Thyroid Cancer 2026

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Objectives

- Classify the main types of thyroid cancer and their general prognosis (Papillary, Follicular, Medullary and Anaplastic)
- Common risk factors for thyroid cancer
- Interpret TSH/radionuclide scintigraphy for low TSH levels
- Initial cost-effective evaluation algorithm for thyroid incidentalomas
- Key: High-risk thyroid nodule ultrasound features (TI-RADS or ATA)
- Fine Needle Aspiration (FNA) biopsy
  - criteria based on nodule size and ultrasound features
  - molecular testing for indeterminant FNA results (Bethesda III/IV)
- Highlight new treatment options for thyroid nodules/thyroid cancer

No conflicts of interest or financial relationships to disclose



Management Guidelines and Statements

- Adults with Thyroid Nodules/Differentiated Thyroid Cancer
- Children with Thyroid Nodules/Differentiated Thyroid Cancer
- Medullary Thyroid Carcinoma
- Recurrent/Persistent Nodal Disease: Surgery *vs* Observation
- Preoperative Imaging for Thyroid Cancer Surgery
- Ultrasound (Pattern-based vs nodule-focused, Criteria for FNA decision-making, US of cervical lymph nodes done at time of nodule US, Reporting standards)
- Hyperthyroidism

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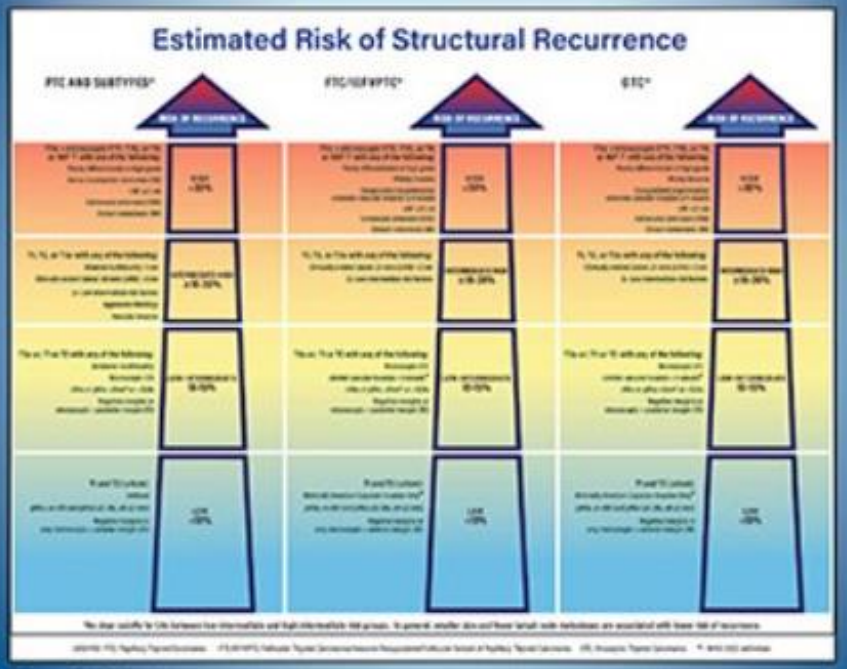
Thyroid®

2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer



The Official Journal of the

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

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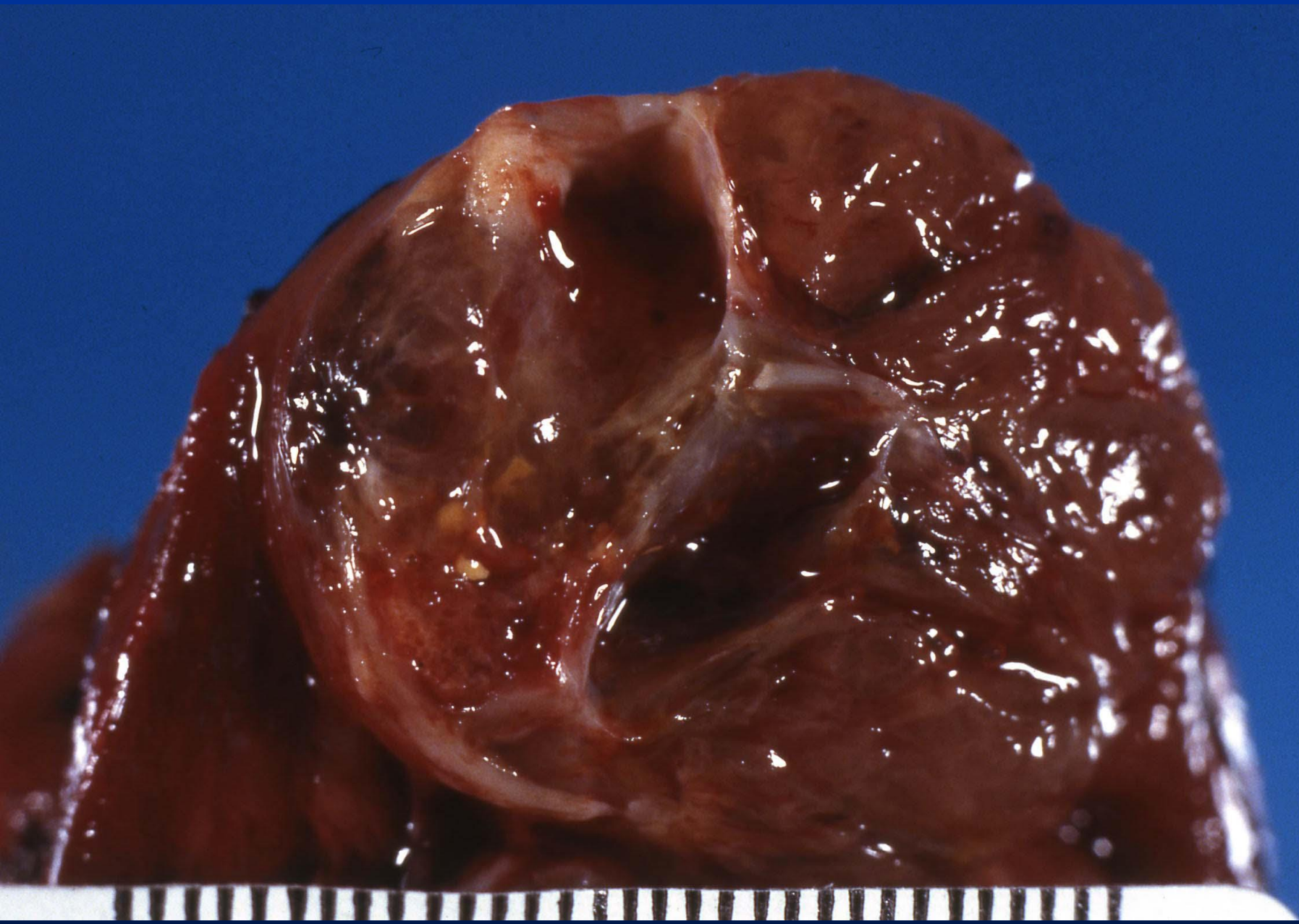
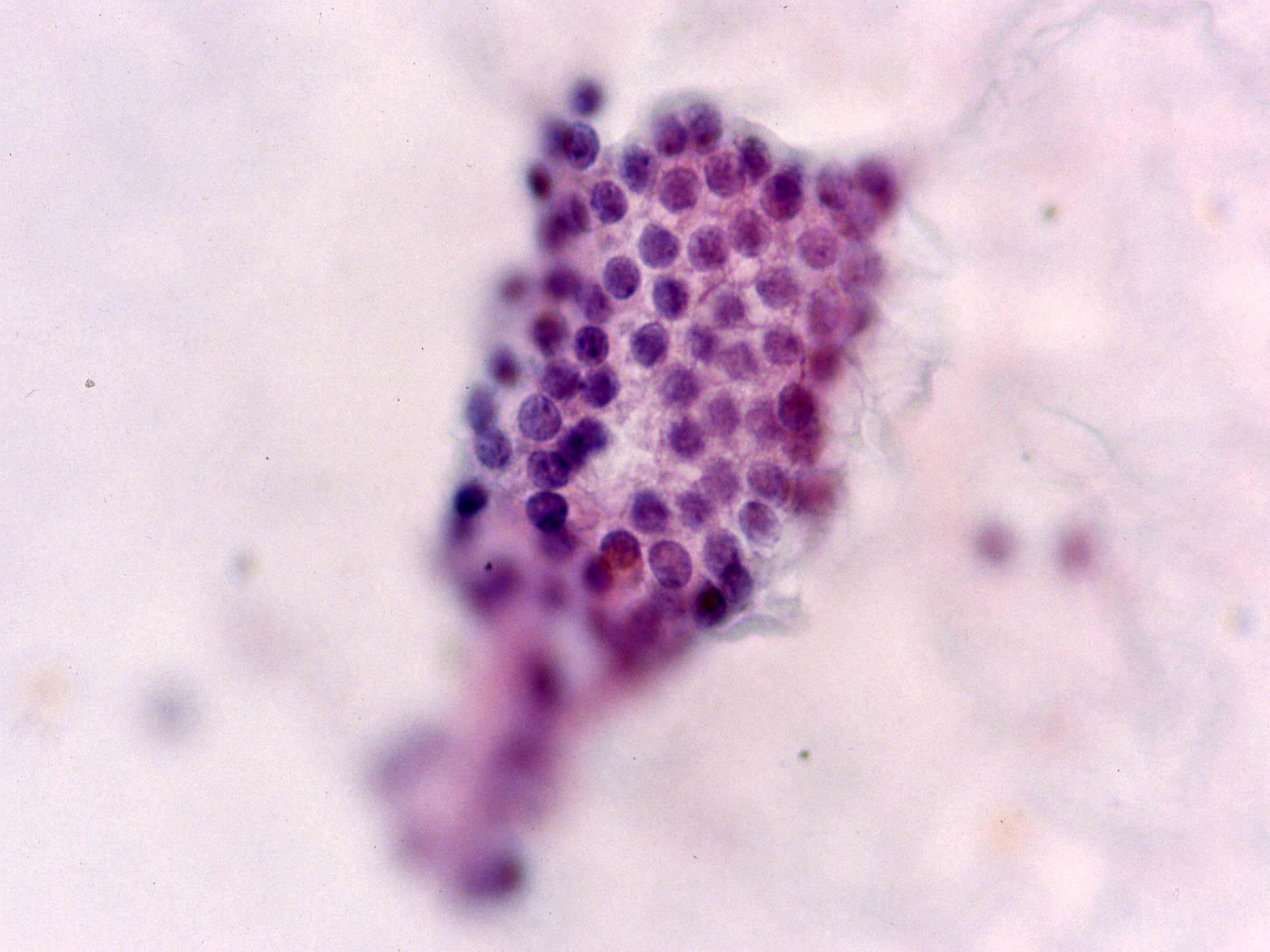
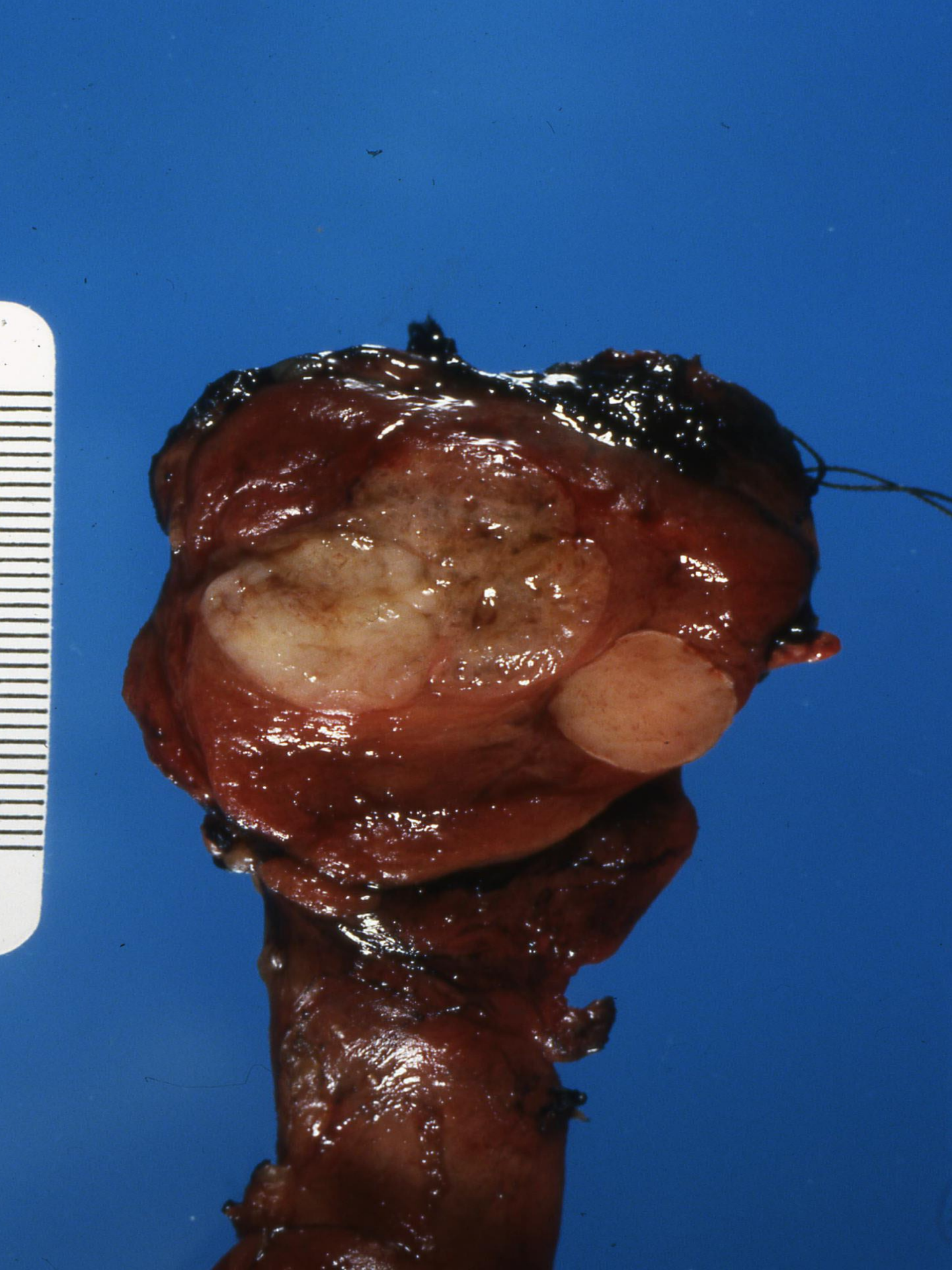
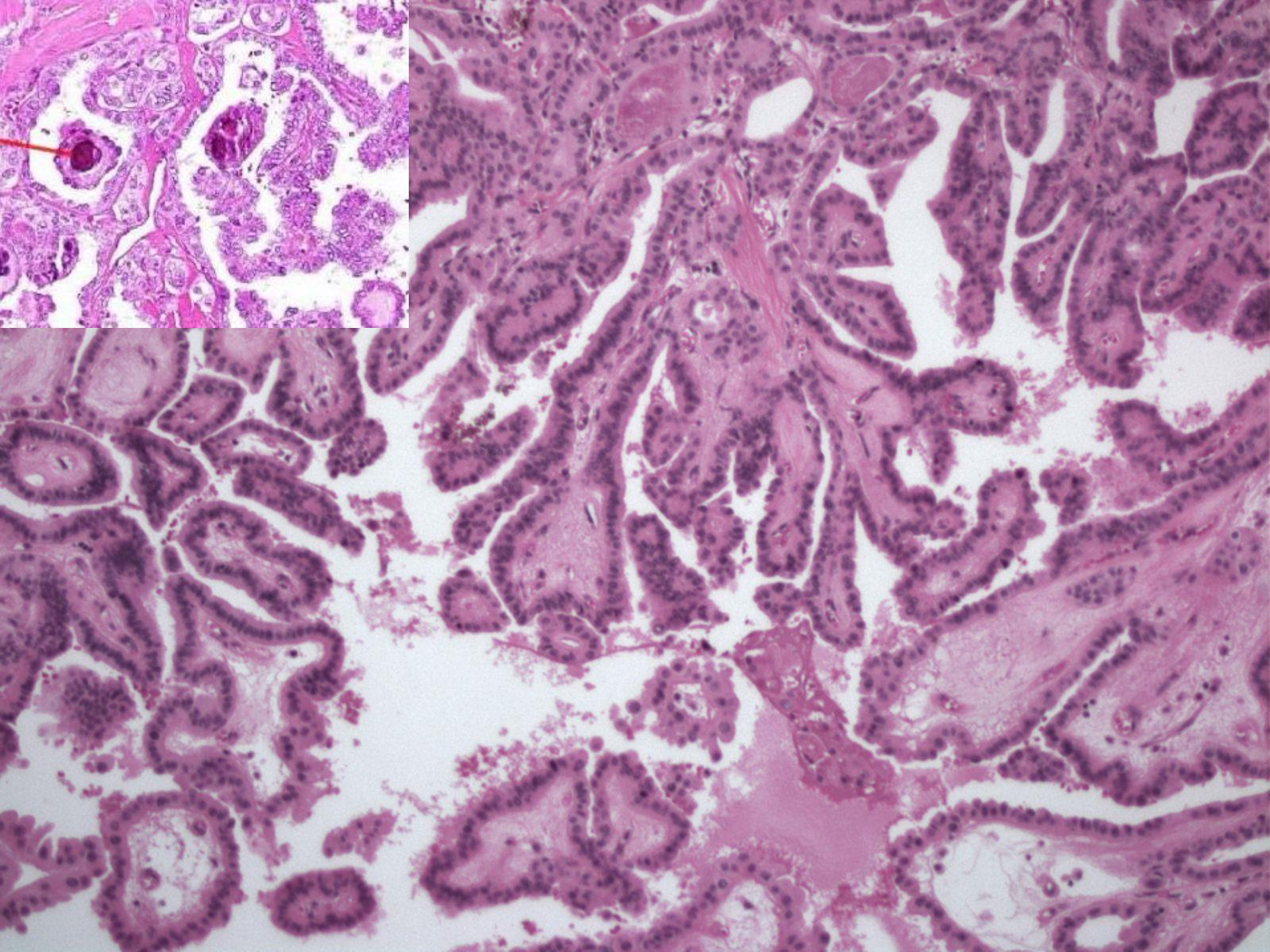
Classify the main types of thyroid cancer and their general prognosis

