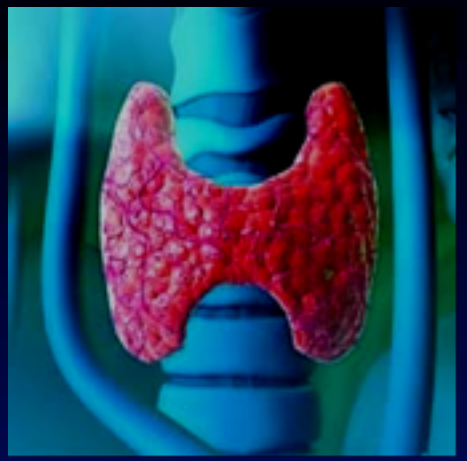
Thyroid Cancer Risk and Management

Joyce Shin, MD, FACS
Surgical Director, Thyroid Center
Department of Endocrine Surgery

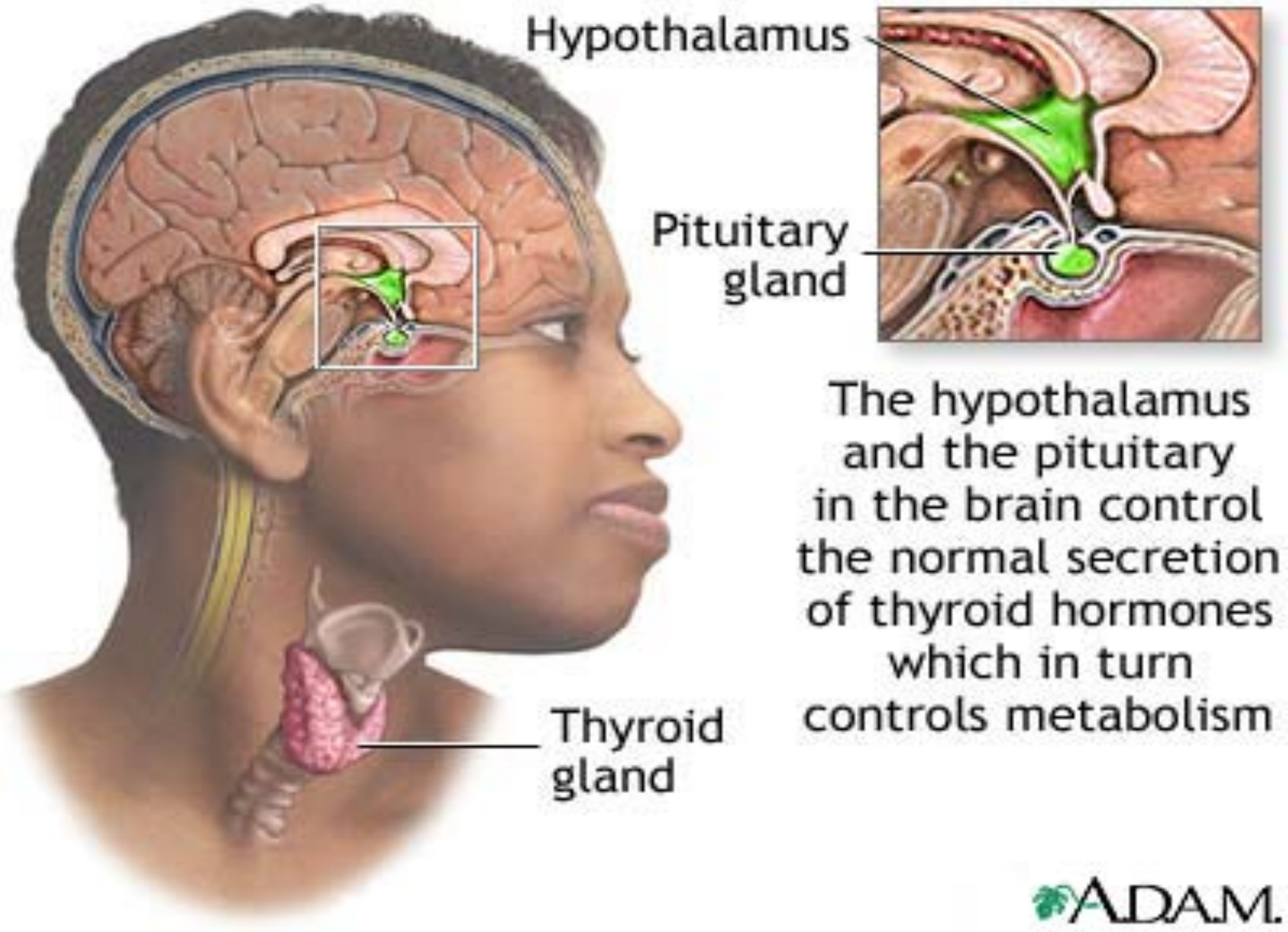
Cleveland Clinic

Outline



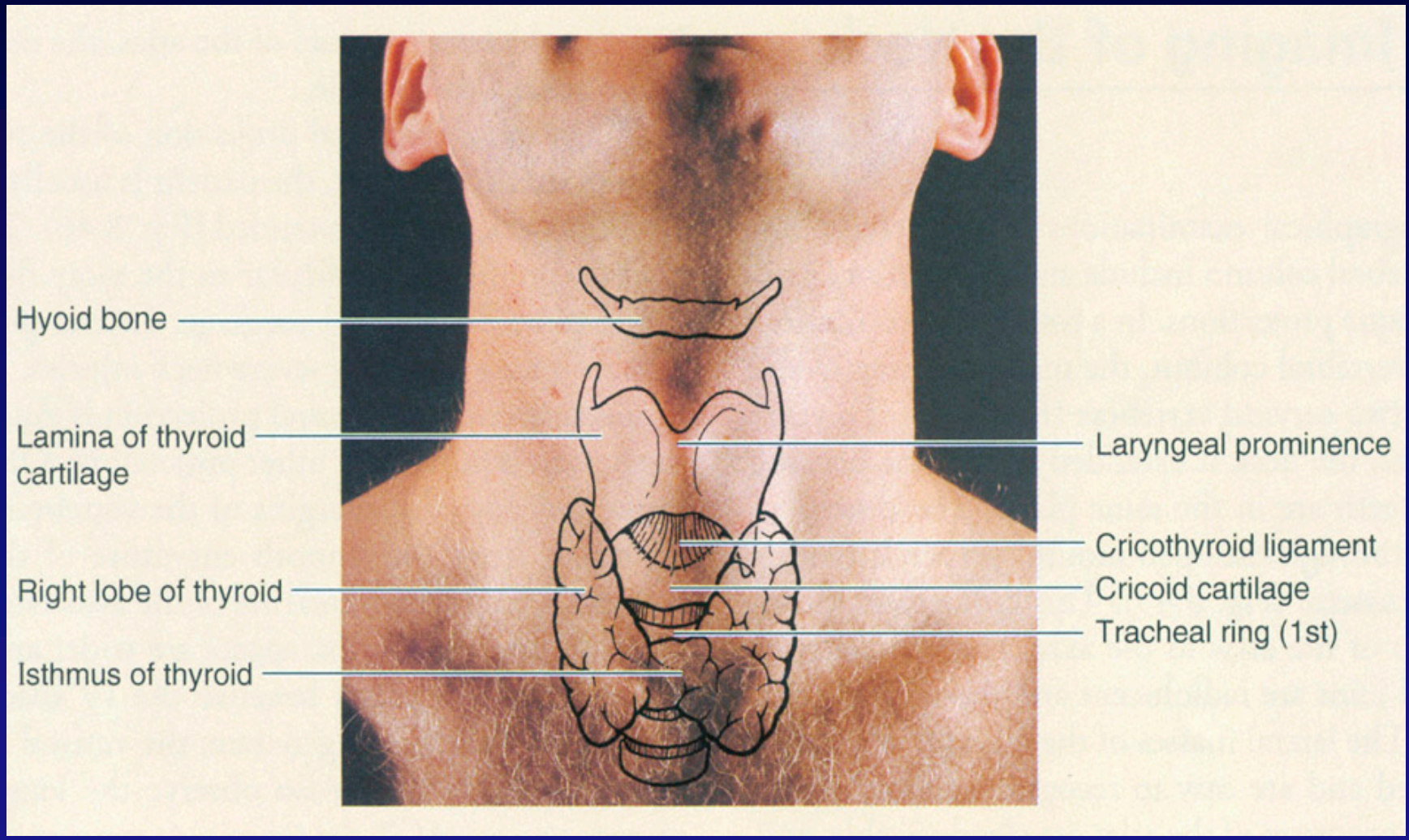
- Overview of the thyroid gland
- Thyroid nodules and cancer in 2017
- Thyroid disease in context of Cowden Syndrome
- Thyroid nodule/cancer management

