)
MDM2(+)	MDM2(-)
Rb(+; preserved), Cyclind D1(+)	Rb(-), Cyclin D1(-)
Parafibromin(+)	Parafibromin(-)
Galectin 3(-)	Galectin 3(+)
Low Ki-67, p53	High Ki-67(according to Papotti et al; >6%), p53



Recent update of endocrine pathology

II) Thyroid and parathyroid gland

A) New concepts and approach for thyroid tumors

I) WHA

II) P new definition

III) thyroidal

ext

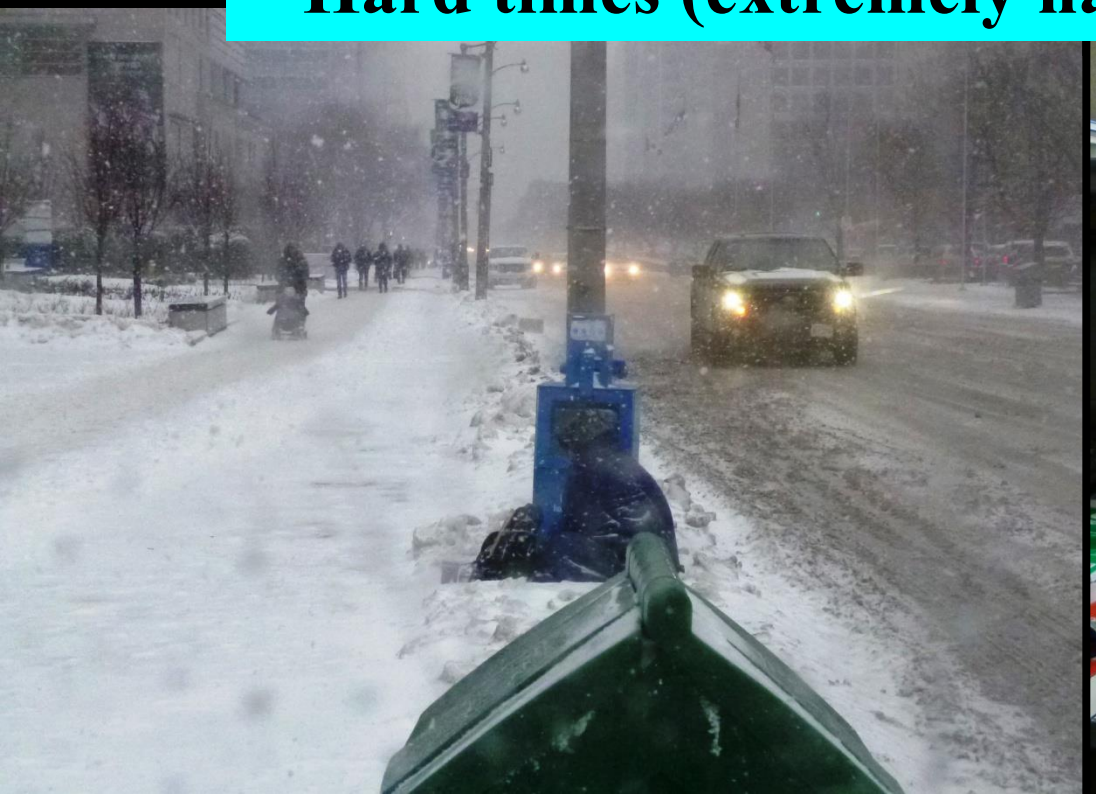
Feed-back for Kagawa University

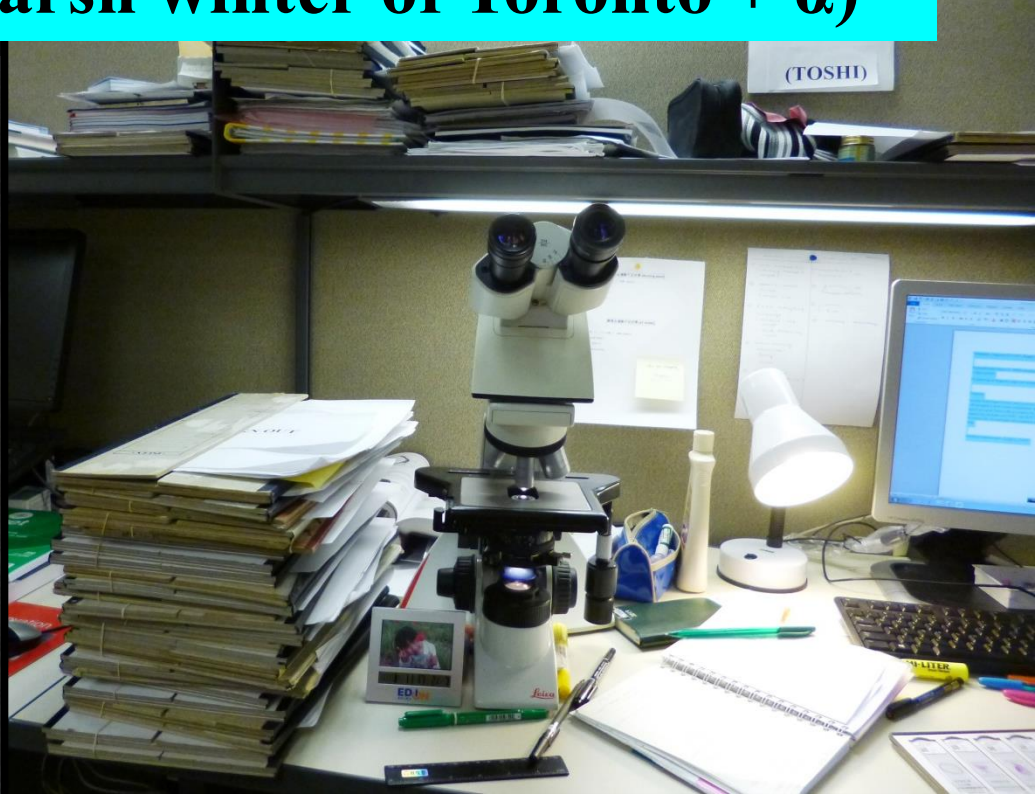
I) Close clinical-pathological correlation (scan, hot nodule, previous FNA history)
II) Histology: gold standard + immunostains (HBME-1, CK19) + careful observation of the background

Dr. METE


TAKE
A BREAK
photograph by Takuya Nagata

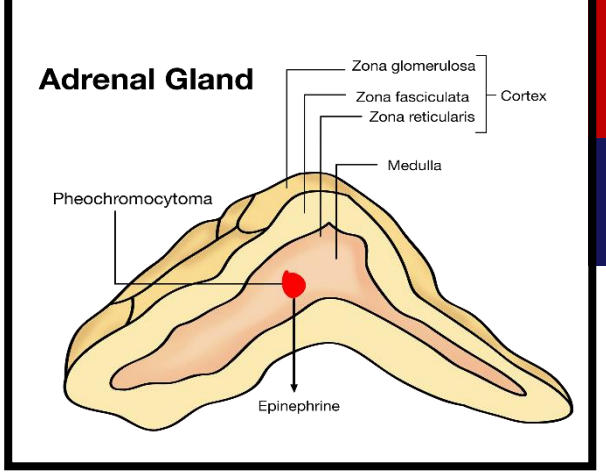
Hard times (extremely harsh winter of Toronto + α)






Hang on here, DAD!!!