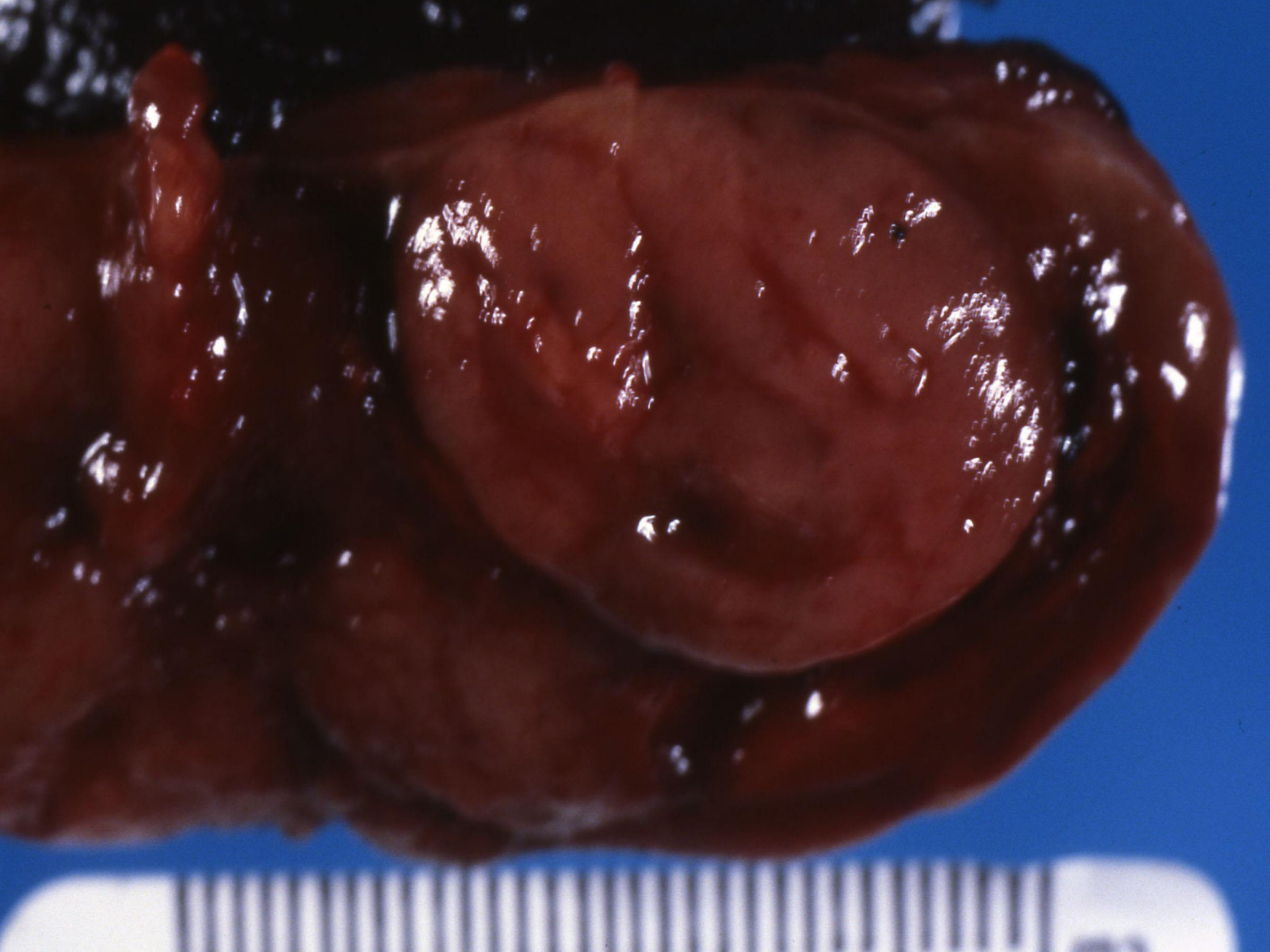
Papillary
Follicular
Medullary
Anaplastic