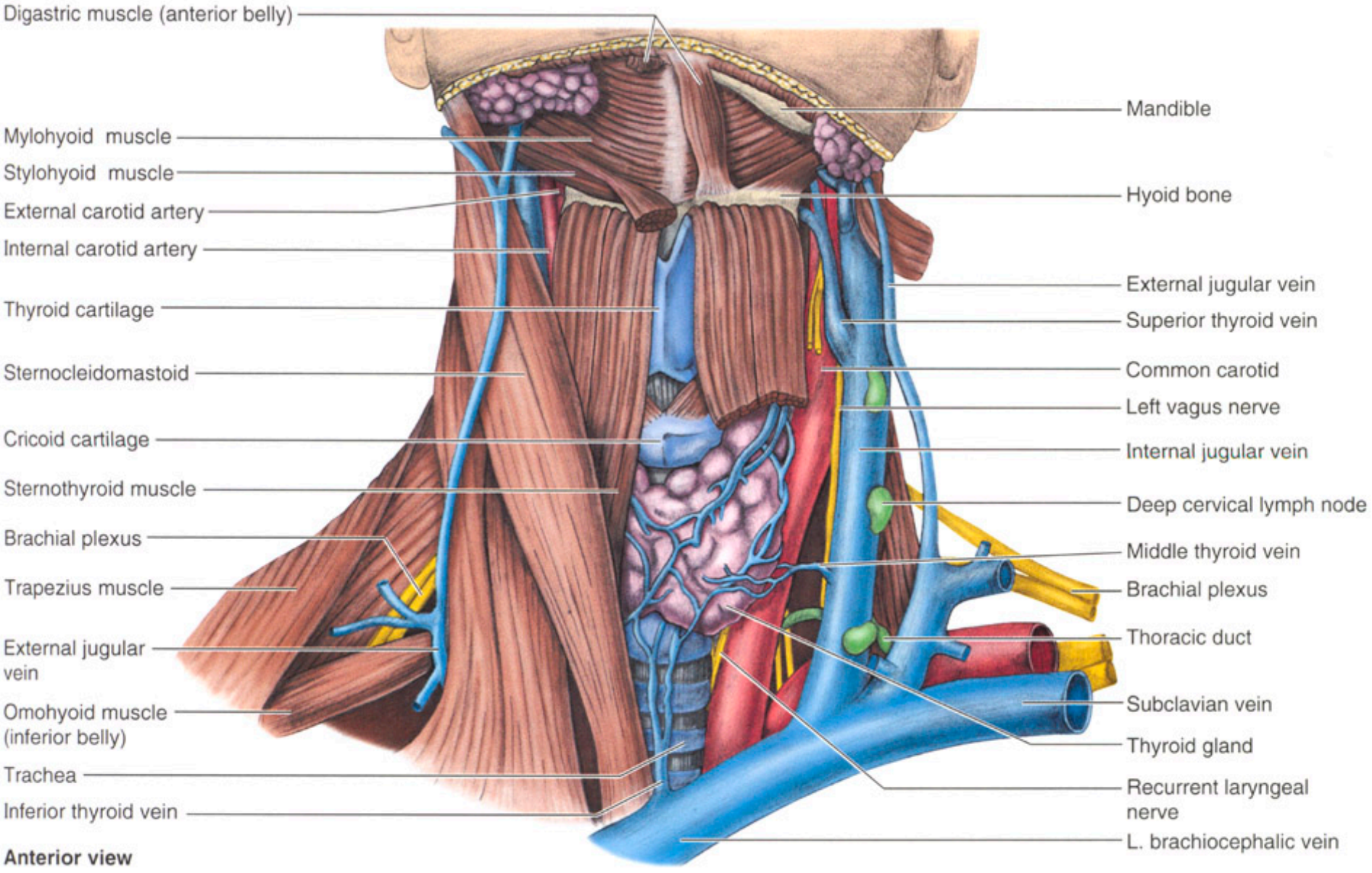
What is the Thyroid Gland?



The hypothalamus and the pituitary in the brain control the normal secretion of thyroid hormones which in turn controls metabolism

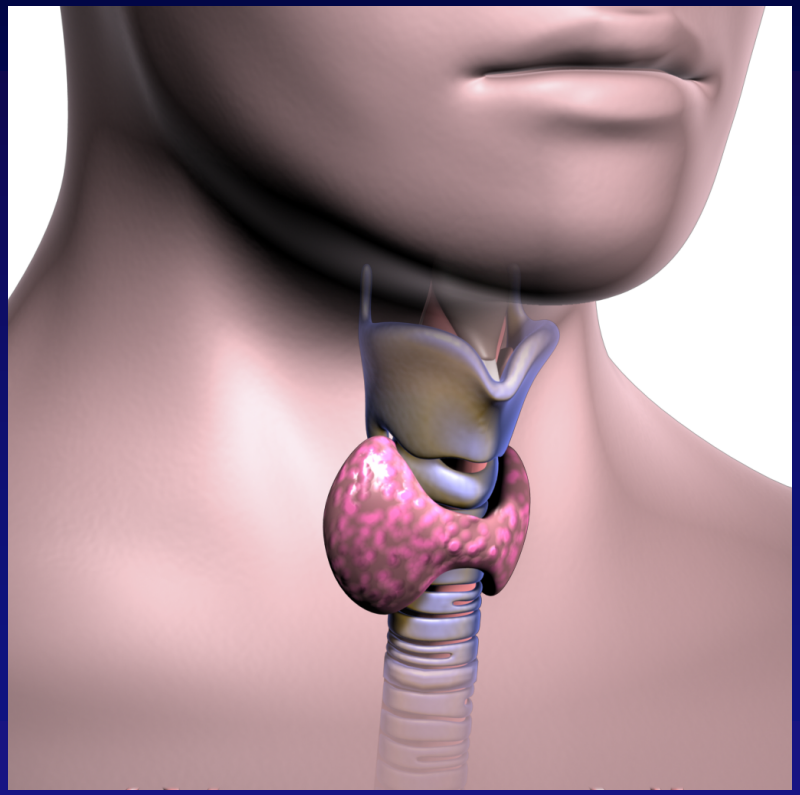
Where is the Thyroid Gland?





