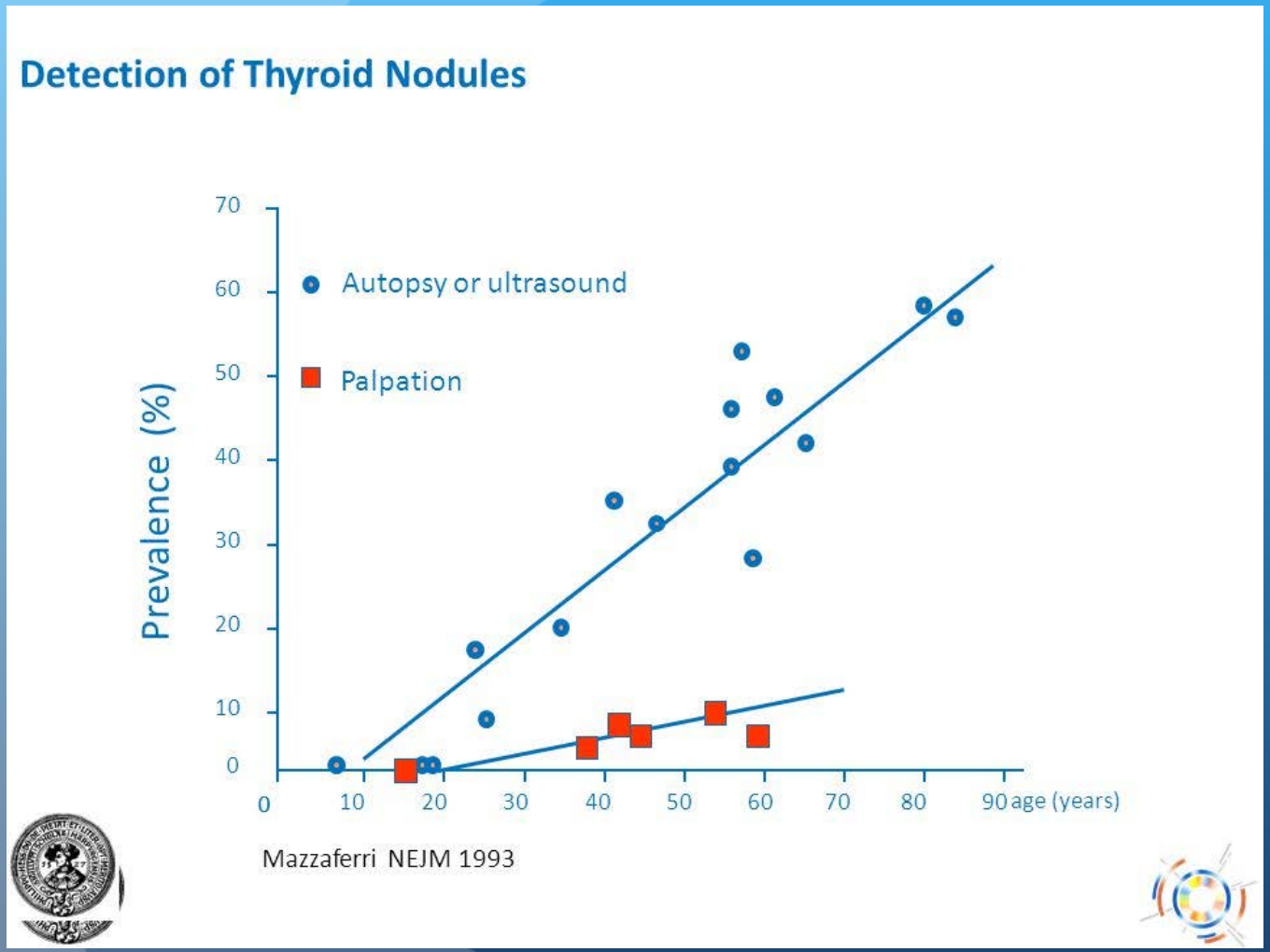
Update in Thyroid Nodules/Cancer

Amanda La Greca, MD, ECNU
Assistant Professor
Endocrinology, Diabetes and Metabolism
Colorado University

Objectives:

- Review diagnostic approach of thyroid nodules
- Discuss current guidelines for UGFNA of thyroid nodules
- Review basics of thyroid cancer diagnosis, management and follow-up
- Highlight the most recent guidelines for the management of thyroid nodules and differentiated thyroid carcinoma (ATA 2015)

How common are nodules?