FOR SIGN OUT
PENDING REPORTS
Fisherbrand
Cat. No: 12-587-10
Leica
EDUN

ENGLISH ONLY ZONE



Recent update of endocrine pathology

III) Adrenal tumor

New concepts and approach for adrenal tumors

I) Defect and inappropriateness of Weiss criteria

II) Proposal of new diagnostic scheme and protocol

III) Angiogenesis and endocrine tumor

Modified Weiss criteria for adrenal cortical carcinoma (ACC):

*Mitotic rate >5 per 50 high-power fields

*Cytoplasm (clear cells comprising 25% or less of the tumor)

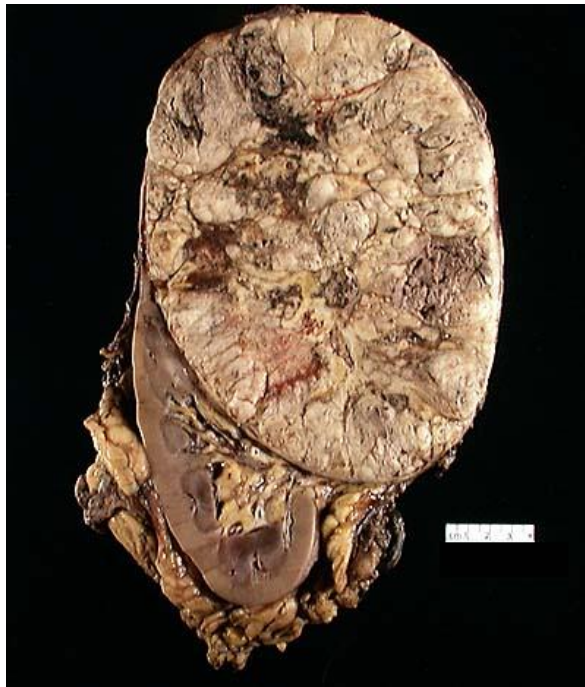
*Abnormal mitoses

*Necrosis

*Capsular invasion

Calculate: 2x mitotic rate criterion + 2x clear cytoplasm criterion + abnormal mitoses + necrosis + capsular invasion (score of 3 or more suggests malignancy, Each criterion is scored 0 when absent and 1 when present in the tumor