Anterior view

Thyroid Nodules/Cancer



- 25-87% prevalence
- Women > Men
- 5% detected on palpation
- 5-15% risk of malignancy
- 56,870 new cases of thyroid cancer (3.4% of all new cancer cases)
- 2,010 deaths from thyroid cancer (0.3% of all cancer deaths)

Cowden Syndrome (CS)

- Characterized by benign hamartomas
- Increased risk of malignant transformation

- Dominantly inherited germline mutation
  - tumor suppressor *PTEN*
  - *PTEN* mut+ is ultimate diagnostic confirmation

International Cowden Consortium (ICC) Operational Criteria for Diagnosis

Pathognomonic	Major	Minor
Mucocutaneous lesions	Breast cancer	Fibrocystic breast disease
Trichilemmomas	Endometrial cancer	Mental retardation
Acral keratoses	Thyroid cancer	Benign thyroid lesions
Papillomas	Macrocephaly	GI hamartomas
Mucosal lesions		Lipomas
Adult Lhermitte-Duclos disease		Fibromas
		GU tumors or malformation
		Renal cell carcinoma
		Uterine fibroids

PTEN mut+ have AV malformations

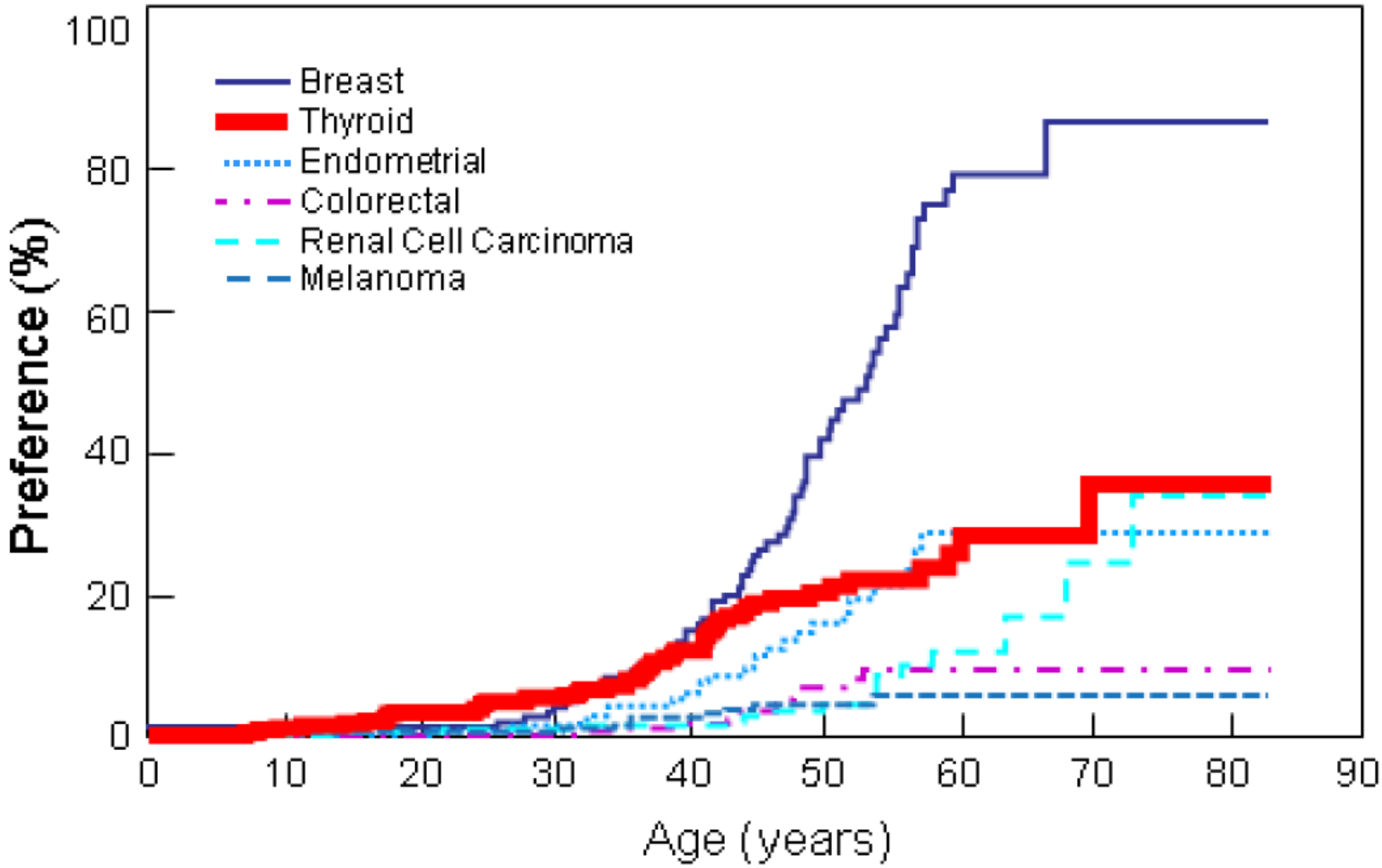
Eng *et al* *J Med Genet* 2000;37:828-30

International Cowden Consortium (ICC) Operational Criteria for Diagnosis

Pathognomonic	Major	Minor
Mucocutaneous lesions	Breast cancer	Fibrocystic breast disease
Trichilemmomas	Endometrial cancer	Mental retardation
Acral keratoses	Thyroid cancer	Benign thyroid lesions
Papillomas	Macrocephaly	GI hamartomas
Mucosal lesions		Lipomas
Adult Lhermitte-Duclos disease		Fibromas
		GU tumors or malformation
		Renal cell carcinoma
		Uterine fibroids

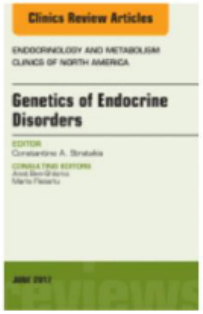
- **2 Major but one must be macrocephaly or LDD**
- **1 Major + 3 Minor**
- **4 Minor**

Of CS-associated cancers, thyroid cancer has the earliest onset and 2nd highest lifetime risk (35%)



Tan et al *Clin Cancer Res* 2012; study population was *PTEN* mut+

Clinical Implications for Germline *PTEN* Spectrum Disorders



Endocrinology and Metabolism Clinics

Volume 46, Issue 2

2017-5-31, Pages I-592

New Issue Alerts: Subscribe

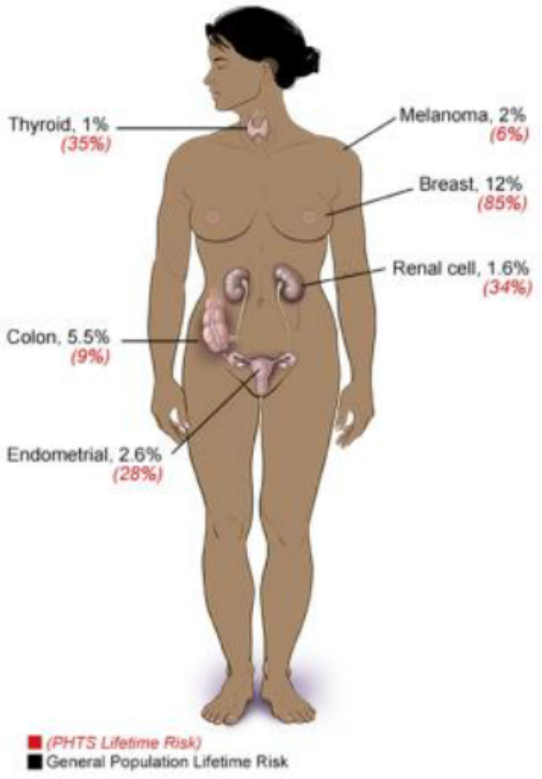
Joanne Ngeow, MBBS, MRCP, MPH[a,b], Kaitlin Sesock, MSc[b,c,d], Charis Eng, MD, PhD[b,c,d,e,f,*]