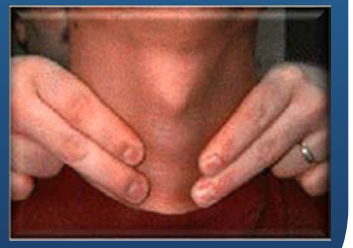
Single thyroid nodules

- Palpable in about 5% of women and 1% of men
- Usually due to benign nodular hyperplasia or thyroid adenomas
- 5% are thyroid carcinomas – the main diagnostic task is diagnosing or excluding thyroid carcinoma

Clinical Presentation

Most thyroid nodules are now diagnosed by imaging tests like CT scans or neck ultrasound done for completely unrelated reasons

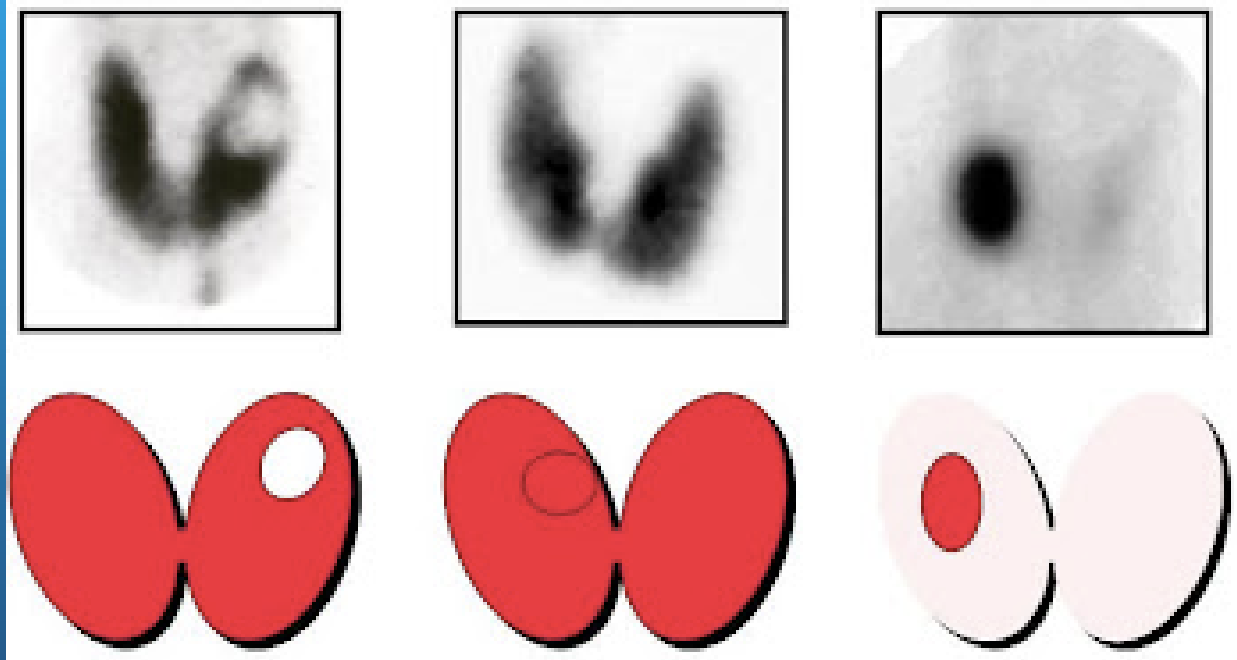
Often present as a painless lump in the neck discovered by the patient or physician



Diagnostic testing

- First test that should be ordered is serum thyrotropin (TSH)
  - IF serum TSH is suppressed – order a radionuclide thyroid scan - A nodule in a hyperthyroid patient is likely to be benign
  - If the TSH is normal or elevated - A radionuclide scan should NOT be performed

Figure 7. Potential Radionuclide Scan Findings in Individuals with a Thyroid Nodule



Thyroid ultrasound

Thyroid sonography should be performed in ALL patients with known or suspected thyroid nodules

ATA guidelines, Haugen el al, Thyroid, 2015

- Is the palpable abnormality a thyroid nodule?
- Are other nodules present?
- Size?
- Suspicious features?
- > 50% cystic?
- Associated abnormal lymph nodes?