Reference: Am J Surg Pathol 2002;26:1612



Modified Weiss criteria:

*Mitotic r

*Cytor

*Abn

*N

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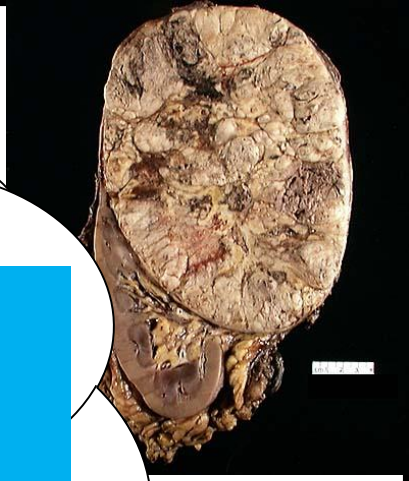


ormal

lignancy,

hor

It's unreliable!!!!!!!!!! (especially for myxoid and oncocytic variant of adrenocortical carcinoma)

Dr. Papotti (University of Torino)

Dr. METE (University of Toronto)

New proposal and panel of immunohistochemistry for ADRENAL CORTICAL CARCINOMAS

Diagnostic algorithm: Reticulin stain + mitosis count + necrosis + vascular invasion

Criteria of malignancy (Histology):

***Low grade carcinomas: mitoses <20/50 HPF**

***High grade carcinomas: mitoses >20/50 HPF**

Overall features:

*P53>90%

*IGF-2: (+)

*β-catenin: nuclear expression

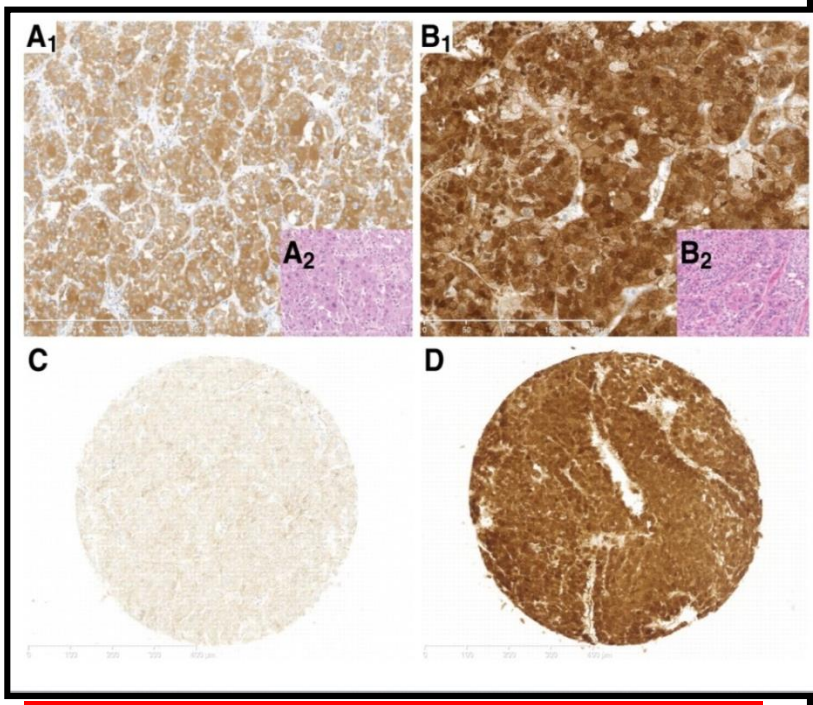
*Vascular invasion

*Macroscopic invasive tumor

*Atypical mitoses

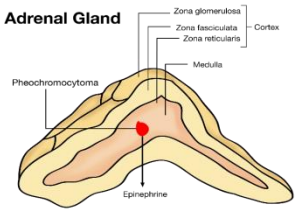
*Diffuse effacement of reticulin stain (but no evident in borderline cases)

***Rule out metastasis (the most common malignancy of adrenal gland)



Aberrant β-catenin expression

Panel of immunostaining: SF-1, Melan A, Inhibin, epithelial markers (usually negative: EMA, CK7), IGF2, β-catenin (nuclear staining), p53



Recent update of endocrine pathology

Angiogenesis and endocrine tumors

Endocr Pathol
DOI 10.1007/s12022-014-9330-y

A Mimic of Sarcomatoid Adrenal Cortical Carcinoma: Epithelioid Angiosarcoma Occurring in Adrenal Cortical Adenoma

Toshitetsu Hayashi · Hasan Gucer · Ozgur Mete

Abstract The adrenal gland is a site of various neoplasms; however, it is rarely involved by sarcomas. We present herein an unusual adrenal neoplasm consisting of epithelioid angiosarcoma and adrenal cortical adenoma. In this report, the authors highlight the diagnostic challenges associated with an epithelioid angiosarcoma occurring in an adrenal cortical neoplasm by providing a comprehensive discussion on the spectrum of vascular proliferations seen in the adrenal gland along with a roadmap for practicing pathologists. The presence of angiosarcoma within an adrenal cortical adenoma may represent a collision tumor; however, one can speculate that the rich vasculature of endocrine lesions can also create a favorable milieu for the occurrence of this phenomenon. While the latter needs to be further clarified, the presented case should be added to the unusual clinical presentations of vascular lesions of the adrenal gland mimicking a sarcomatoid adrenal cortical carcinoma.