Table 2
Cancer risks and screening recommendations for *PTEN* hamartoma tumor syndrome

Cancer	General Population Risk (%)	Lifetime Risk with *PTEN* Hamartoma Tumor Syndrome (%)	Age at Presentation	Screening Recommendations
Breast	12	~85	40s	Starting at age 30 Annual mammogram Consider MRI for patients with dense breasts
Thyroid	1	35	30s–40s	Baseline ultrasound examination at diagnosis Annual ultrasound and clinical examination
Endometrial	2.6	28	40s–50s	Starting at age 30 Annual endometrial biopsy or transvaginal ultrasound examination
Renal cell	1.6	34	50s	Starting at age 40 Renal imaging every 2 y
Colon	5	9	40s	Starting at age 40 Colonoscopy every 2 y
Melanoma	2	6	40s	Annual dermatologic examination

Data from Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res 2012;18(2):400–7.

Lifetime Risks of Cancer for Patients with PHTS



Should patients with Cowden syndrome undergo prophylactic thyroidectomy?

Mira Milas, MD,[a] Jessica Mester, MS, CGC,[b,c] Rosemarie Metzger, MD, MPH,[d] Joyce Shin, MD,[d] Jamie Mitchell, MD,[d] Eren Berber, MD,[d] Allan E. Siperstein, MD,[d] *and* **Charis Eng, MD, PhD,[b,c,e]**
Portland, OR, and Cleveland, OH

Background. *Cowden syndrome (CS) is dominantly inherited and predisposes patients to tumors in multiple organs. We characterized CS-associated malignant and benign thyroid disease.*
Methods. *Of data from 3,477 prospectively recruited CS patients with known genetic analysis, we analyzed 225 PTEN mutation+ patients whose treatment occurred at our center (n = 25) or other hospitals nationwide (n = 200).*
Results. *A total of 32 of 225 PTEN mutation+ patients (14%) had thyroid cancer: 52% papillary, 28% follicular-variant papillary, 14% follicular, and 6% anaplastic. Median age at diagnosis was 35 years compared with 49 years for Surveillance Epidemiology and End Results population data. Initial thyroid ultrasonography in 16 of 25 patients revealed thyroiditis/goiters in all >13 years age, leading to FNA in 7 (64%), thyroidectomy in 3 (27%), and new cancer diagnosis in 2 (18%). Three with severe autism required intraoperative sedation for ultrasonography. A total of 9 of 25 patients were monitored after multiple partial thyroidectomies for goiters by age 42 (n = 5), thyroiditis, or cancer detected by age 36 (n = 3).*
Conclusion. *PTEN mutation+ patients with CS have an enormous prevalence of thyroid disease. Earlier screening may be advisable because thyroiditis and nodules are seen by the time patients reach adolescence, and cancer diagnosis occurs on average 14 years earlier than expected. Furthermore, the risks observed may justify prophylactic total thyroidectomy in select, if not all, patients, particularly those with developmental disorders. (Surgery 2012;152:1201-10.)*

Should patients with Cowden syndrome undergo prophylactic thyroidectomy?

- Goiter → 60%
- Hashimoto's thyroiditis → 40%
- Thyroiditis and nodules as young as age 12
- Thyroid cancer → 20% of screened; 14% of larger PTEN mut+ population
- Median age of cancer → 35 (in comparison with 49 in general population)

Screening for Thyroid Cancer

- Screen at time of diagnosis, regardless of age
- Physical exam is not reliable to detect thyroid nodules
- Ultrasound is an effective, noninvasive, and inexpensive test

30% of Surgeons in USA perform their own ultrasound

CLINIC

High-frequency
linear
small parts
transducer

FNAB

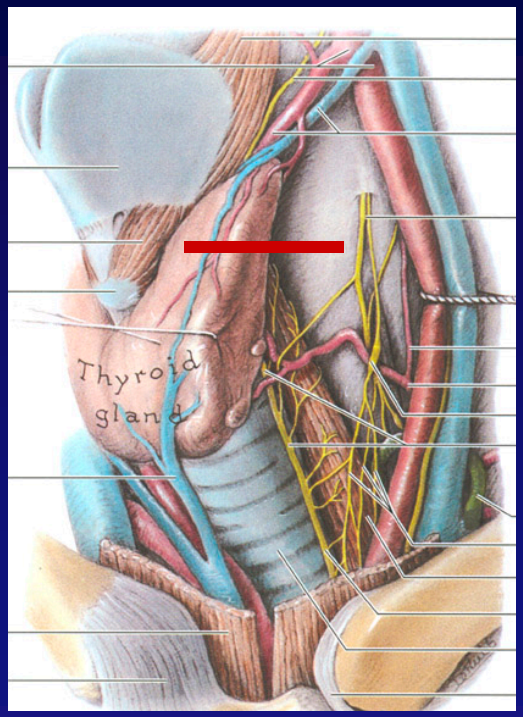
22 gauge needle
>1 cm nodules
atypical appearance
lymph nodes