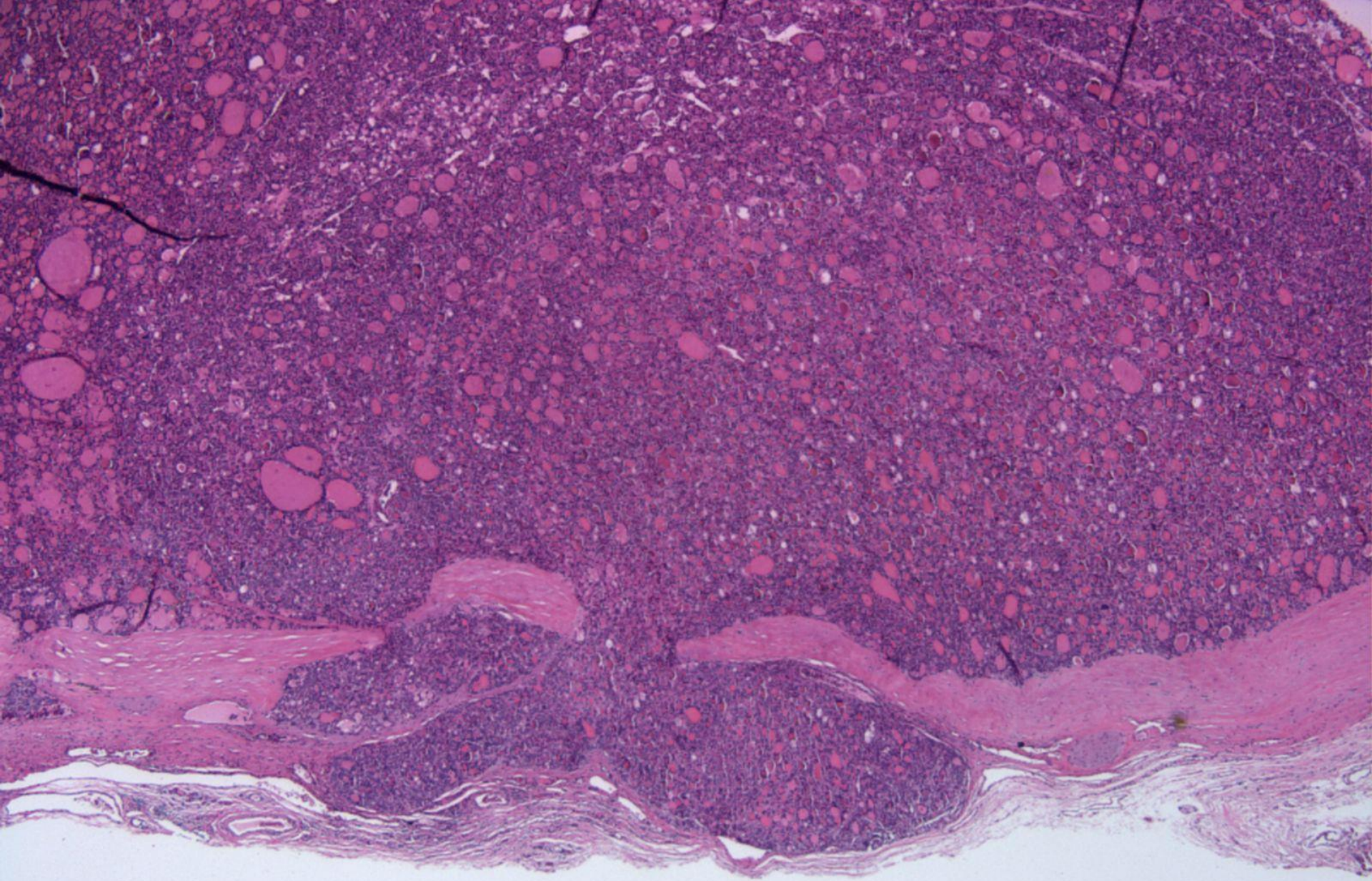


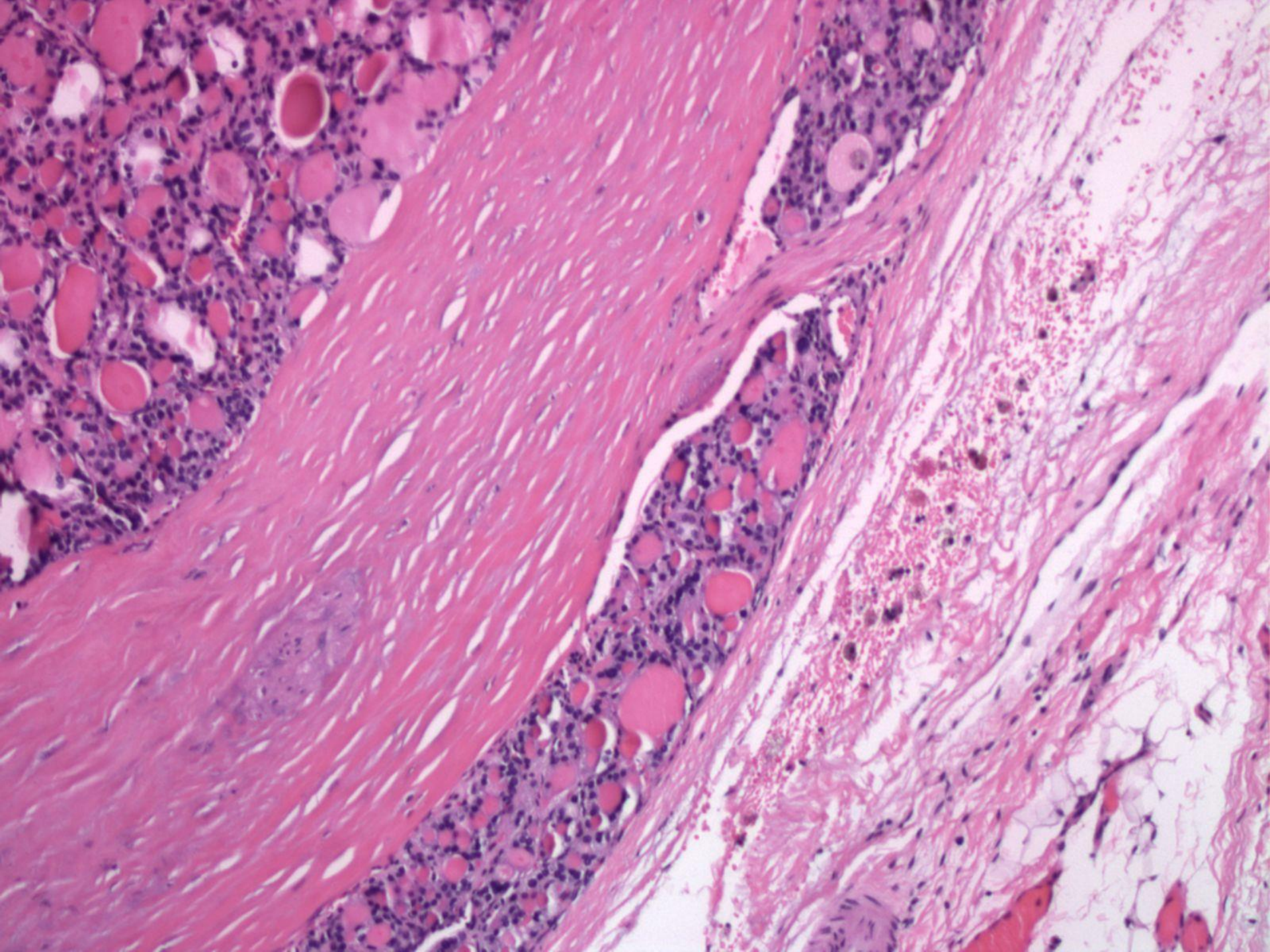


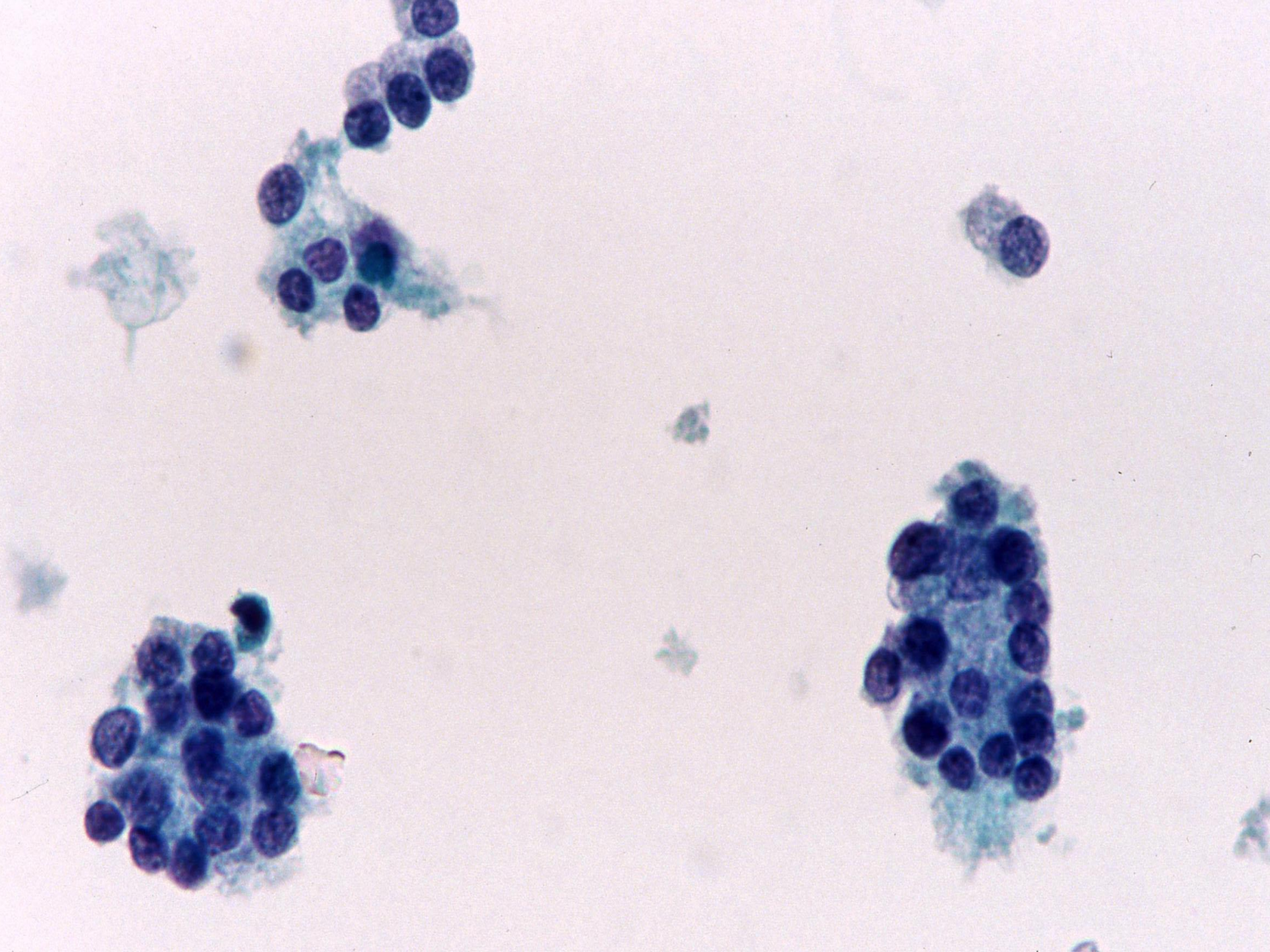


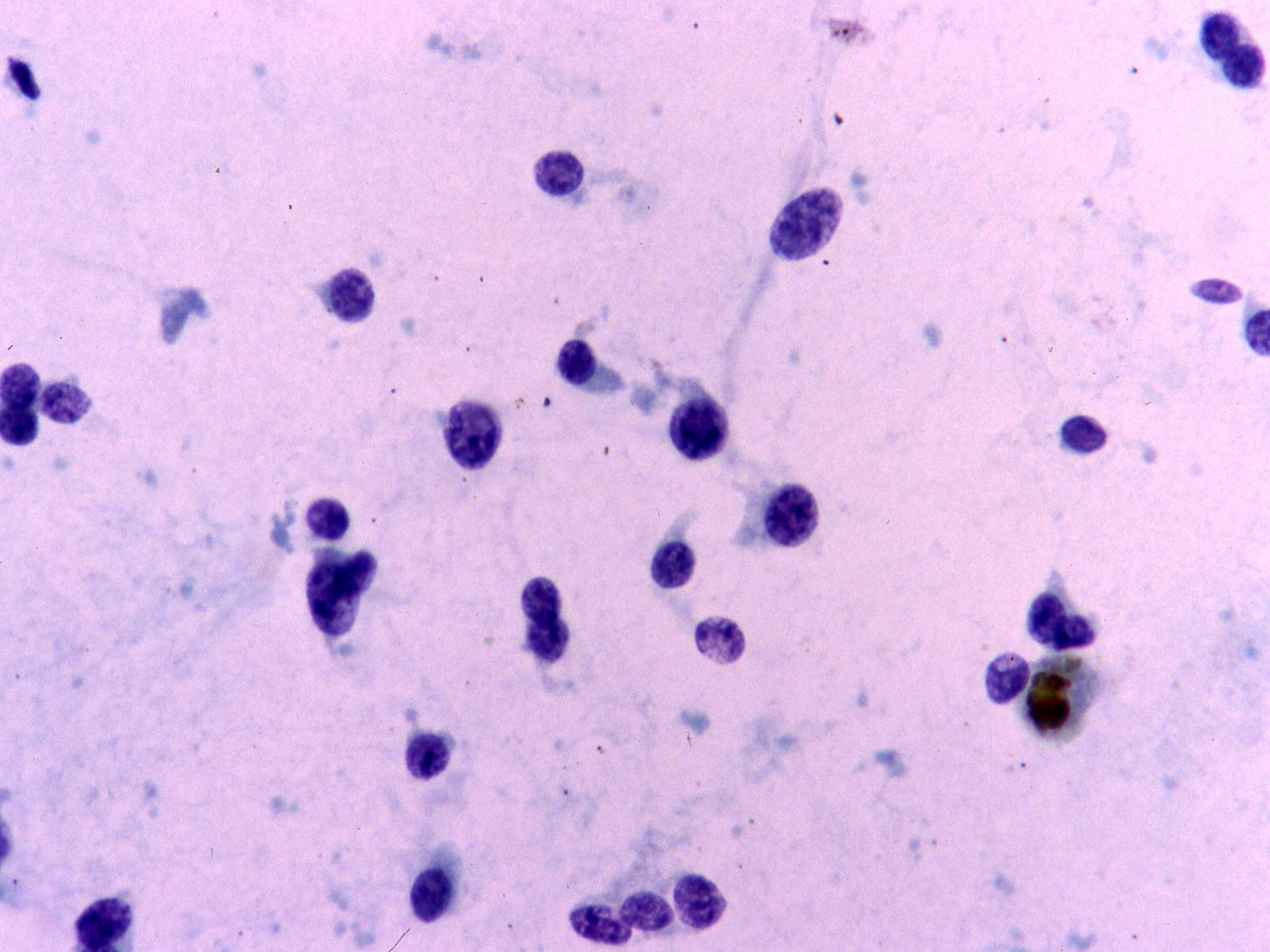


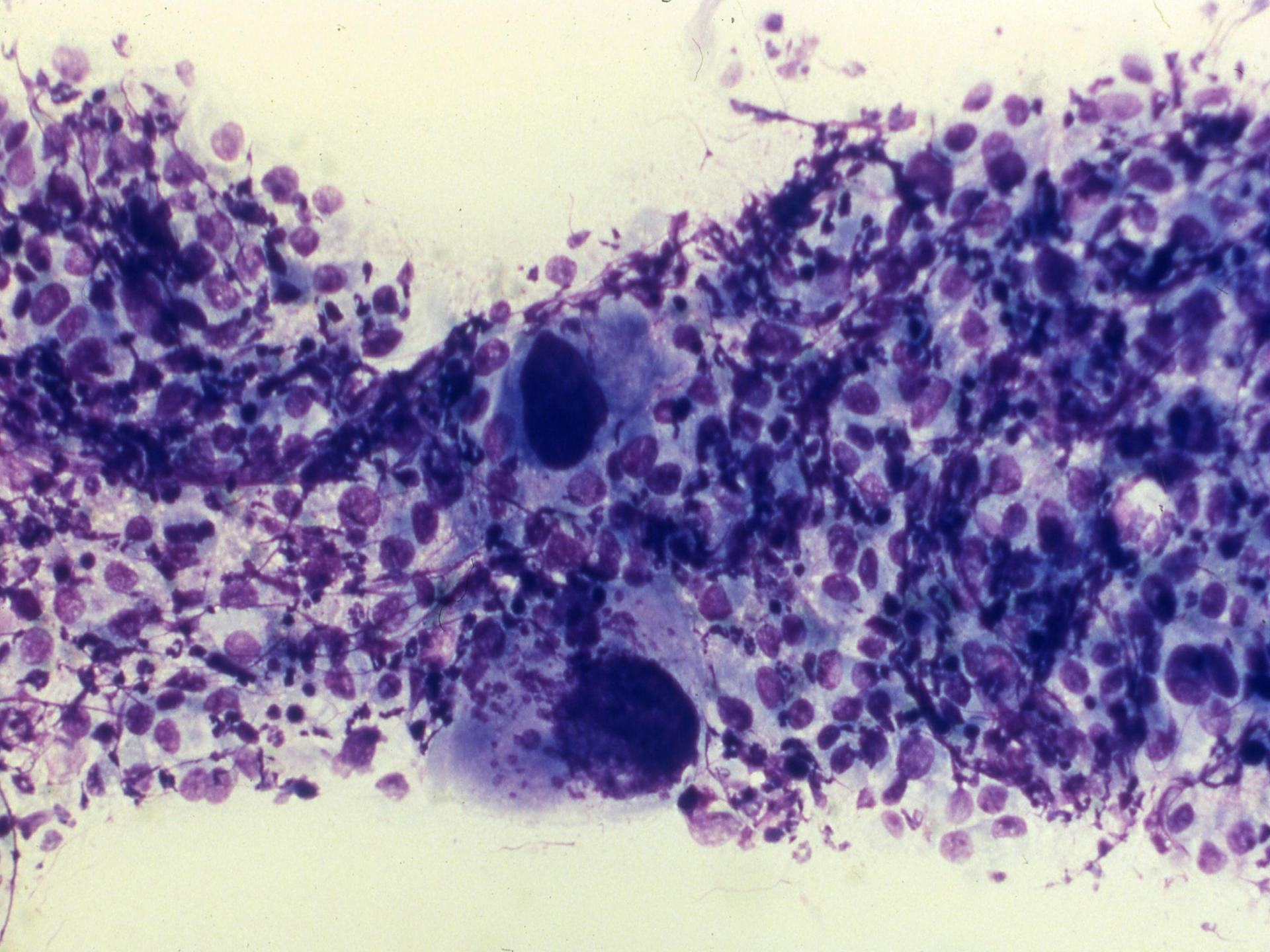








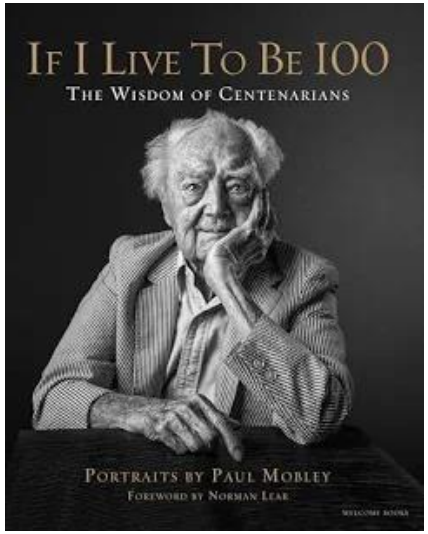




Risk	Annual Deaths	Lifetime risk
Heart disease	652,486	1 in 5
Cancer	553,888	1 in 7
Stroke	150,074	1 in 24
Hospital infections	99,000	1 in 38
Flu	59,664	1 in 63
Car accidents	44,757	1 in 84
Suicide	31,484	1 in 119
Accidental poisoning	19,456	1 in 193
MRSA	19,000	1 in 197
Falls	17,229	1 in 218
Drowning	3,306	1 in 1,134
Bike accident	762	1 in 4,919
Air/space accident	742	1 in 5,051
Excessive cold	620	1 in 6,045
Sun/heat exposure	273	1 in 13,729
Shark attack*	62	1 in 60,453
Lightning	47	1 in 79, 746
Train crash	24	1 in 156,169
Fireworks	11	1 in 340,733