Keywords Epithelioid angiosarcoma · Adrenal cortical adenoma · Adrenal cortical carcinoma · Sarcomatoid carcinoma · SF-1

Introduction

Angiosarcomas are malignant neoplasms recapitulating both morphological and functional features of endothelium to a variable degree. While these neoplasms are often seen in the skin and soft tissue, visceral forms have also been described in many organs [1]. Malignant vascular endothelial neoplasms in which epithelioid cells predominate are classified as epithelioid angiosarcomas. Epithelioid angiosarcomas can easily be mistaken for carcinomas because of their morphologic and immunohistochemical similarities [1, 2]. While most adrenal angiosarcomas represent metastases from another primary tumor site, primary angiosarcoma of the adrenal gland is uncommon and usually of epithelioid type, with only 29 reported cases in the literature [3–22] (Table 1). We present herein an unusual adrenal neoplasm consisting of composite epithelioid angiosarcoma and adrenal cortical adenoma that mimics a sarcomatoid adrenal cortical carcinoma. In this report, the authors aimed to discuss the diagnostic challenges associated with an epithelioid angiosarcoma occurring in an adrenal cortical neoplasm by providing a comprehensive discussion on the spectrum of vascular proliferations seen in the adrenal gland along with a road map for practicing pathologists.

Case Report

A 63-year-old man with a previous history of smoking-related chronic obstructive pulmonary disease was admitted to hospital due to progressive dyspnea and progressive marked weight loss along with abdominal discomfort of 6-month duration. Both abdominal ultrasound and computed tomography scan identified a large right adrenal mass measuring up to 7.8 cm. In addition, enlarged mediastinal lymph nodes with a predominant right hilar 3-cm nodule were detected. While the imaging studies were highly suspicious for tumor metastasis, no endobronchial lesion was identified on bronchoscopy. Bronchial biopsy and bronchoalveolar lavage smears were negative for malignancy or granulomatous inflammation. Multiple dynamic and functional tests (ACTH stimulation

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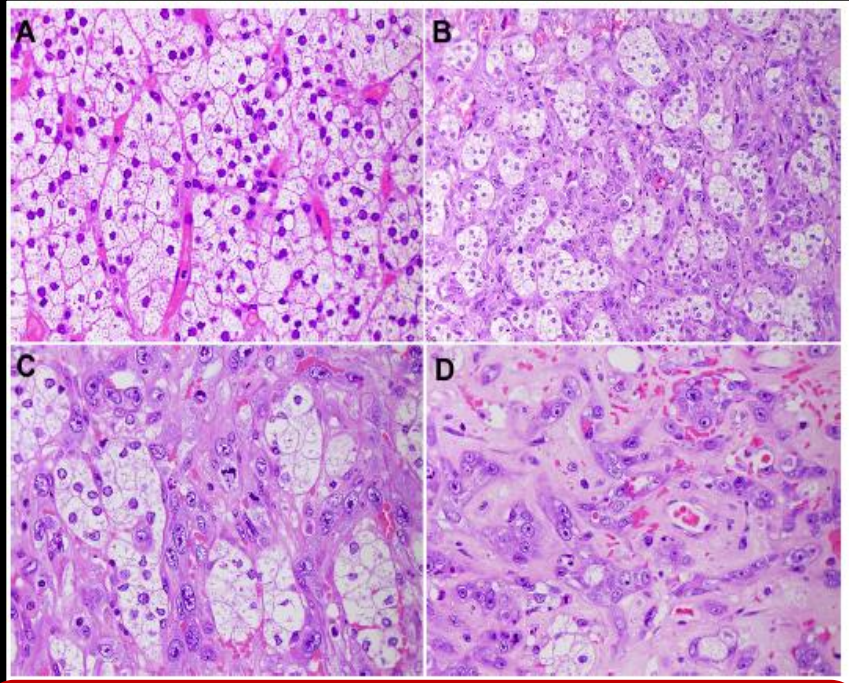
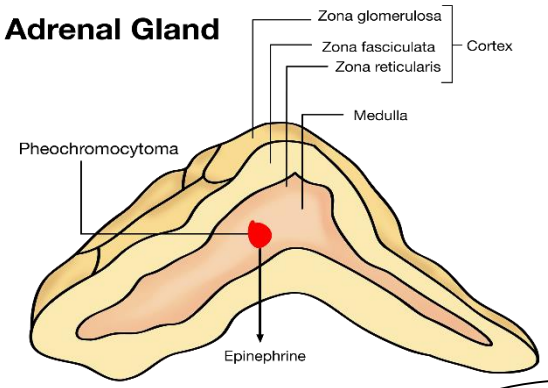
Published online: 23 September 2014