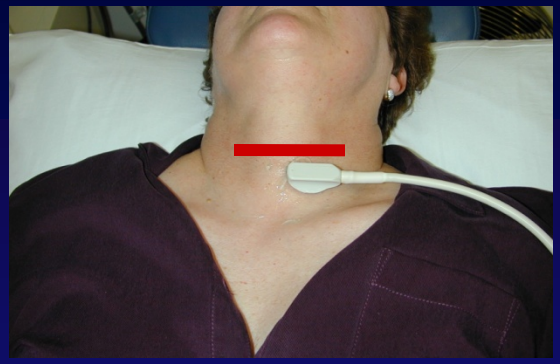
OR

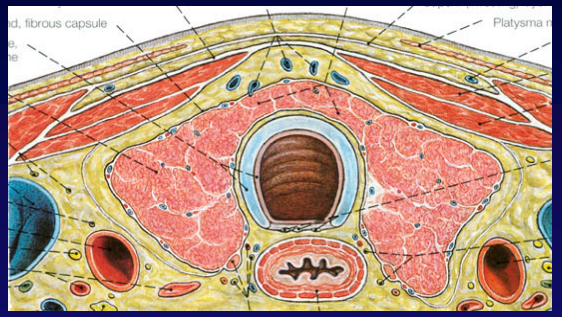
Pre-operative
Intra-operative

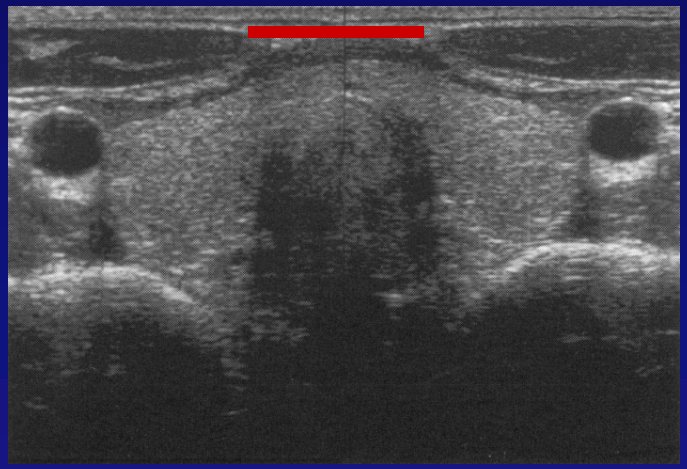
Cleveland Clinic

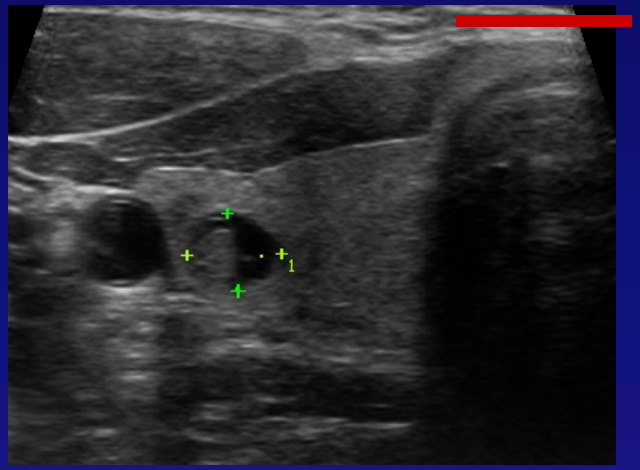
Transverse Views of Thyroid







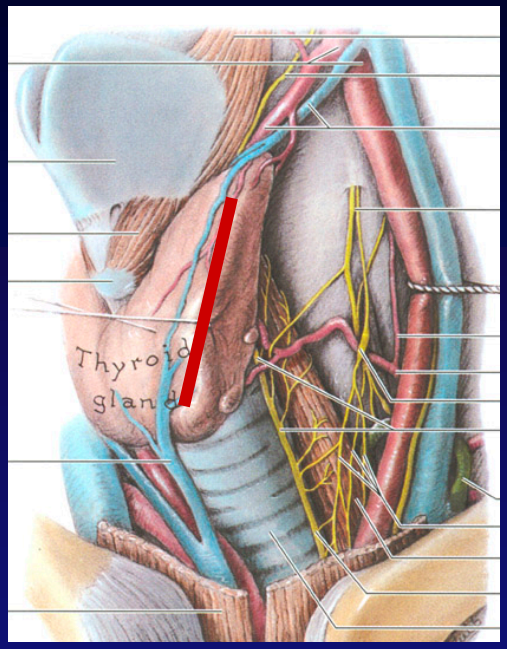


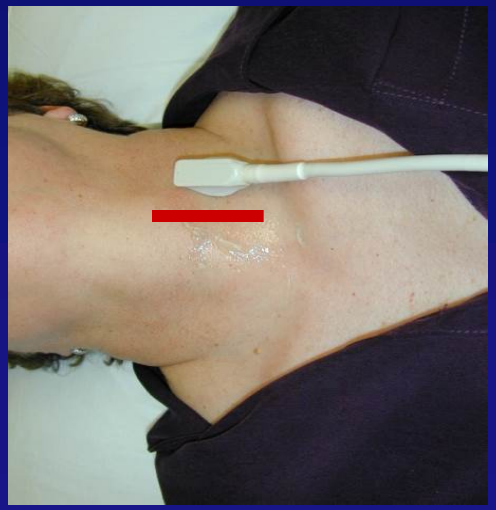


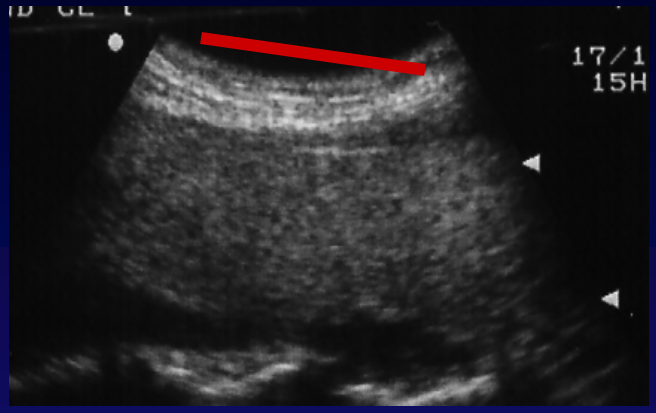
NORMAL

ABNORMAL

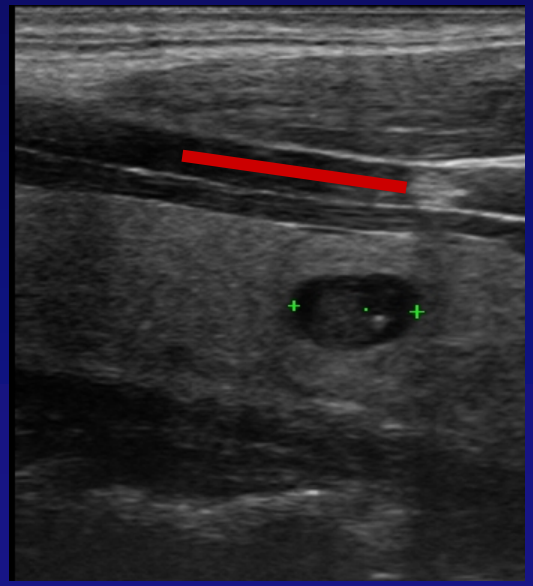
Longitudinal Views of Thyroid