The Good Old Days

FNA indicated
Most palpable nodules
Clinically/biochemically euthyroid

Most were benign
Did identify clinically significant thyroid cancer

Neck Ultrasonography
An epidemic of thyroid nodules

Majority are benign
Did identify clinically significant thyroid cancer
Also identified a huge pool of very small thyroid cancers

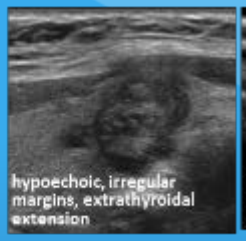
Which nodules need FNA??

Epidemic of Nodules

- Can no longer FNA all nodules > 1 cm
- Current ATA, AACE and Korean guidelines rely on recognition of sonographic features of low-risk and high-risk thyroid nodules

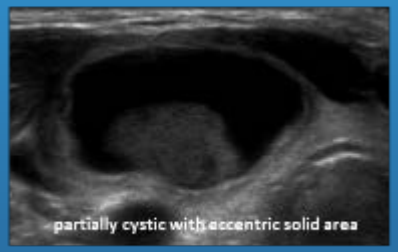
ATA Nodule Sonographic Pattern Risk of Malignancy

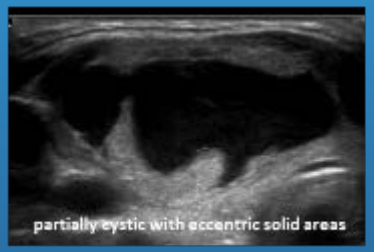
High Suspicion 70-90%



Intermediate Suspicion 10-20%

Low Suspicion 5-10%





Very low Suspicion <3%

Benign <1%

Risk of malignancy

Haugen et al, ATA 2015 Guidelines

Bethesda System for reporting thyroid cytopathology

Diagnostic category	Description	Risk of malignancy (%)
I	Non-diagnostic/unsatisfactory	1–4
II	Benign	0–3
III	Atypia or follicular lesion of undetermined significance	5–15
IV	Follicular neoplasm or suspicious for follicular neoplasm	15–30
V	Suspicious for malignancy	60–75
VI	Malignant	97–99

Source: Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. J Am Soc Cytopathol. 2017;6:217–222. https://doi.org/10.1016/j.jasc.2017.09.002

Molecular testing

- For nodules with indeterminate cytology:
  - Repeat FNA or
  - Molecular testing to supplement risk of malignancy
  - Surveillance or diagnostic surgical excision – usually lobectomy

Molecular testing

Preoperative molecular markers in patients with indeterminate FNA cytology :

- New tests that examine genes in the DNA of thyroid nodules
- Several companies: Afirma, Thyroseq, ThyGenX
- No single optimal molecular test that can definitely rule in or rule out malignancy in all cases of indeterminate cytology, long-term outcome data needed - ATA

Evaluation of multiple thyroid nodules:

- Patients with multiple thyroid nodules ≥ 1 cm should be evaluated in the same fashion as patients with a solitary nodule ≥ 1 cm (each nodule that is > 1 cm carries an independent risk of malignancy and therefore multiple nodules may require FNA).

- In patient with low or low-normal TSH – FNA should be considered only for the nonfunctioning nodules

What is our goal?

To diagnose every thyroid cancer?

To diagnose clinically significant thyroid cancer?

Does very early detection of thyroid cancer lead to improved outcomes?