[2, 22, 36–39]. An interesting feature of the presented case is the identification of angiosarcoma within an adrenal cortical adenoma. Lepoutre-Lussey et al. reported an adrenocortical adenoma presenting with hypokalemic hypertension in a young man associating with a primary adrenal angiosarcoma [8]. While this phenomenon may represent a possible collision tumor phenomenon [8], one can speculate that the rich vasculature of endocrine lesions creates a favorable milieu for neoplastic transformation. However, the latter still remains unproven. In summary, the presented case should be added to the unusual clinical presentations of vascular lesions of the adrenal gland mimicking a sarcomatoid adrenal cortical carcinoma.



Recent update of endocrine pathology

III) Adrenal tumor

New cor…nors

I) We…a

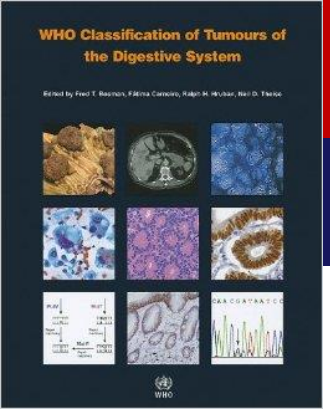
II)Prop…

II) An…

Feed-back for Kagawa University

I) Be careful with the modified Weiss criteria for adrenal cortical carcinoma (ACC)

II) Immunohistochemical panel for ACC and proposal of the new criteria



Recent update of endocrine pathology

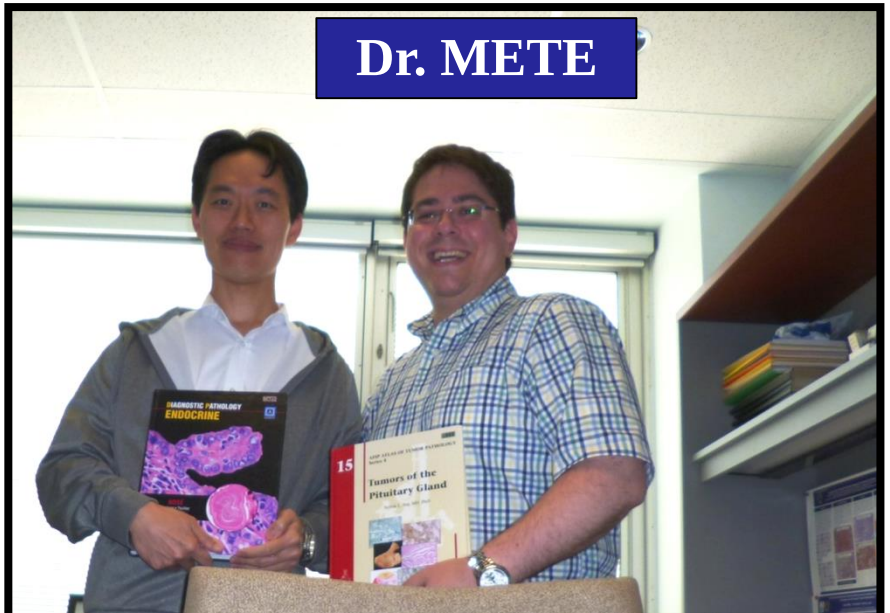
IV) Neuroendocrine tumors (NET)

New concepts and approach for NET and paraganglioma (PGL)

I) New WHO classification of GEPNET (2010)

II) All NETs are potentially malignant

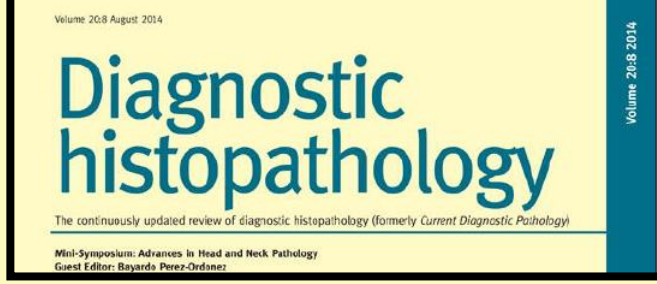
III) Diagnostic algorithm of paraganglioma



Beware of NET: Wolf in sheep's clothing

- NETs are **clinically & pathologically heterogeneous.**
- **Functionality** depends on the presence of clinical symptoms. However, **hormone immunohistochemistry can provide important information.**
- Long term follow-up data indicates that all **neuroendocrine tumors are malignant.**
- **Grading** and **Staging** are important factors, and they are still **evolving** in neuroendocrine tumors
  - **Grading:** Ki67: at least 2000 cells, hot spots
    Mitotic count: at least 50 HPF, hot spots
  - **Staging (TNM):** extent of spread of the tumor
- The status of **differentiation** should be present in the report.
- **Rule out paraganglioma** when dealing with a keratin- and transcription factor-negative NET!