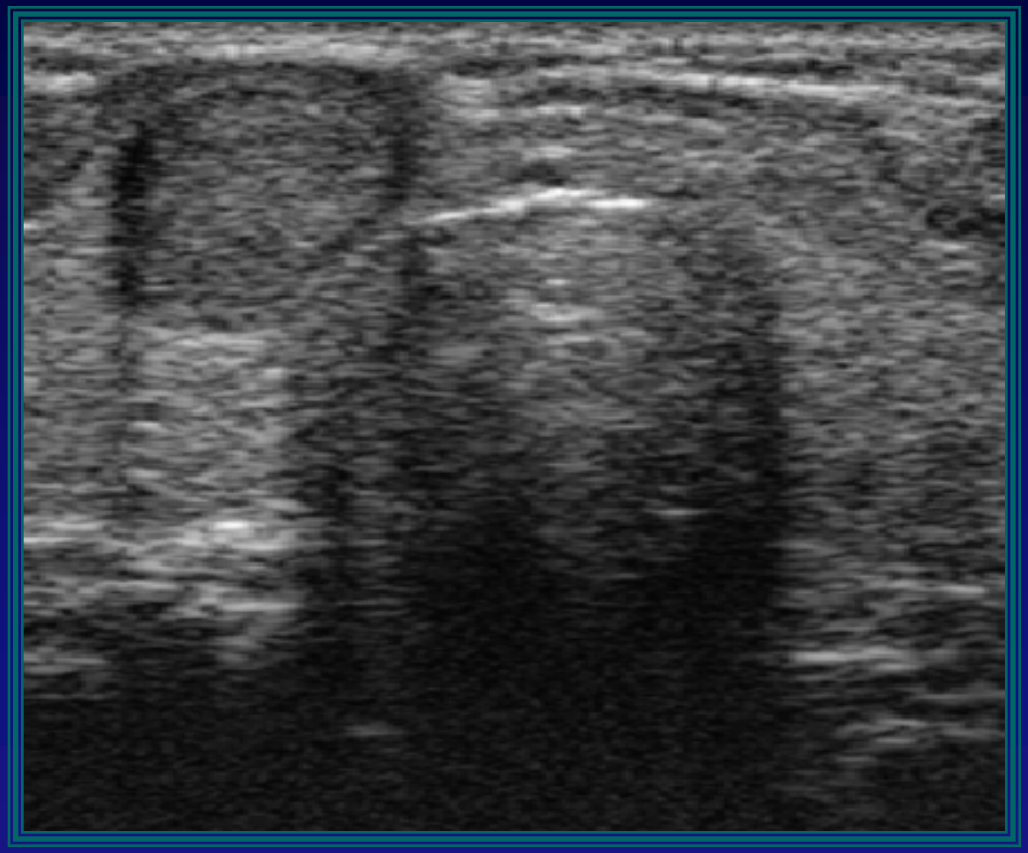


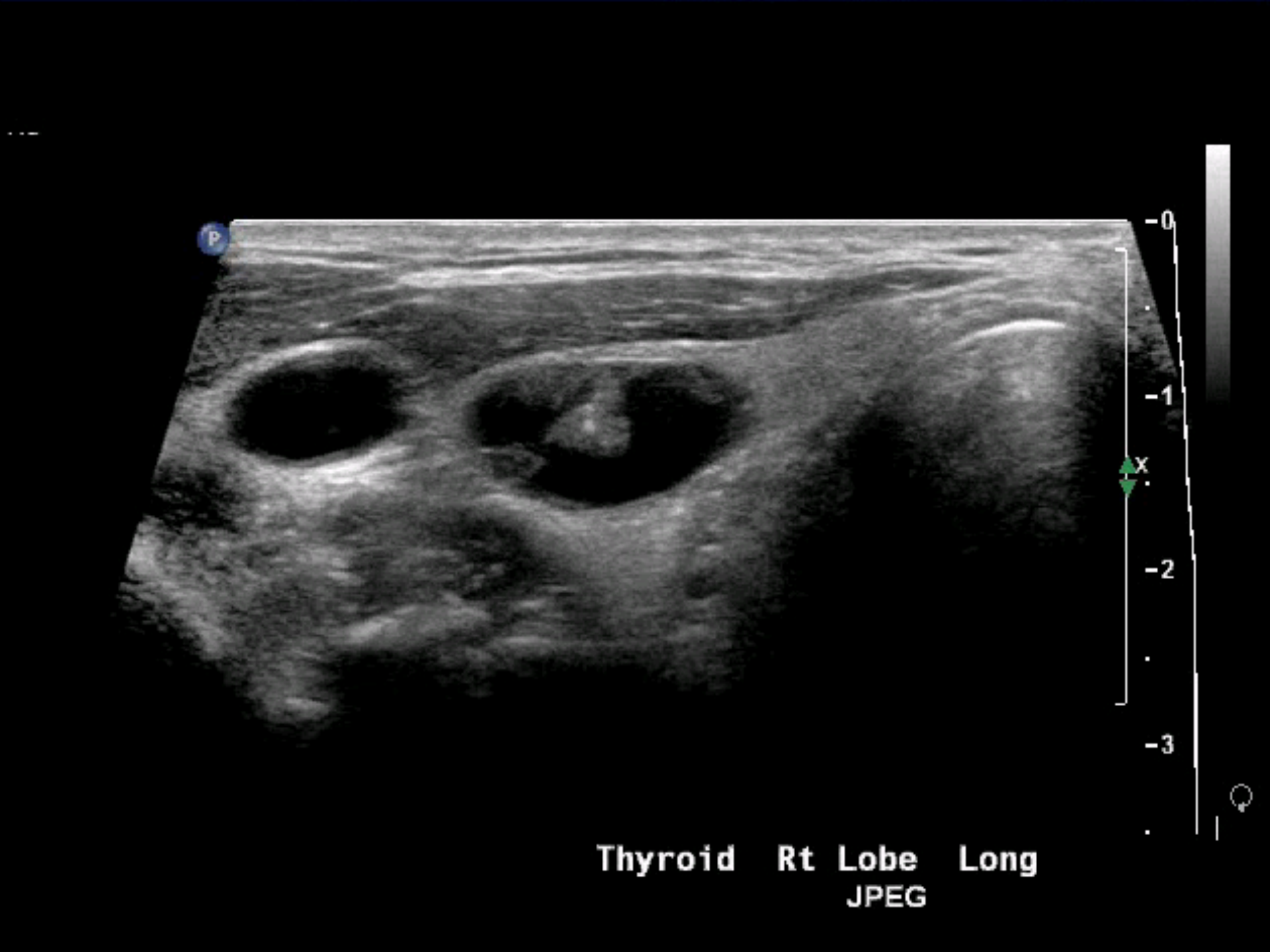
NORMAL



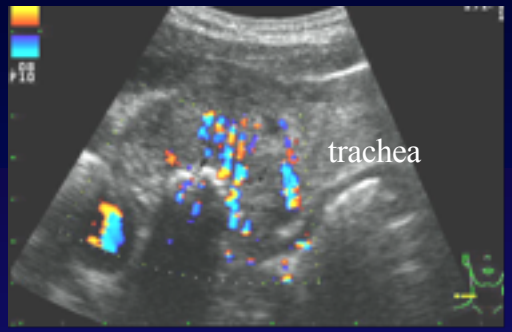
ABNORMAL

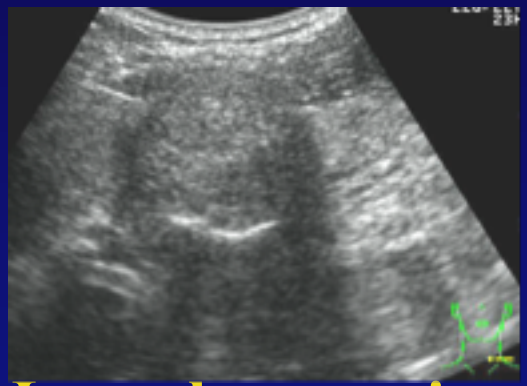
Thyroid Nodules

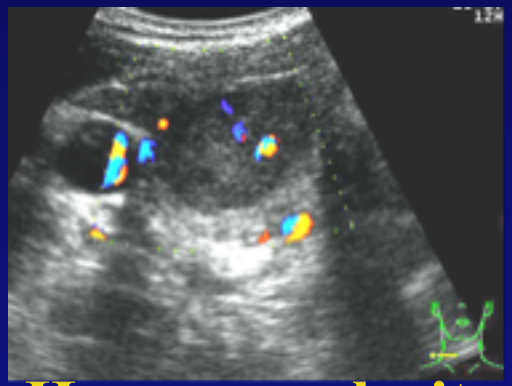



Thyroid Rt Lobe Long
JPEG

Ultrasound Features Suspicious for Thyroid Malignancy







	Irregular margins	Hypervascularity	Microcalcifications
SN	77%	74%	14-35%
SP	85%	81%	>90%
PPV	30%	24%	33-66%