Moving toward a more individualized management approach

The last 10-15 years

"Traditional Paradigm"
One Size Fits All
Total thyroidectomy
RAI remnant ablation
All with same follow up

"Risk Adapted Paradigm"
Management recommendations based individualized risk assessment

Why the change?

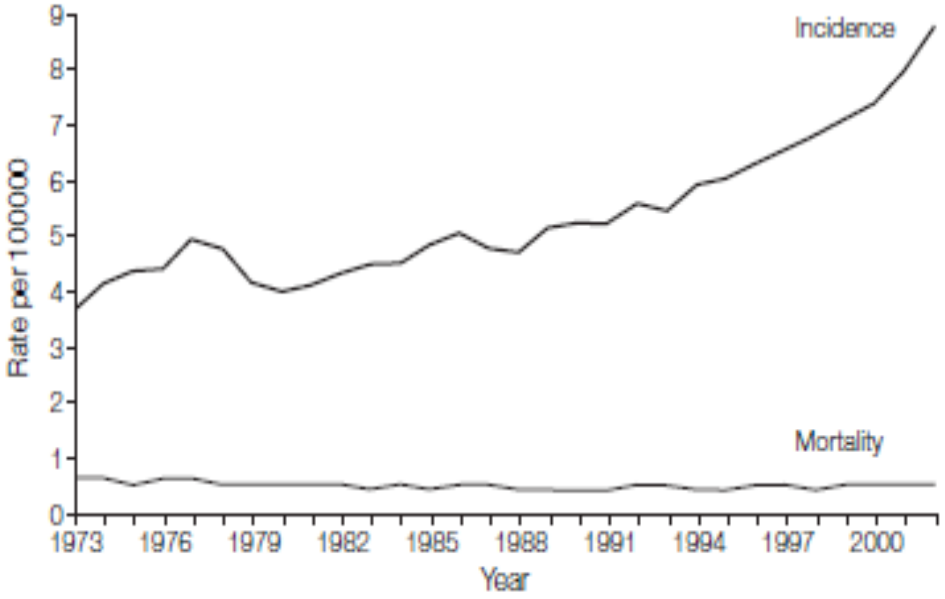
In the past, disease was detected by symptoms and physical examination (large volume)

Today, marked shift to diagnosing small volume thyroid cancers with/without microscopic lymph node mets

Thyroid Cancer

The rising incidence of thyroid cancer

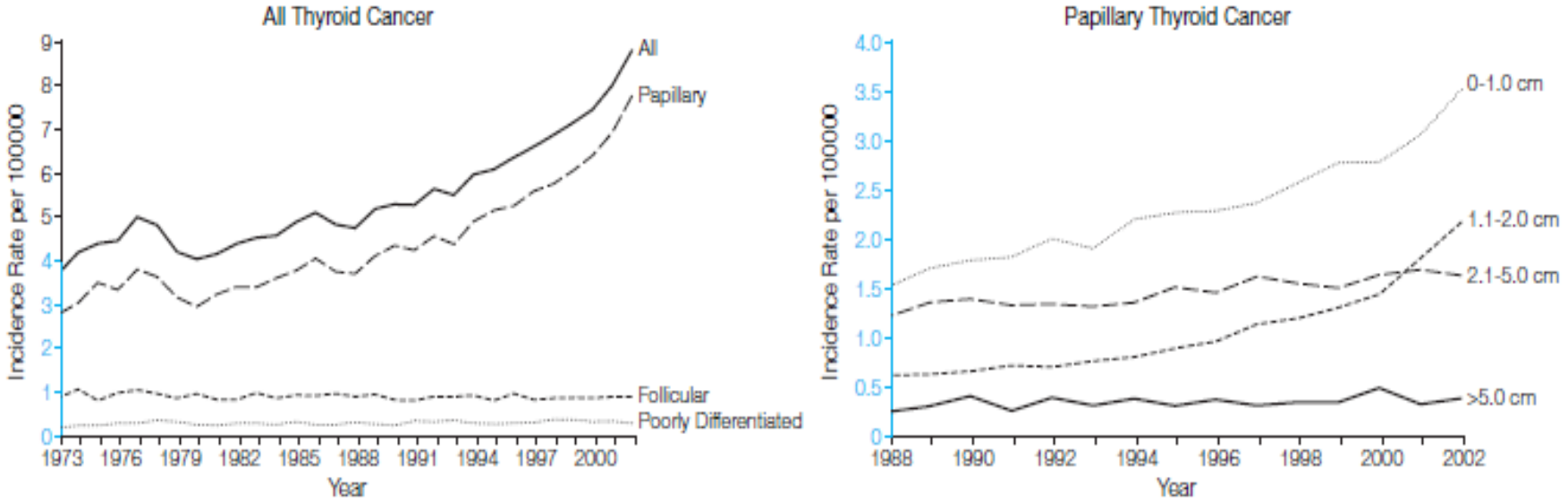
Figure 2. Thyroid Cancer Incidence and Mortality, 1973-2002