2000 annual deaths
Life time risk of dying from
Thyroid cancer 0.06 (%)

Source: NY times
NSC – National Safety Council 2007



Papillary Thyroid Cancer	
SEER Stage	**5-year survival rate**
Localized	> 99.5%
Regional	99%
Distant	74%
All stages combined	> 99.5%

Follicular Thyroid Cancer	
SEER Stage	**5-year survival rate**
Localized	> 99.5%
Regional	98%
Distant	67%
All stages combined	98%

Medullary Thyroid Cancer	
SEER Stage	**5-year survival rate**
Localized	> 99.5%
Regional	92%
Distant	43%
All stages combined	91%

Anaplastic Thyroid Cancer	
SEER Stage	**5-year survival rate**
Localized	39%
Regional	11%
Distant	4%
All stages combined	8%

T

N

M

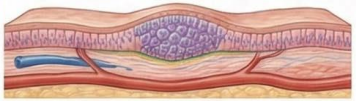
TNM Cancer Staging System

How Tumor Size, Lymph Nodes, and Metastasis Define Cancer Stage

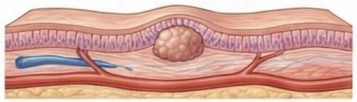
PANEL 1 – T (PRIMARY TUMOR)

T0 – No primary tumor found

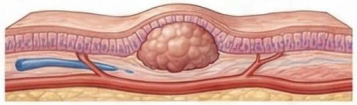
Tis – Carcinoma in situ (non-invasive)



T1 – Small localized tumor

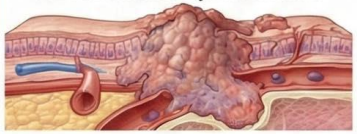


T2 – Larger tumor, confined to organ



T3 – Tumor extends into nearby tissues

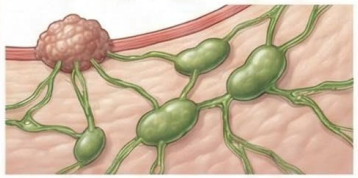
T4 – Tumor invades adjacent structures



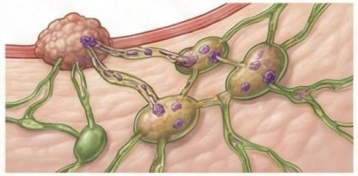
Tumor size and local invasion vary by cancer type

PANEL 2 – N (LYMPH NODE INVOLVEMENT)

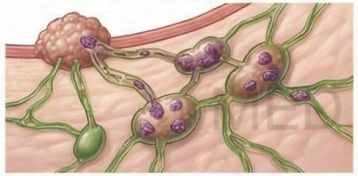
N0 – No lymph node involvement



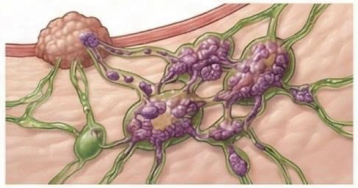
N1 – Few nearby lymph nodes involved



N2 – Multiple or larger regional nodes involved



N3 – Extensive regional lymph node involvement

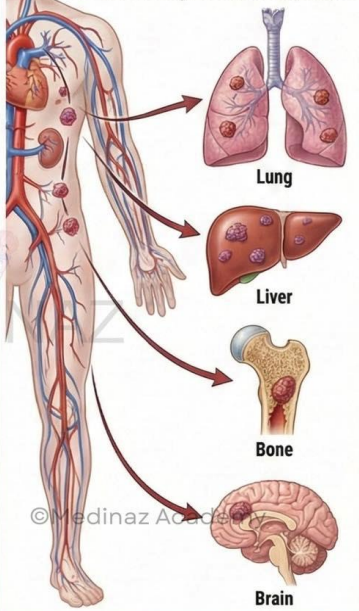


Only regional lymph nodes are included in N staging

PANEL 3 – M (DISTANT METASTASIS)

M0 – No distant metastasis

M1 – Distant organ metastasis present



Any distant spread = metastatic disease

COMBINED STAGING STRIP (IMPORTANT)

How TNM Becomes a Cancer Stage

T1 N0 M0 → Stage I

T2 N1 M0 → Stage II

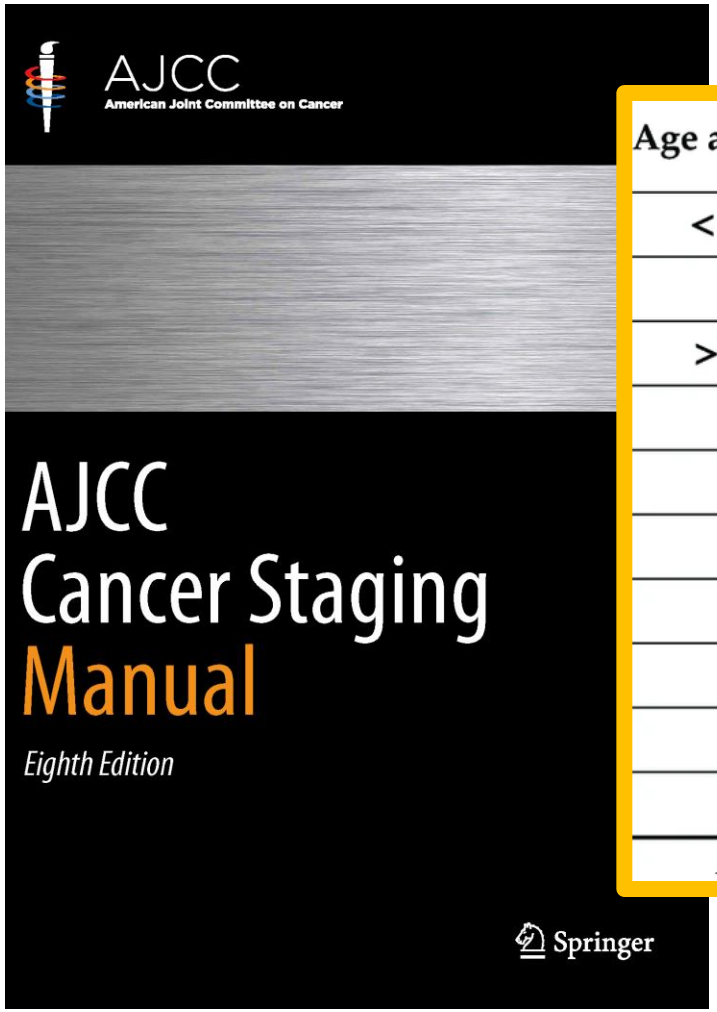
T3 N2 M0 → Stage III

Any T, Any N, M1 → Stage IV

MEDINAZ

"TNM staging varies by cancer type."
"Final stage grouping depends on cancer-specific guidelines."
"TNM staging guides treatment and prognosis."

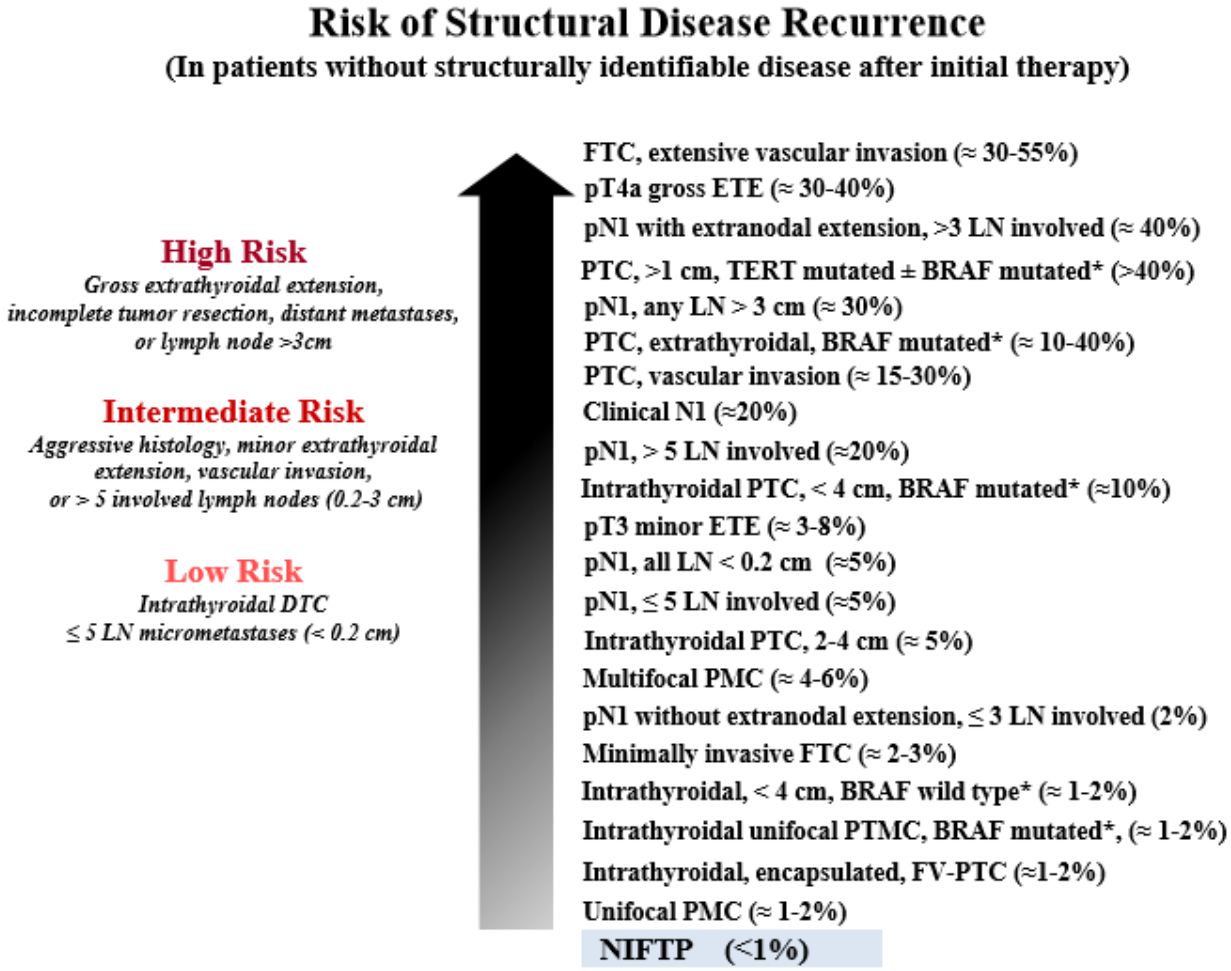
AJCC 8th Edition Staging for ***Survival***



Age at Diagnosis	T Staging	N Staging	M Staging	Stage
< 55 years	Any T	Any N	M0	I
	Any T	Any N	M1	II
>55 years	T1	N0/Nx	M0	I
	T1	N1	M0	II
	T2	N0/Nx	M0	I
	T2	N1	M0	II
	T3a/T3b	Any N	M0	II
	T4a	Any N	M0	III
	T4b	Any N	M0	IVA
	any T	any N	M1	IVB

Adapted from [24], with permission from Mary Ann Liebert, Inc., 2020.