Steps in the diagnostic assessment of head and neck paragangliomas



Chromogranin-A (+) and synaptophysin (+)

Tyrosine hydroxylase (–)

Negative for keratins
AE1/AE3, CAM5.2
Negative for transcription factors
TTF-1 (–), PAX8 (–), CDX2 (–)
Negative for some secretory peptides
PTH, monoclonal CEA

No evidence of catecholamine excess

Unusual anatomic locations

The diagnosis of PGL cannot be rendered

Additional studies including ultrastructure, other site-specific transcription factors and hormones are required to better characterize this lesion

Carotid body*

Increased blood and/or urinary catecholamines or their metabolites
*Dopamine/methoxytyramine
*Norepinephrine/normetanephrine
*Epinephrine/metanepinephrine

PGL

Tyrosine hydroxylase (+)

PGL

Loss of SDHB expression

Genetic testing for SDHx genes
SDHD
SDHB
SDHC
SDHA
SDHAF2

Intact SDHB expression

Genetic testing for other genes associated with inherited disease

Ref: Hayashi T. et al, Diagnostic histopathology Vol 20:8 Aug 2004 (Review)

Practice points

- The possibility of a paraganglioma should be questioned when dealing with a keratin- and transcription factor-negative neuroendocrine tumor.
- The diagnosis of paraganglioma should be confirmed with positivity for tyrosine hydroxylase, especially in unusual localizations.
- Positivity for chromogranin-A and tyrosine hydroxylase is usually weaker and more variable in parasympathetic than in sympathetic paragangliomas and can sometimes be negative especially in carotid body paragangliomas.
- The identification of S100-positive sustentacular network is often linked to paragangliomas; however, this finding can also be seen in other neuroendocrine neoplasms.
- At least 30–40% of paragangliomas are associated with inherited disease.
- The bulk of hereditary disease in the head and neck paraganglioma is associated with *SDHD*, *SDHC*, *SDHB*, and *SDHAF2* mutations.
- Loss of SDHB expression is regarded as a surrogate marker for inherited paraganglioma syndromes caused by any *SDH* mutation.
- Malignancy of paragangliomas is determined by the presence of metastases to sites where paraganglial tissue is not formally found.
- Genotype-biochemical phenotype correlation exists in paragangliomas, and predicts the likelihood of metastasis.
- The optimal clinical management of head and neck paragangliomas depends on their location, extent and genotype–phenotype correlation.

Head and neck paragangliomas: what does the pathologist need to know?

Toshitetsu Hayashi

Ozgur Mete

Abstract

Paragangliomas can occur in a variety of anatomic locations in the head and neck region and can create diagnostic challenges for practicing pathologists. The most recent data suggest that at least 30–40% of paragangliomas are associated with inherited disease. Occasional VHL-, TMEM127-, and SDHA-related head and neck paragangliomas have been described; however, the bulk of hereditary disease in the head and neck paraganglioma is associated with *SDHD*, *SDHC*, *SDHB*, and *SDHAF2* mutations. While the distinction of paragangliomas from other head and neck neoplasms is very important, the clinical responsibility of surgical pathologists has evolved and also includes the integration of SDHB immunohistochemistry into the routine pathology practice. In this article, we highlight an approach to clinicopathological diagnosis of head and neck paragangliomas along with a comprehensive discussion on genotype–biochemical profile correlation and synoptic report approach in paragangliomas.

Keywords catecholamines; genotype–phenotype correlation; paragangliomas; succinate dehydrogenase; synoptic report; tyrosine hydroxylase

Introduction

Head and neck paragangliomas (PGLs) are neuroendocrine neoplasms arising from chief cells of the paraganglia.[1] These neoplasms account for approximately 3% of all PGLs.[2] Head and neck PGLs often present with a slow-growing painless mass in middle-aged adults.[3] PGLs can occur in a variety of anatomic locations in the head and neck regions; however, the most common sites are the carotid bodies. Less frequently these neoplasms can originate from the skull base and temporal bone regions along the length of the vagus nerve, sellar region, pineal gland, cerebellum, sinonasal cavities, nasopharynx, along proximal cervical branches of the aorta, larynx, trachea, cervical esophagus, thyroid, parathyroid, orbit, external ear, tongue, and skin.[2,4–19] The most recent data suggest that at least 30–40% of PGLs are associated with inherited disease.[20–28] Patients with inherited disease often present at younger ages and are more likely to have multifocal disease including pheochromocytomas arising from intra-adrenal sympathetic paraganglia. In this review, we discuss the clinical, biochemical, radiological, morphological, and molecular features of the head and neck PGLs to highlight the timely topics in this field by emphasizing the role of pathologist in the management of these neoplasms.