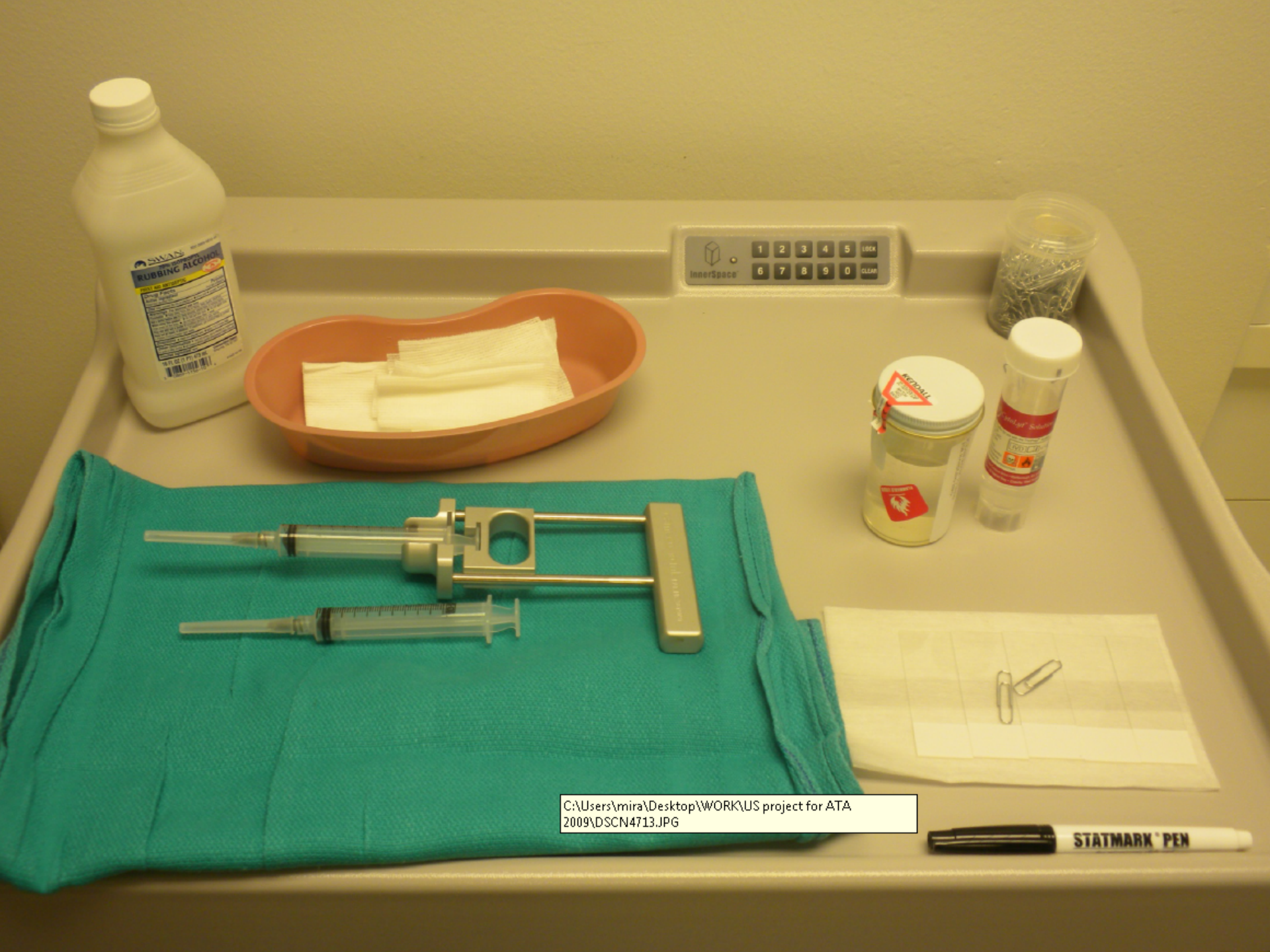
Papini et al. J Clin Endocrinol Metab 2002.

Fine Needle Aspiration Biopsy

Non-diagnostic	--------	Repeat biopsy
Benign	**0-3%**	US in 6 months, then yearly
Atypia of Undetermined Significance	**5-15%**	Repeat biopsy in 3 months
Suspicious for a follicular neoplasm (Hürthle cell)	**15-30%**	Lobectomy vs. TT
Cannot exclude malignancy	**45-55%**	TT ± CNLND
Suspicious for malignancy	**60-75%**	TT ± CNLND
Positive for malignant cells	**97-99%**	TT ± CNLND

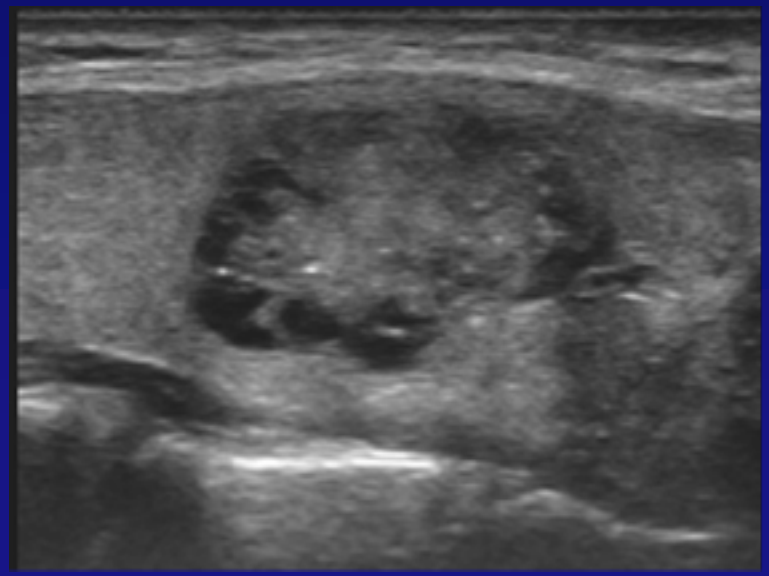
Cibas et al. The Bethesda System for Reporting Thyroid Cytopathology. Am J Clin Pathol 2009.


C:\Users\mira\Desktop\WORK\US project for ATA 2009\DSCN4712.JPG


RUBBING ALCOHOL
InnerSpace
1 2 3 4 5 LOCK
6 7 8 9 0 CLEAR
C:\Users\mira\Desktop\WORK\US project for ATA 2009\DSCN4713.JPG
STATMARK PEN

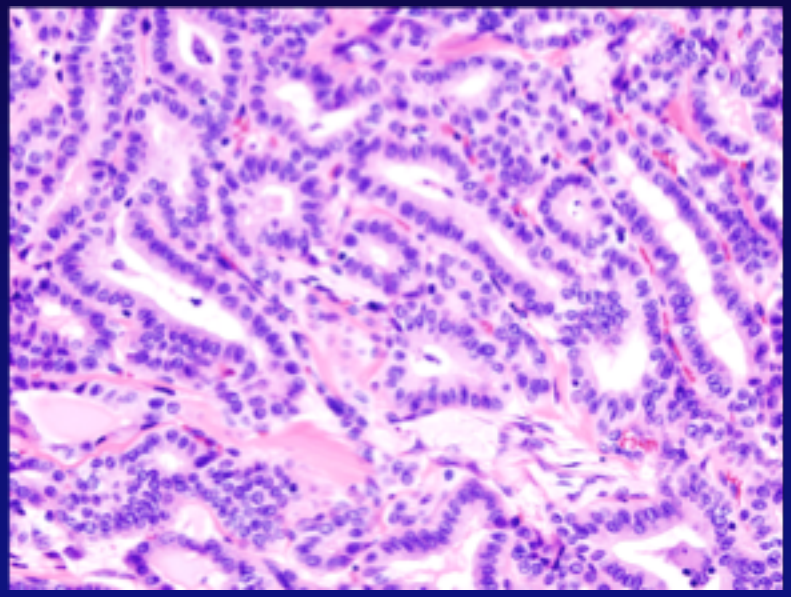
Thyroid Cancer

- Papillary Carcinoma (70-80%)
  - Follicular, classical
  - Tall cell, insular, columnar, solid, diffuse sclerosing
- Follicular Carcinoma (10%)
  - Hürthle Cell Carcinoma
- Medullary Carcinoma (3-10%)
- Anaplastic Carcinoma (<1%)
- Primary Thyroid Lymphoma (1-5%)