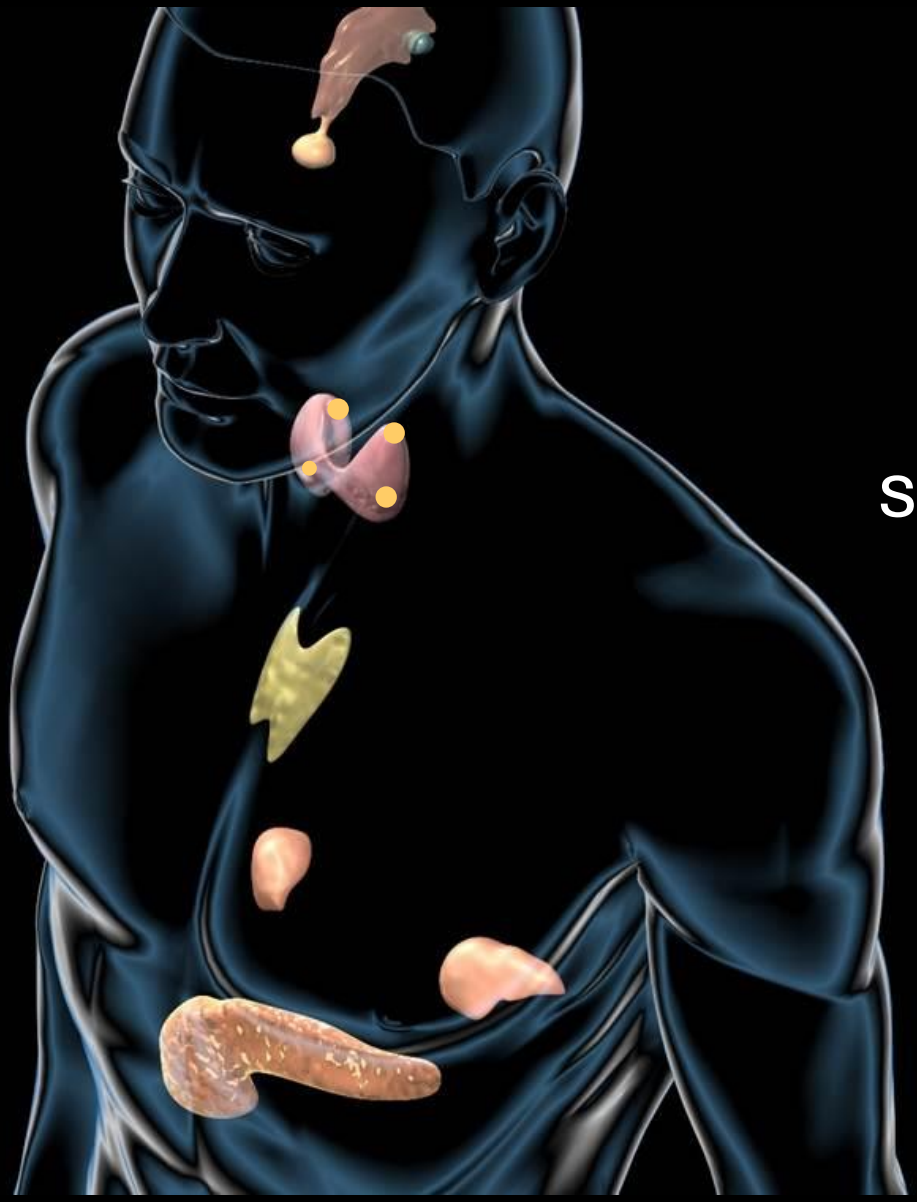
ATA Dynamic Risk Stratification for ***Recurrence***



Common risk factors for thyroid cancer

XRT exposure
Smoking
Obesity
Women age 30-60
Men solitary nodule
Asian ethnicity
Family Hx/Genetics
MEN, Cowden, FAP
Hashimoto’s
Low iodine diet


HOW SCARY IS THAT RADIOACTIVITY FROM JAPAN?!!



Interpret TSH

Radionuclide scintigraphy for low TSH levels

TSH Levels

Distribution In Healthy Population (mUI/L)

Source: Vejbjerg, Clin Endocrinol (2009)

Radioactive Iodine Uptake Test

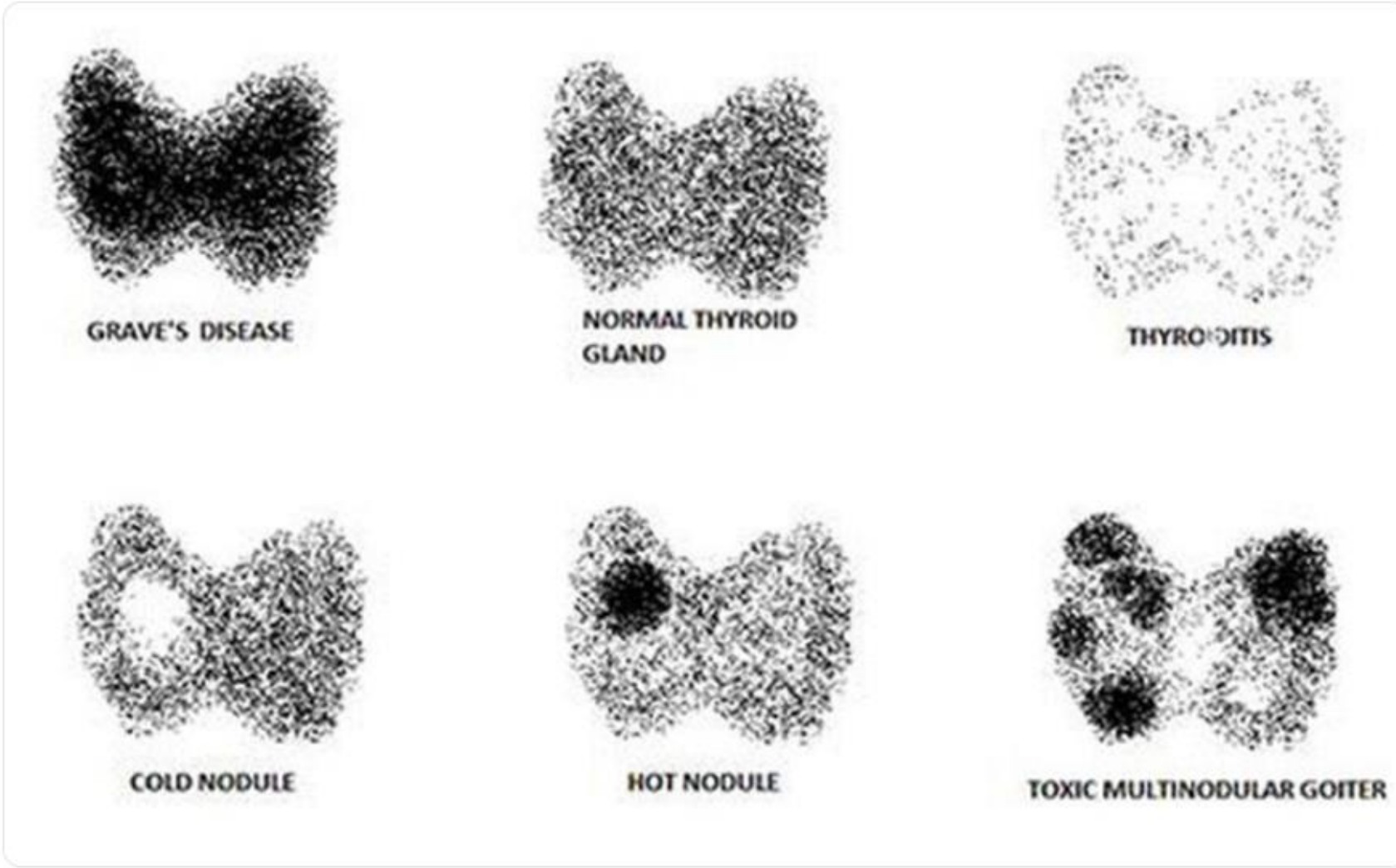
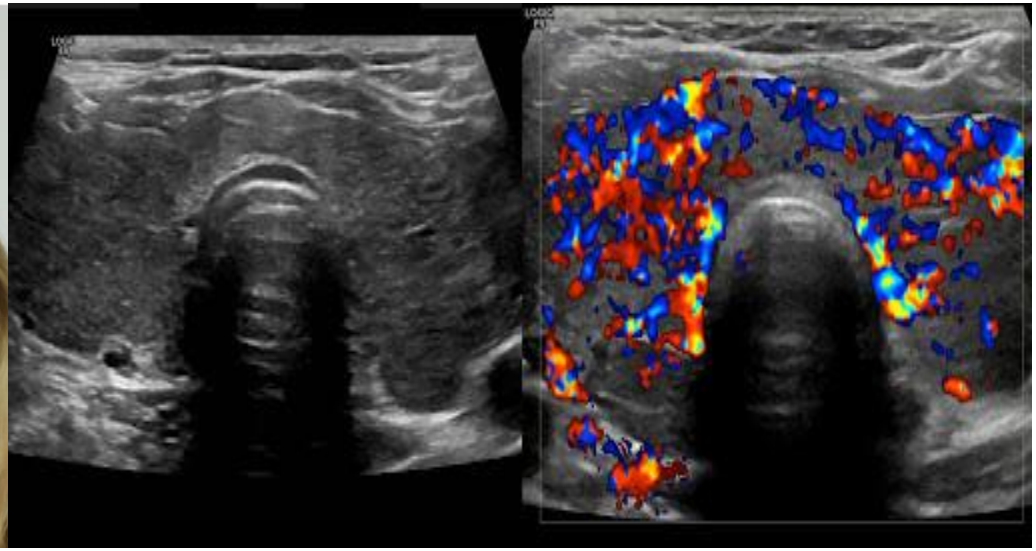