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Ozgur Mete MD *Consultant Endocrine Pathologist, Department of Pathology, University Health Network, Toronto, Ontario, Canada; Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada; Endocrine Oncology Site Group, Princess Margaret Cancer Centre, Toronto, Ontario, Canada. Conflict of interest: none declared.*

The normal paraganglia

In order to better understand the clinicopathological features of head and neck paragangliomas, one has to know the basic characteristics of the normal paraganglia.

Clinical anatomy

Head and neck paraganglia is typically seen in close association with vascular structures, ganglia and nerve branches of the autonomic nervous system, especially along the cranial and thoracic branches of the glossopharyngeal and vagus nerves.[29] With the exception of the carotid bodies, head and neck paraganglia are highly variable in both number and location.[29,30] Four major parasympathetic paraganglia have been defined in the head and neck region as follows: (a) carotid body paraganglia, (b) jugulotympanic paraganglia, (c) vagal paraganglia, and (d) laryngeal paraganglia.[29] In fact, PGLs arising from these four paraganglia refer to general locations, rather than to specific anatomic structures.[29,31] Occasionally PGLs can also occur in sites other than these four anatomic structures including paravertebral cervical sympathetic ganglia.[29] Tympanic PGLs arise from dispersed paraganglia along the tympanic nerve (also known Jacobson' nerve, a branch of the glossopharyngeal nerve) in the middle ear cavity; whereas jugular PGLs arise from anatomically dispersed paraganglia near the base of the skull and lateral temporal bone.[29,31] Vagal PGLs collectively encompass PGLs arising from multiple dispersed paraganglia located within or adjacent to the vagus nerve, especially at the level or just below the lower border to the ganglion nodosum.[29] On the other hand, laryngeal PGLs arise from either superior or inferior components of multiple dispersed paraganglia located near the larynx, in relation to the cricoid and thyroid cartilages.[11,29] For example, thyroid and laryngeal PGLs are linked to disperse elements of laryngeal paraganglia.[11,14,29] Of note, rare PGLs arising from orbit, pituitary gland, pineal gland, cerebellum, sinonasal cavity, nasopharynx, along proximal cervical branches of the aorta, trachea, cervical esophagus, thyroid, parathyroid, external ear, tongue, and skin have also been described justifying the wide spectrum of PGLs arising from miscellaneous paraganglia of the head and neck region.[2,4–19]

Functional histology

The paraganglia are of neuroectodermal origin, and are found among or near the components of the autonomous nervous system.[29,30] Even at the earliest developmental stage, primitive precursor cells that will be differentiating into neural, glial, and neuroendocrine cells have the ability to produce catecholamines.

FOCUS ON
NEUROENDOCRINE TUMORS

Recent update of Endocrine Pathology

Practical points

1. Neuroendocrine neoplasms: peculiar tumors with precursor lesions, genetic background and familiar syndromes.

2. Biochemical, clinical and morphological correlation is mandatory for an appropriate diagnosis.

3. Long term following data suggest that all NETs are malignant.

4. Beware and rule out paraganglioma when dealing with cytokeratin and transcription factor negative NET.

A happy ending of my 1 year Canadian program and…

Short-term follow up

My adventure continues and……..