Davies, Welch. JAMA. 2006;295:2164-2167

INCREASING INCIDENCE OF THYROID CANCER IN THE UNITED STATES, 1973-2002

Figure 1. Trends in Incidence of Thyroid Cancer (1973-2002) and Papillary Tumors by Size (1988-2002) in the United States



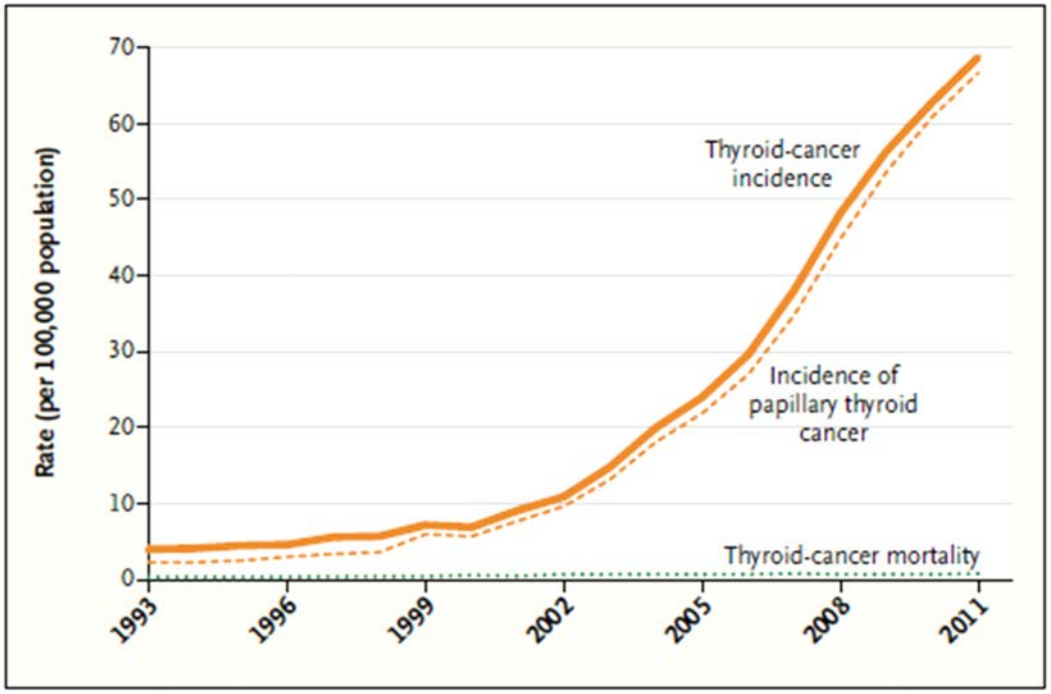
87% of the increase is due to primary tumors < 2cm
49% of the increase is due to primary tumors < 1 cm

Davies, Welch. JAMA. 2006;295:2164-2167

Korea's Thyroid-Cancer "Epidemic" — Screening and Overdiagnosis

New Eng J Med 2014

Hyeong Sik Ahn, M.D., Ph.D., Hyun Jung Kim, M.P.H., Ph.D., and H. Gilbert Welch, M.D., M.P.H.