Image Source: Medizzy

Graves' Disease

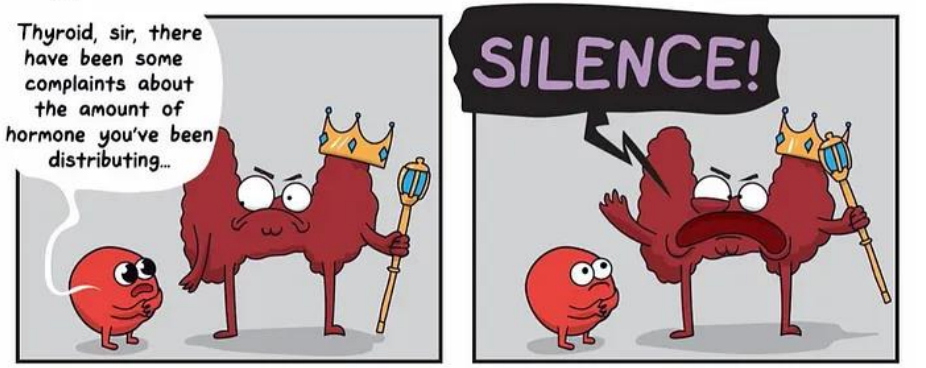


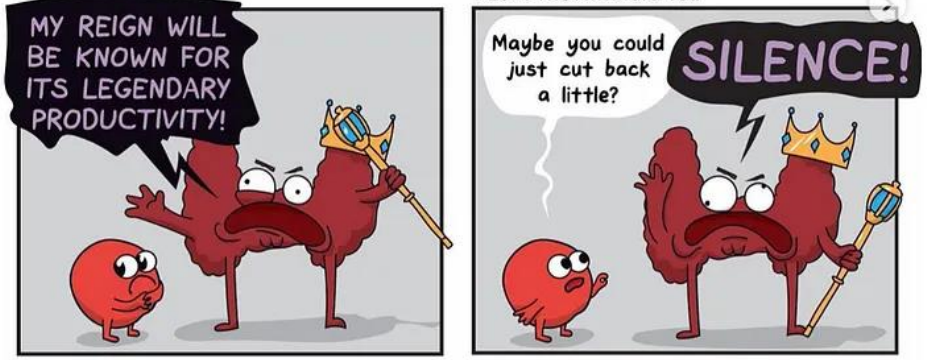
TSH <0.1

T4/T3 high

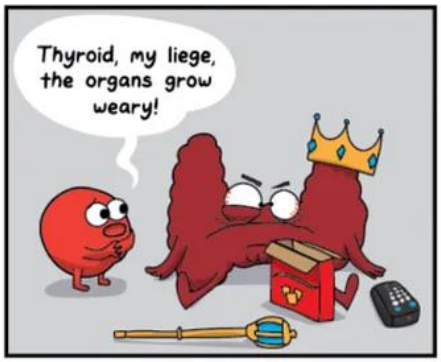
TRAB/TSI high

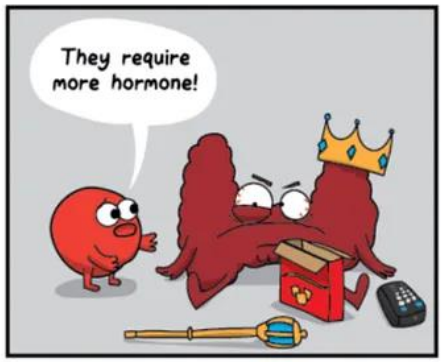
Hyper

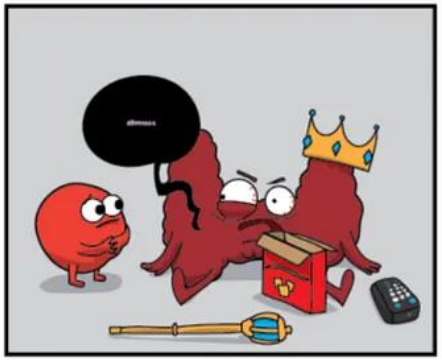


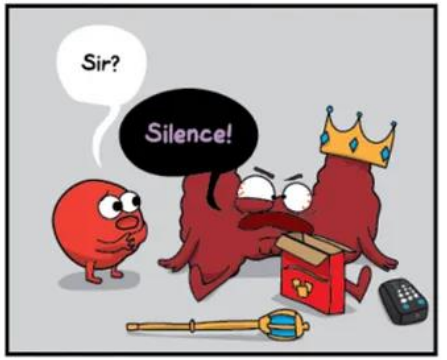


Hypo



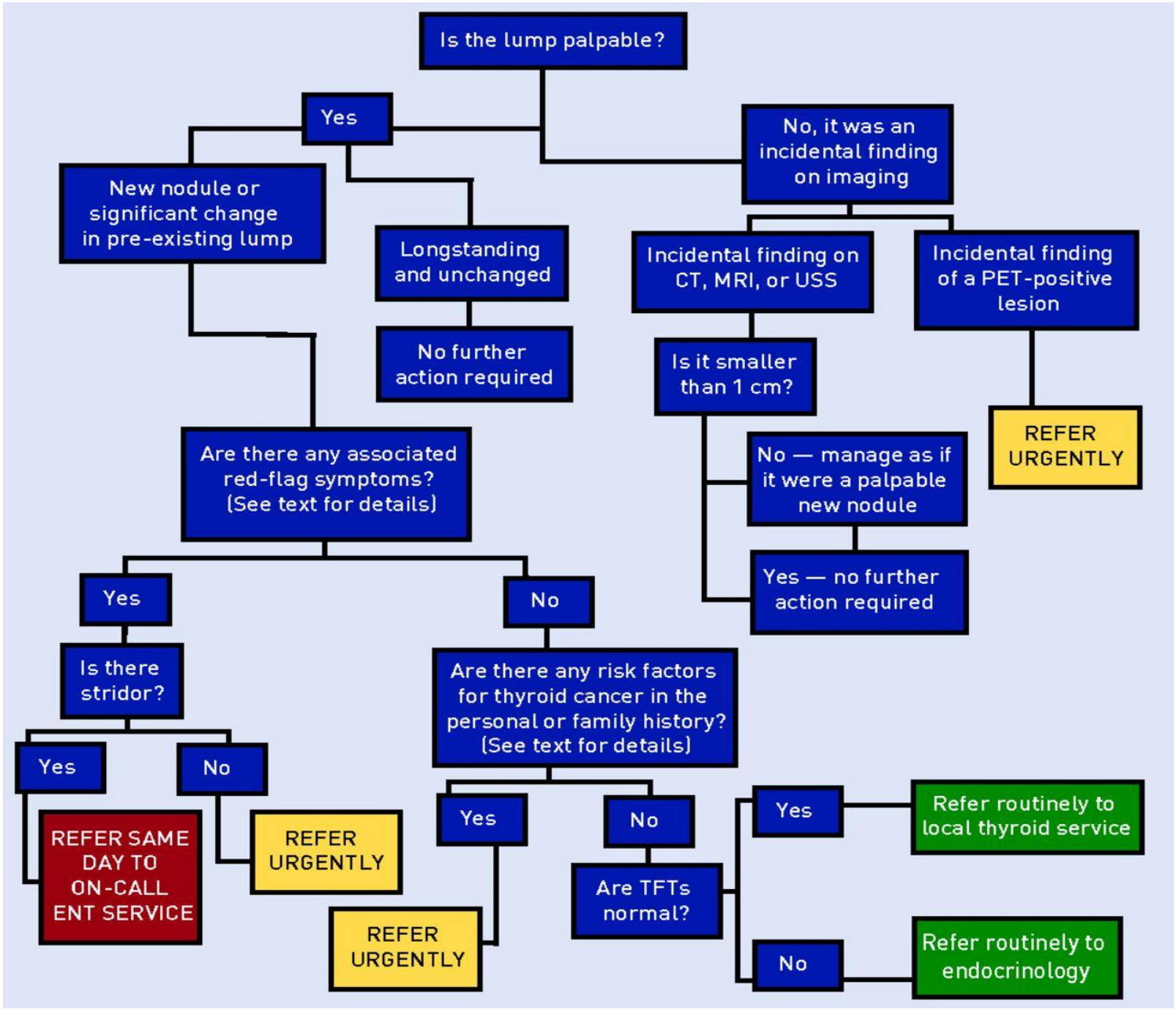






Initial cost-effective evaluation algorithm for thyroid incidentalomas

High-risk thyroid nodule ultrasound features (TI-RADS or ATA)


Is the lump palpable?
Yes
No, it was an incidental finding on imaging
New nodule or significant change in pre-existing lump
Longstanding and unchanged
No further action required
Incidental finding on CT, MRI, or USS
Incidental finding of a PET-positive lesion
Is it smaller than 1 cm?
REFER URGENTLY
No — manage as if it were a palpable new nodule
Yes — no further action required
Are there any associated red-flag symptoms? (See text for details)
Yes
No
Is there stridor?
Yes
No
REFER SAME DAY TO ON-CALL ENT SERVICE
REFER URGENTLY
Are there any risk factors for thyroid cancer in the personal or family history? (See text for details)
Yes
No
REFER URGENTLY
Are TFTs normal?
Yes
No
Refer routinely to local thyroid service
Refer routinely to endocrinology


BJGP
HEALTH TECHNOLOGY

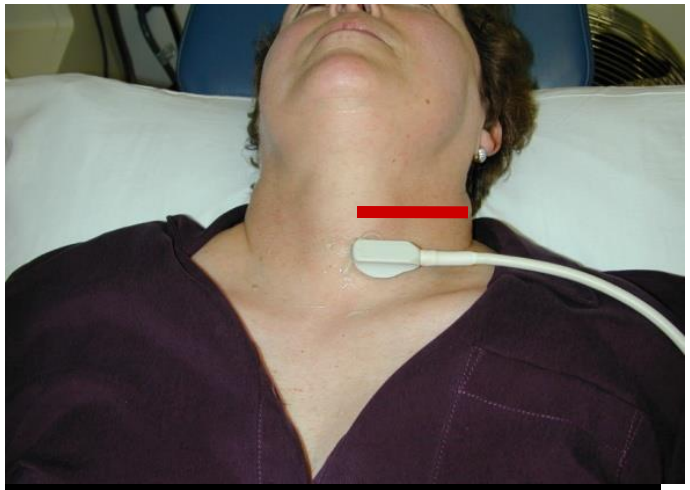
TSH + ULTRASOUND

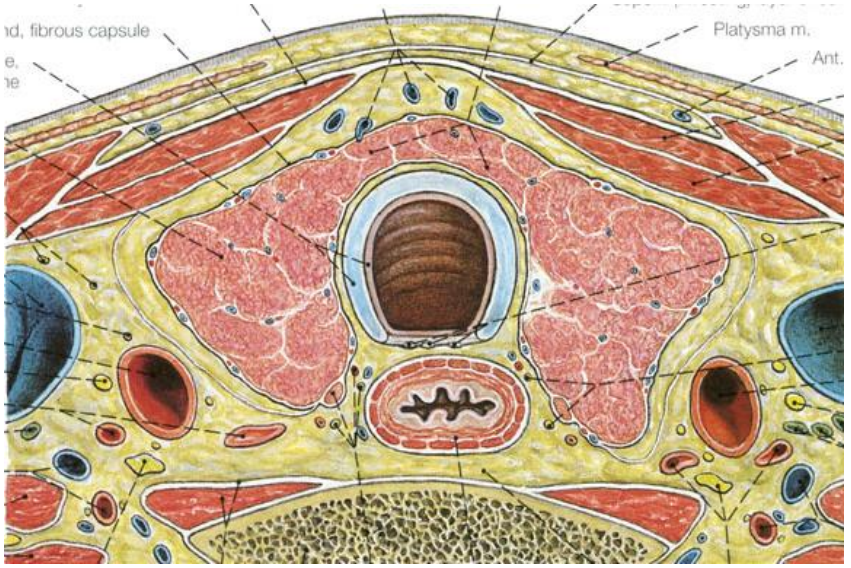
TSH LOW
Graves' Disease
Toxic Goiter
Toxic Nodule

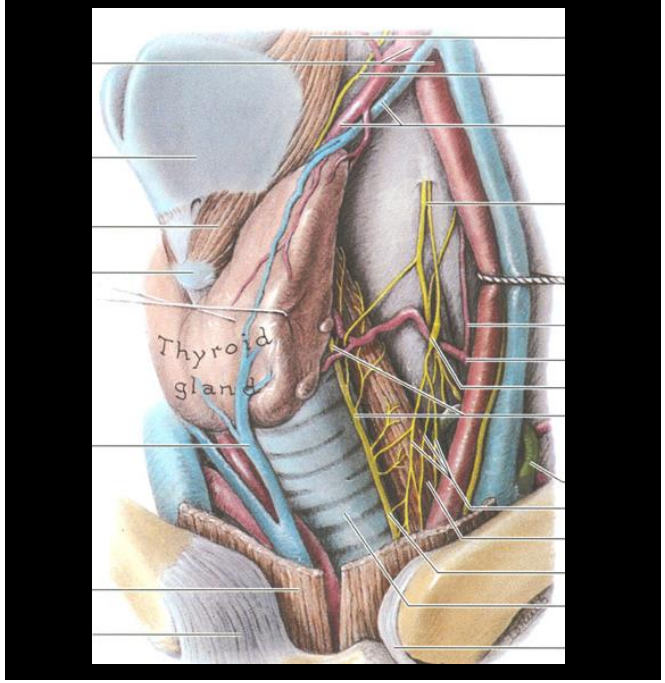
TSH NORMAL
Cancers

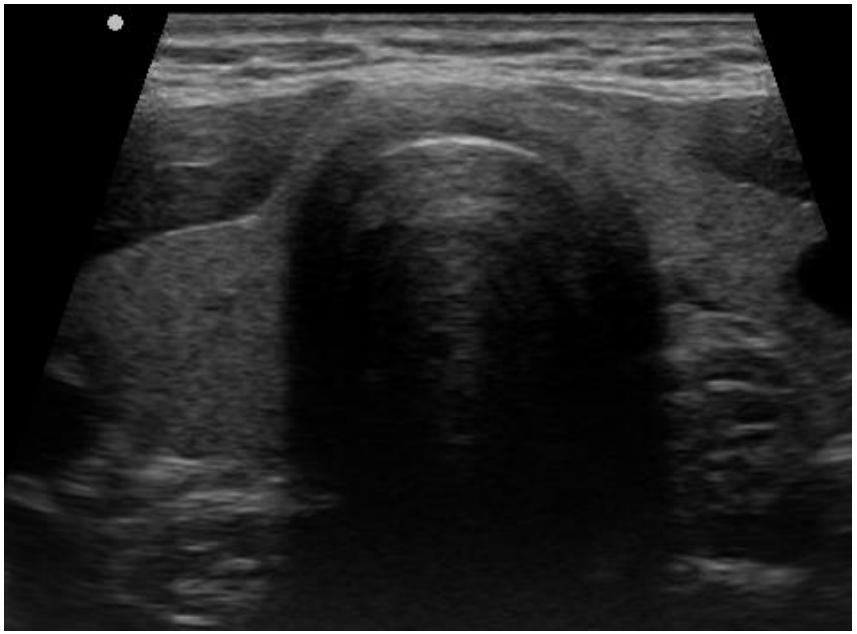
TSH HIGH
Hashimoto's
Thyroiditis

Transverse Views of Thyroid

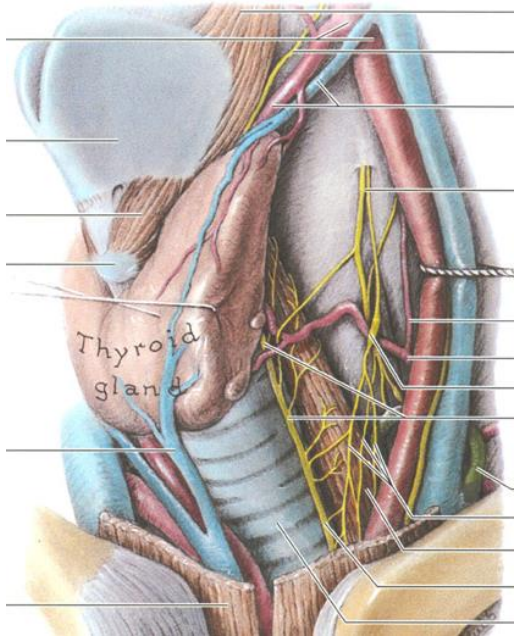


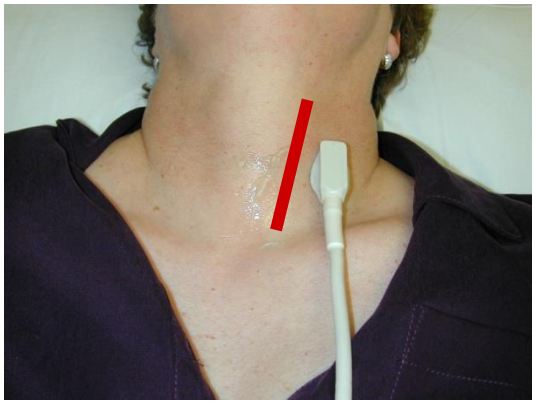






Longitudinal/Sagittal Views of Thyroid



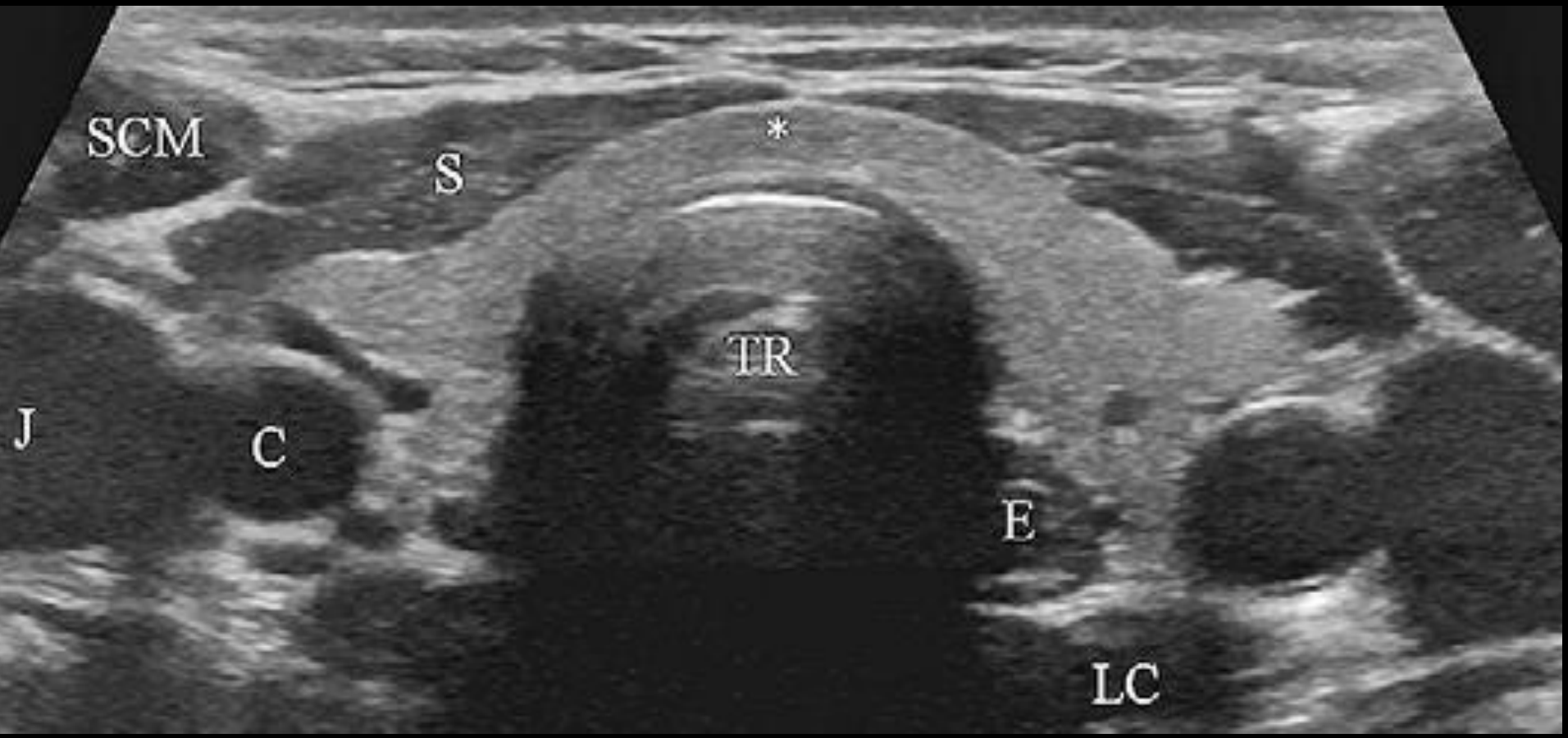


Ultrasonography for the Endocrine Surgeon

Mira Milas, MD,[a] Antonia Stephen, MD,[b] Eren Berber, MD,[a] Kristin Wagner, MD,[c] Judiann Miskulin
and Allan Siperstein, MD,[a] *Cleveland, Ohio, Boston, Mass, and Charlotte, NC*

Surgery 2005;138:1193-201


DIVISI
ASSOCIATES
GENERAL SURGERY
F.C.C.M.
F.A.C.S.
F.A.C.S.