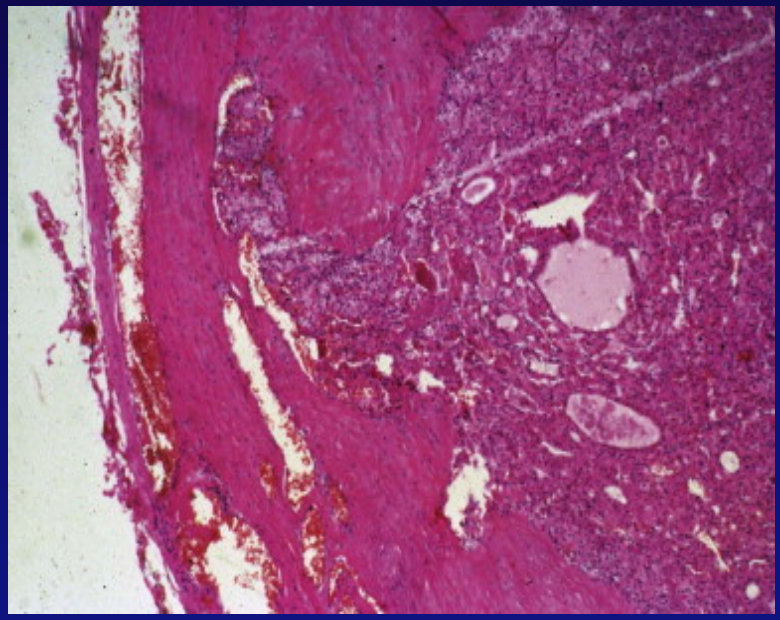
Thyroid Cancer

- Papillary Thyroid Carcinoma
  - Differentiated thyroid carcinoma arising from thyroid follicular epithelial cells
  - Most common type
  - Usually no symptoms
  - Usually metastasizes to lymph nodes in the neck
  - Best prognosis



Thyroid Cancer

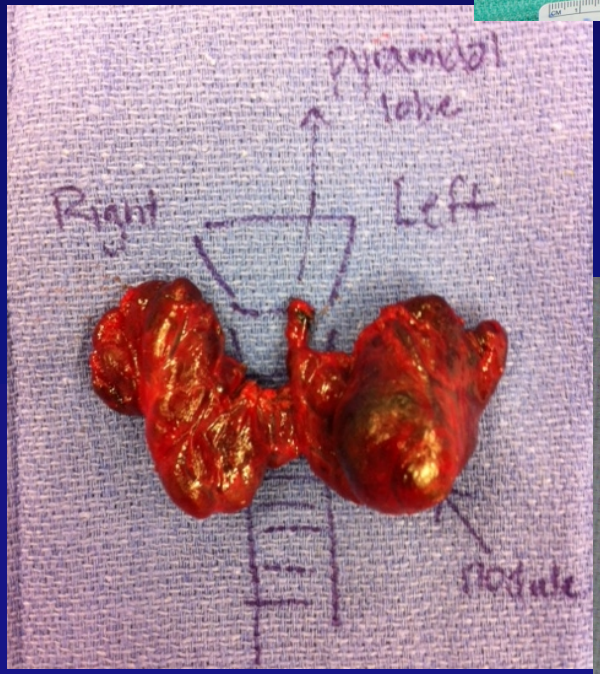
- Follicular Thyroid Carcinoma
  - Differentiated thyroid carcinoma
  - Second most common type
  - Most often associated with CS
  - Can occur at any age but more likely in older people
  - Hematogeneous metastasis (e.g., lung, bone)
  - Second best prognosis

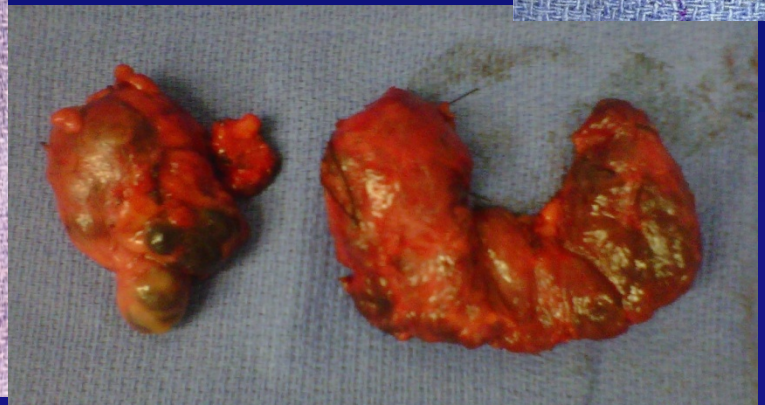


Mainstays of Treatment

- Total thyroidectomy ± appropriate compartment lymph node dissection (PTC/FTC)
  - Different for MTC, anaplastic, lymphoma
- Radioactive iodine ablation
- Thyroid hormone replacement at higher doses
- Long-term surveillance
- No “chemotherapy” or “external beam radiation”

All That Work For This???





Thyroid Hormone Replacement

- Healthy, young patients → full replacement doses of LT4 (1.6 mcg/kg/day)
- Elderly patients and patients with known or suspected cardiac disease → slightly lower doses of LT4
- Benign pathology → target TSH should be close to preoperative TSH
- Thyroid cancer → TSH suppression

FDA-approved T4 Products

Name of Product	Manufacturer
Synthroid	Abbott Laboratories
Levoxyl	King Pharmaceuticals
Unithroid	Jerome Stevens Pharmaceuticals
Levo-T	Mova-pharmaceuticals
Levothyroxine sodium	Mylan Laboratories Inc.
Novothyrox	Genpharm Inc.

CONSISTENCY

Symptoms/Signs of Hypothyroidism

- Lack of energy (even after sleeping)
- Cold intolerance
- Dry, scaly skin; coarse, dry hair; brittle nails and increased hair loss
- Constipation
- Heavy menstrual periods
- Propensity to weight gain
- Muscle aches, stiffness, and tenderness
- Join pain, stiffness, and swelling
- Muscle weakness/cramps
- Depressed mood
- Difficulty remembering and focusing
- Slowed heart rate

Symptoms/Signs of Hyperthyroidism

- Anxiety, irritability, nervousness
- Difficulty sleeping (especially falling asleep)
- Heat intolerance
- Increased perspiration
- Heart palpitations
- Fatigue
- Muscle weakness, especially in the upper arms and legs
- Weight loss, despite normal appetite
- Tremor of hands and fingers
- Lighter and less frequent menstrual periods
- Brittle hair
- Brisk muscle reflexes

Screening for Thyroid Disease

- Baseline neck ultrasound
- Screen at time of diagnosis, regardless of age
- ***Normal*** ultrasound → follow-up yearly with TSH level
- ***Abnormal*** ultrasound → FNAB → surgery


Thank You!

Cleveland Clinic

Every life deserves world class care.