Thyroid-Cancer Incidence and Related Mortality in South Korea, 1993–2011.

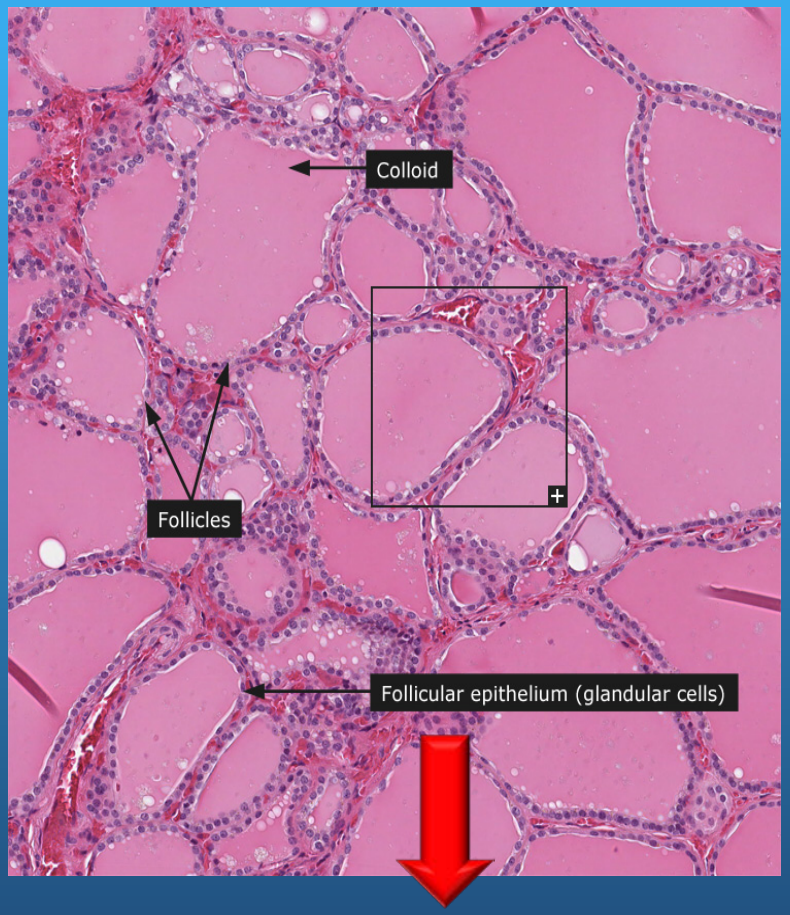
Data on incidence are from the Cancer Incidence Database, Korean Central Cancer Registry; data on mortality are from the Cause of Death Database, Statistics Korea. All data are age-adjusted to the South Korean standard population.

Thyroid cancer is now the most commonly diagnosed cancer in Korea (2014)

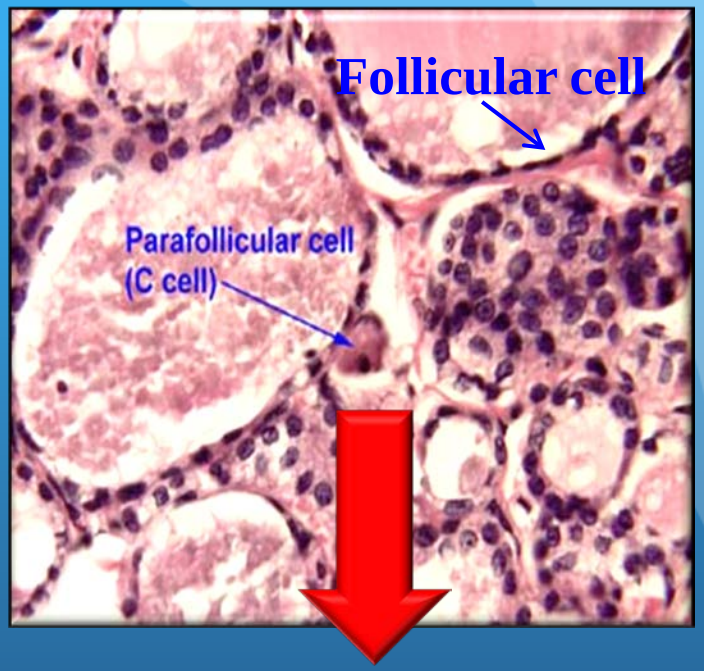
Clinical Presentation

- Thyroid cancer usually presents as an asymptomatic thyroid nodule
- Not painful or tender
- It does not cause hyperthyroidism or hypothyroidism
- Diagnostic procedure of choice: Fine Needle Aspiration Biopsy