SCM
S
*
TR
J
C
E
LC

Your Patient

46 yrs old woman is referred to you for a palpable and visible midline thyroid nodule. Medical/family history is unremarkable. TSH is normal.

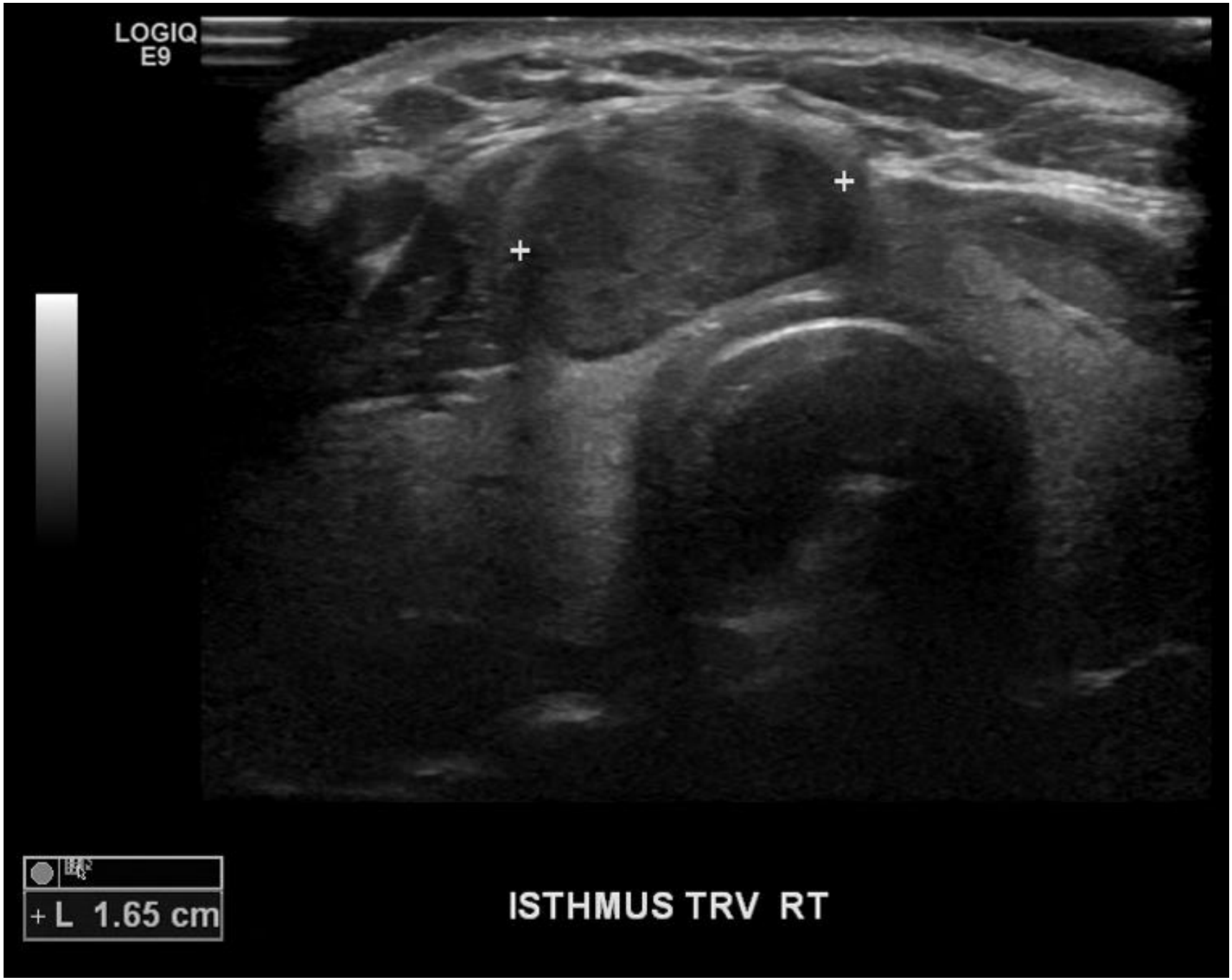
PROCEDURE REASON: CYSTIC THYROID NODULE
* * * * Physician Interpretation * * * *

RESULT:
HISTORY : nodule on physical exam.

Right thyroid lobe measures 4.4 x 2.1 x 1.9 cm. Left lobe measures 4.0 x 1.9 x 1.4 cm. Solid mid pole nodule within it measures 0.7 x 0.6 x 0.6 cm.

The isthmus measures 0.5 cm. Within the isthmus toward the right is a dominant solid nodule of 2.2 x 1.2 x 1.7 cm.

IMPRESSION: Dominant solid nodule within the isthmus. This corresponds to the palpable abnormality. Further evaluation is necessary.


LOGIQ
E9
+ L 1.65 cm
ISTHMUS TRV RT


LOGIQ
E9
LT THYROID TRV S-I

“Code words” in US reports that suggest high suspicion of malignancy

Microcalcifications

Coarse/peripheral calcifications (eggshell gaps)

Indistinct borders/local invasion/infiltrating or irregular margins

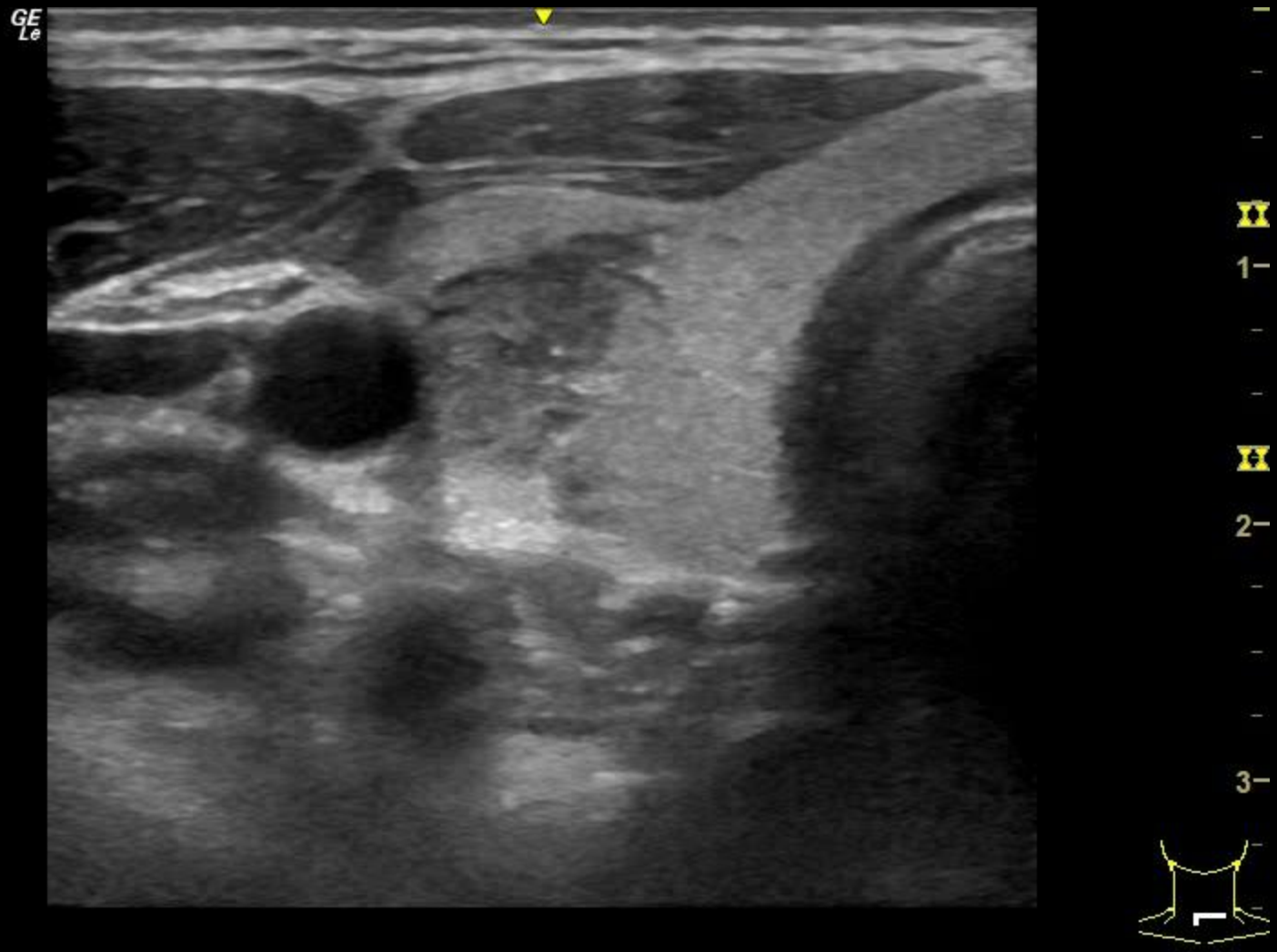
Lymphadenopathy

Taller than wide

Markedly hypoechoic

Intranodular hypervascularity


GE
Le
2
3


GE
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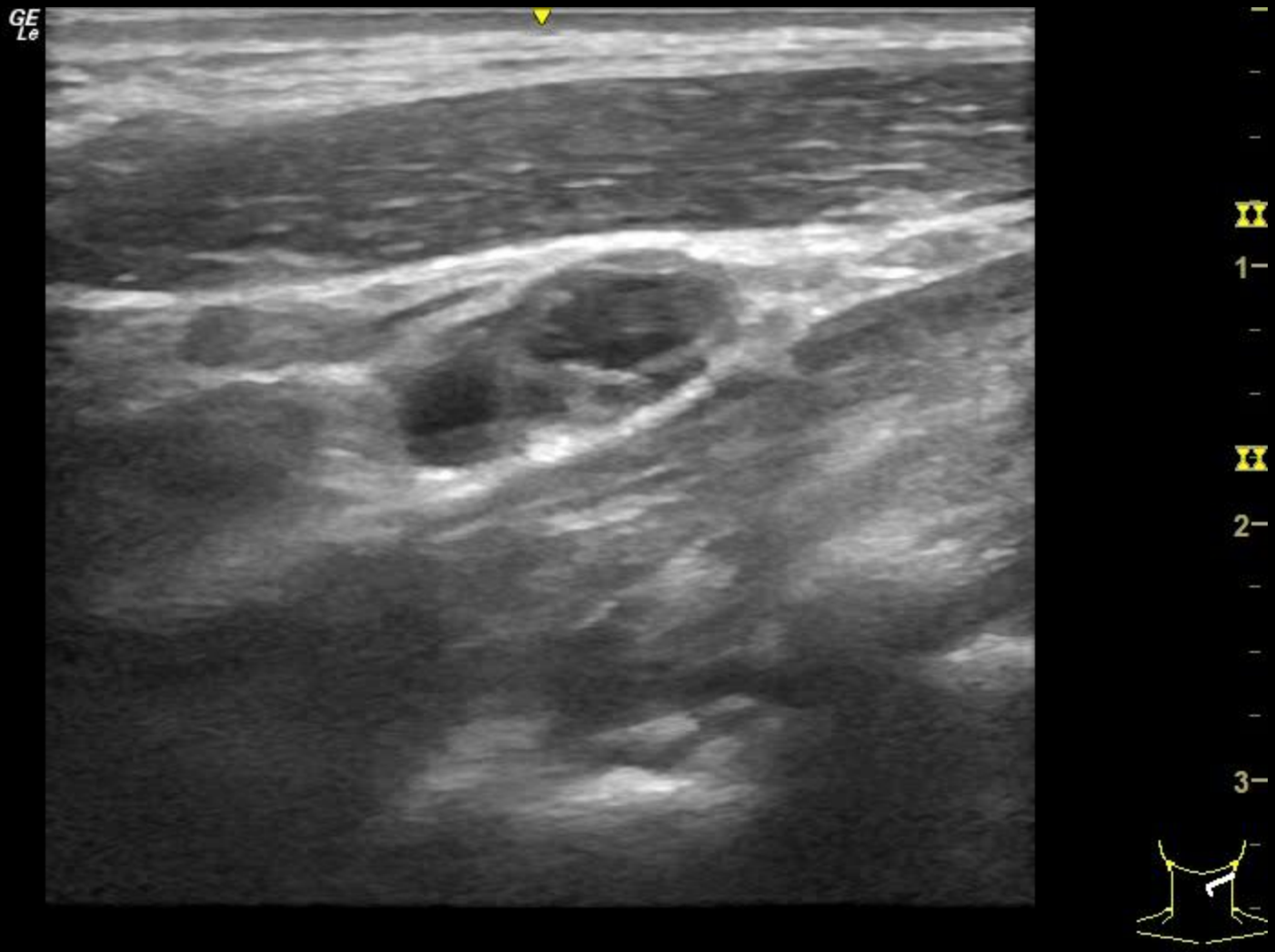
1
2
3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ATA “patterns”