October 6, 2014 **03:00-05:30 PM**

Session code: SY04-2

Symposium: Vascular Pathology

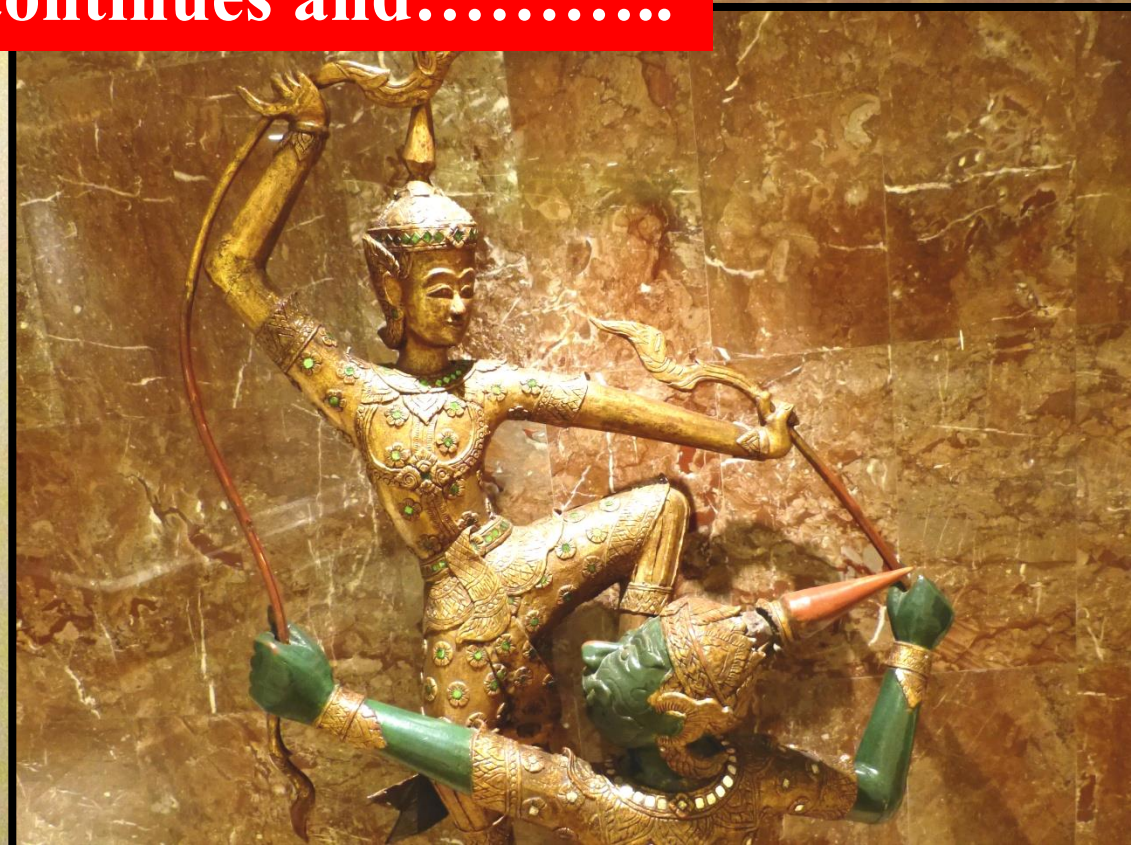
Room: Lotus Suite 3

Moderator: Jagdish Butany
University of Toronto, University Health Network, Toronto, ON, Canada

Speakers: Jagdish Butany
University of Toronto, University Health Network, Toronto, ON, Canada

Pradeep Vaideeswar
Seth GS Medical College, Mumbai, Maharashtra, India

Toshitetsu Hayashi
Department of Diagnostic Pathology, Faculty of Medicine, Kagawa University, Kagawa, Japan



第３回

日本甲状腺病理学会総会・学術集会

IN HAMANAKO

Work hard and play hard!

一般演題2　15：45-16：40　（座長 隈病院 廣川 満良）

9. 肺高血圧症患者剖検例における甲状腺腫大　杏林大学 千葉 知宏

10. 甲状腺濾胞性病変におけるNras Q61Rの免疫組織化学的同定　山梨大学 大石 直輝

11. A comparative study of the carcinomas of the thyroid with predominant squamous differentiation and othe squamous lesions of the thyroid　高松赤十字病院 林 俊哲

Guided visit tour of Takamatsu Red Cross Hospital

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アプリ

For further details please visit our homepage

カナダからの留学報告

香川大学医学部附属病院病理診断科・病理部　林　俊哲

平成20年より香川大学医学部附属病院病理診断科・病理部に入局致しました林俊哲と申します。入局から約4年が経過しましたが、その間に病理専門医と細胞診専門医の資格を取得し、平成24年8月よりカナダのトロント大学/University Health Network(UHN)に臨床留学をしています。以下、留学中の研究活動と生活環境について記載しますが、この内容がこれから入局を希望される先生方や、臨床留学を希望される方に、何かご参考になれば幸いです。

私は現在、カナダのオンタリオ州（Province of Ontario）のトロント（City of Toronto）に所在するトロント大学/UHNの病理部神経内分泌診断部門に留学しておりま

ントは、都市圏に約600万人の人口を抱え、北米では

goに次ぐ4番目の大都市となっています。また、トロン

々な人種・国籍の人々が共存する国際都市でもありま

並ぶ北米経済の中心地でありますが、観光名所としても

イギリス風の建造物も散見されます。

大学で、世界的にも評価が非常に高い大学です。私が所

院病理診断科・病理部の業務の中心は病理診断であり、

、特に神経内分泌病理を専門分野として専攻していきた

病理研究の世界的権威であるトロント大学病理部門の

Thanks for your kind attention

"Boys, be ambitious! Be ambitious not for money or for selfish aggrandizement, not for that evanescent thing which men call fame. Be ambitious for the attainment of all that a man ought to be."