Thyroid Gland



Papillary thyroid cancer
Follicular thyroid cancer
Anaplastic thyroid cancer



Medullary thyroid cancer

Medullary Thyroid Cancer

- Arises from C cells (parafollicular cells)
- Plasma Calcitonin and CEA are elevated and useful for the diagnosis
- Most cases are sporadic. However, MTC is a component of MEN2A and 2B as well as familial MTC syndrome, which are all caused by mutations of different regions of the RET proto-oncogene.

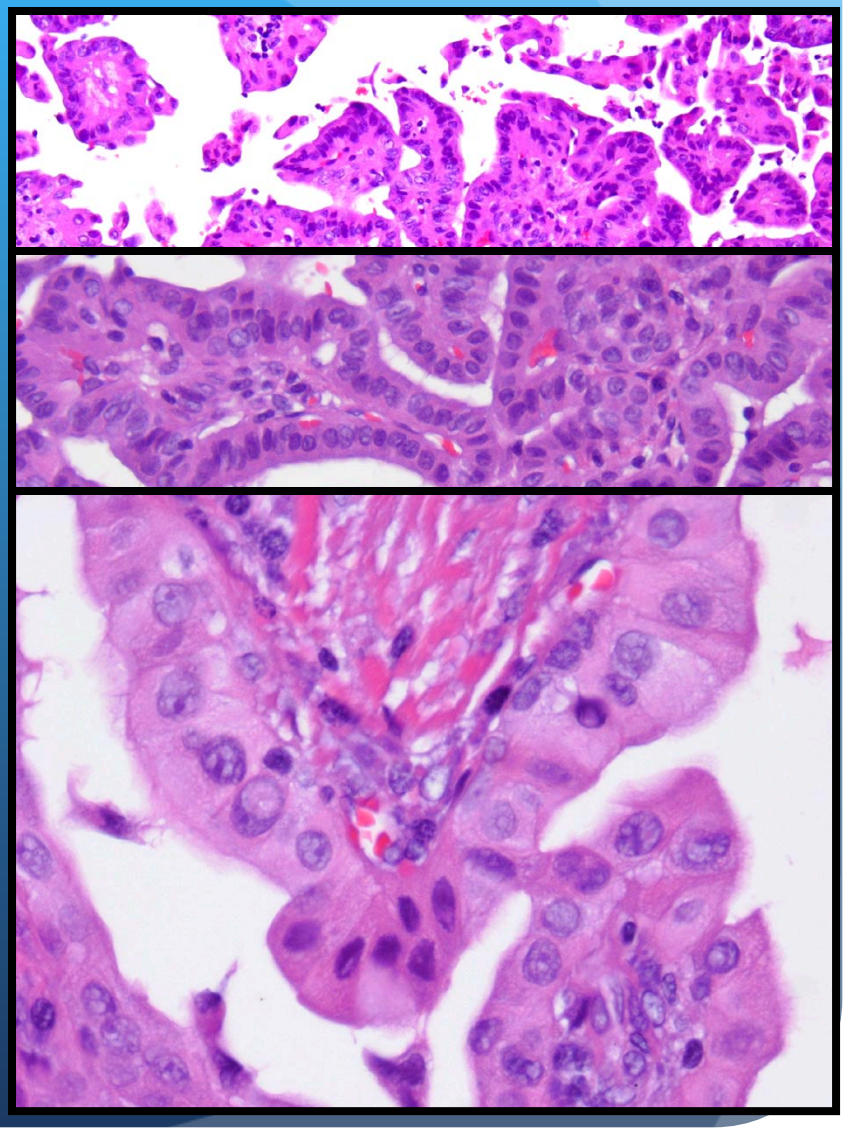
Medullary Thyroid Cancer

Treatment:

- Total thyroidectomy. If advanced, EBRT and systemic therapy
- Genetic testing for RET mutation
- Plasma Calcitonin and CEA – used to monitor patients for recurrence
- Levothyroxine – keep TSH level normal
- RAI is NOT useful

Papillary Thyroid Cancer

- Arise from follicular cells
- 80% of all thyroid carcinomas
- Females out number males 2:1
- Median age at Dx: 30-40 yrs
- Frequent LN mets
- Retain many properties of normal thyroid cells
  - Take up iodine
  - Synthesize Thyroglobulin
  - Their grow and function is stimulated by TSH



Follicular Thyroid Carcinoma

- 15% of thyroid cancers
- More aggressive than papillary thyroid carcinoma, can metastasize early to lungs and bone
- Usually does not metastasize to cervical lymph nodes

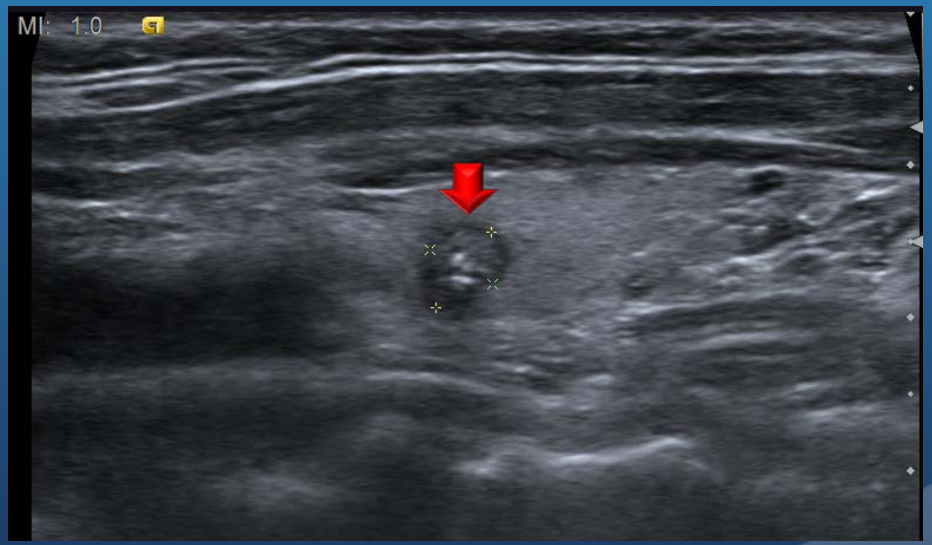
Treatment of Papillary and Follicular Thyroid Carcinoma

- Partial/Total thyroidectomy
- Radioactive iodine – when TSH is elevated
  - Thyroid remnant ablation/treatment
- Levothyroxine to suppress plasma TSH (to inhibit growth of residual tumor cells) – suppression only on high risk thyroid cancer!
- Lifelong monitoring with plasma Thyroglobulin and neck ultrasounds

Case Example

75 year old male

- Asymptomatic
- Normal thyroid function test
- US for carotid artery evaluation
  - Normal carotid
  - 6 mm thyroid nodule with very suspicious features



[A14] Malignant Cytology

- **RECOMMENDATION**

A cytology diagnostic for a primary thyroid malignancy will almost always lead to thyroid surgery. However, an active surveillance management approach can be considered as an alternative to immediate surgery in:

(a) Very low risk tumors (e.g. papillary microcarcinomas without clinically evident metastases or local invasion)

(b) High surgical risk because of co-morbid conditions,

(c) Relatively short life span (e.g. serious cardiopulmonary disease, other malignancies, very advanced age), or

(d) Concurrent medical or surgical issues that need to be addressed prior to thyroid surgery.

Haugen et al, Thyroid 2015

Thank you

Questions?

amanda.lagreca@cuanschutz.edu