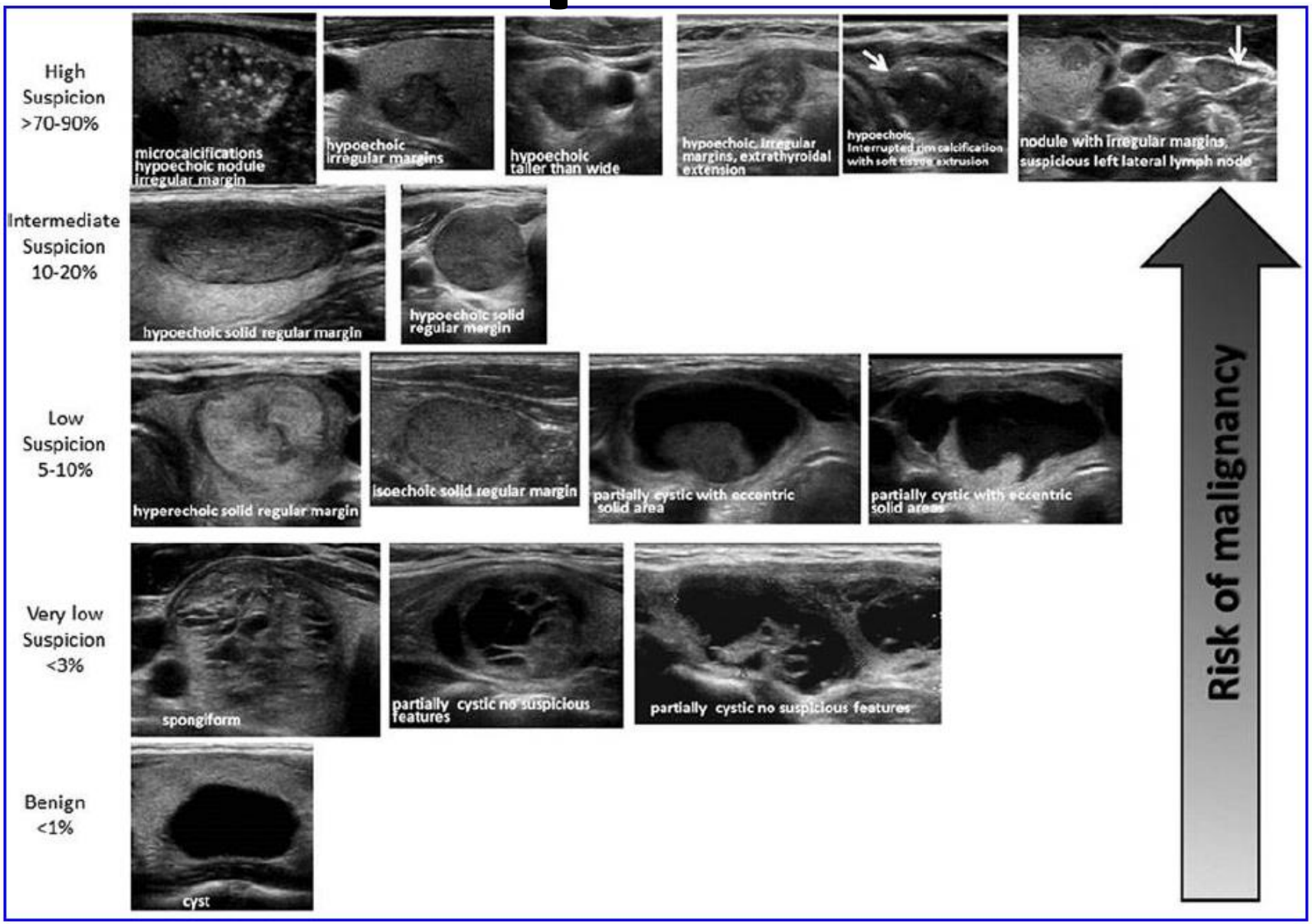


Table 6. Sonographic Patterns, Estimated Risk of Malignancy, and Fine-Needle Aspiration Guidance for Thyroid Nodules

Sonographic pattern	*US features*	*Estimated risk of malignancy, %*	*FNA size cutoff (largest dimension)*
High suspicion	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule ***with*** one or more of the following features: irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with small extrusive soft tissue component, evidence of ETE	>70–90[a]	Recommend FNA at ≥1 cm
Intermediate suspicion	Hypoechoic solid nodule with smooth margins ***without*** microcalcifications, ETE, or taller than wide shape	10–20	Recommend FNA at ≥1 cm
Low suspicion	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, ***without*** microcalcification, irregular margin or ETE, or taller than wide shape.	5–10	Recommend FNA at ≥1.5 cm
Very low suspicion	Spongiform or partially cystic nodules ***without*** any of the sonographic features described in low, intermediate, or high suspicion patterns	<3	Consider FNA at ≥2 cm Observation without FNA is also a reasonable option
Benign	Purely cystic nodules (no solid component)	<1	No biopsy[b]

US-guided FNA is recommended for cervical lymph nodes that are sonographically suspicious for thyroid cancer (see Table 7).

[a]The estimate is derived from high volume centers, the overall risk of malignancy may be lower given the interobserver variability in sonography.

[b]Aspiration of the cyst may be considered for symptomatic or cosmetic drainage.

ETE, extrathyroidal extension.

TIRADS “points”

The Point-Based Scoring System

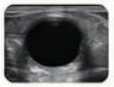
Category 1: Composition (1)

Cystic or completely spongiform (0 pts)

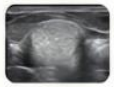
Mixed cystic and solid (1 pt)

Solid or almost completely solid (2 pts)

Category 2: Echogenicity (2)



Anechoic (0 pts)



Hyperechoic or isoechoic (1 pt)

Hypoechoic (2 pts)

Very hypoechoic (3 pts)

Category 3: Shape (3)

Wider-than-tall (0 pts)

Taller-than-wide (3 pts)

Category 4: Margin (4)

Smooth (0 pts)

Ill-defined (0 pts)

Lobulated or irregular (2 pts)

Extra-thyroidal extension (3 pts)

Category 5: Echogenic Foci (5)

None or large comet-tail artifacts (0 pts)

Macrocalcifications (1 pt)

Peripheral/Rim calcifications (2 pts)

Punctate echogenic foci (3 pts)

A Cumulative Approach: Points are assigned across five categories; the total sum determines the TI-RADS (TR) level.

Risk Levels and Malignancy Rates

TR1: Benign (0 Points)	TR2: Not Suspicious (2 Points)	TR3: Mildly Suspicious (3 Points)	TR4: Moderately Suspicious (4–6 Points)	TR5: Highly Suspicious (≥7 Points)
<0.3% Malignancy Risk	<1.5% Malignancy Risk	~4.8% Malignancy Risk	~9.1% Malignancy Risk	~35% Malignancy Risk

Management Thresholds

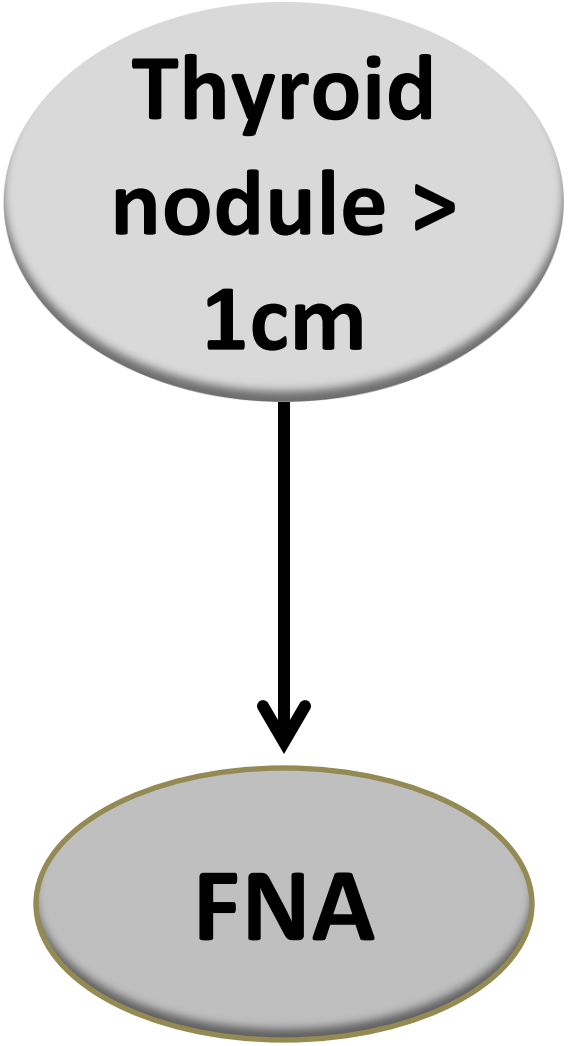
TR Level	FNA (Biopsy) Threshold	Follow-up US Threshold
TR1 (Benign)	No FNA	No Follow-up
TR2 (Not Suspicious)	No FNA	No Follow-up
TR3 (Mildly Suspicious)	≥ 2.5 cm	≥ 1.5 cm
TR4 (Moderately Suspicious)	≥ 1.5 cm	≥ 1.0 cm
TR5 (Highly Suspicious)	≥ 1.0 cm	≥ 0.5 cm

Fine Needle Aspiration (FNA) biopsy

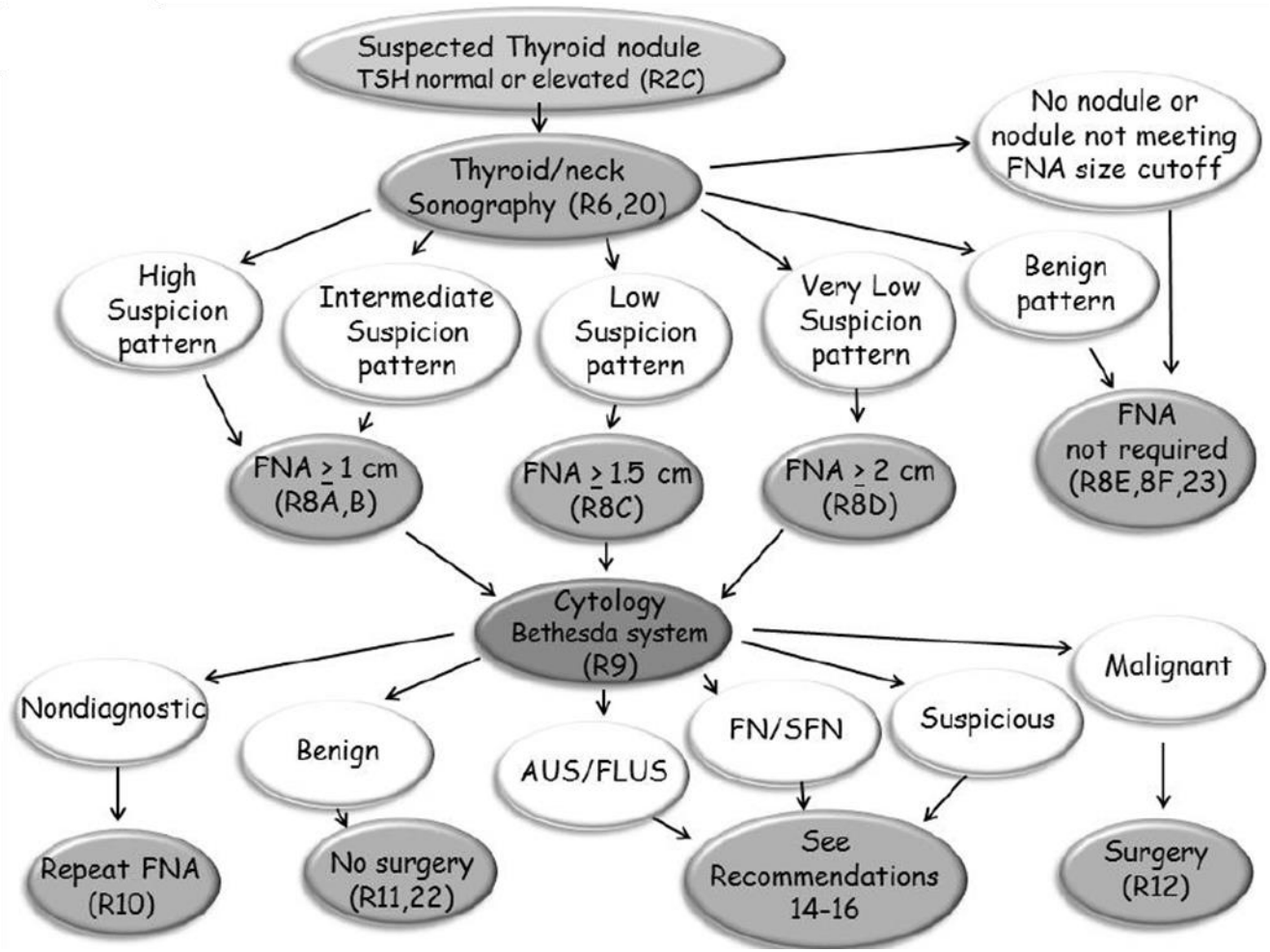
criteria based on nodule size and ultrasound features

molecular testing for indeterminant FNA results (Bethesda III/IV)

2004



2016



2015 ATA Guidelines for Thyroid Nodule/Cancer Management
http://www.ncbi.nlm.nih.gov/pubmed/?term=haugen+b+2016+thyroid+nodule+guidelines
Haugen et al. Thyroid. 2016 Jan;26(1):1-133

The Context

Discovery of thyroid nodule → History and Exam

TSH → **US** → FNA

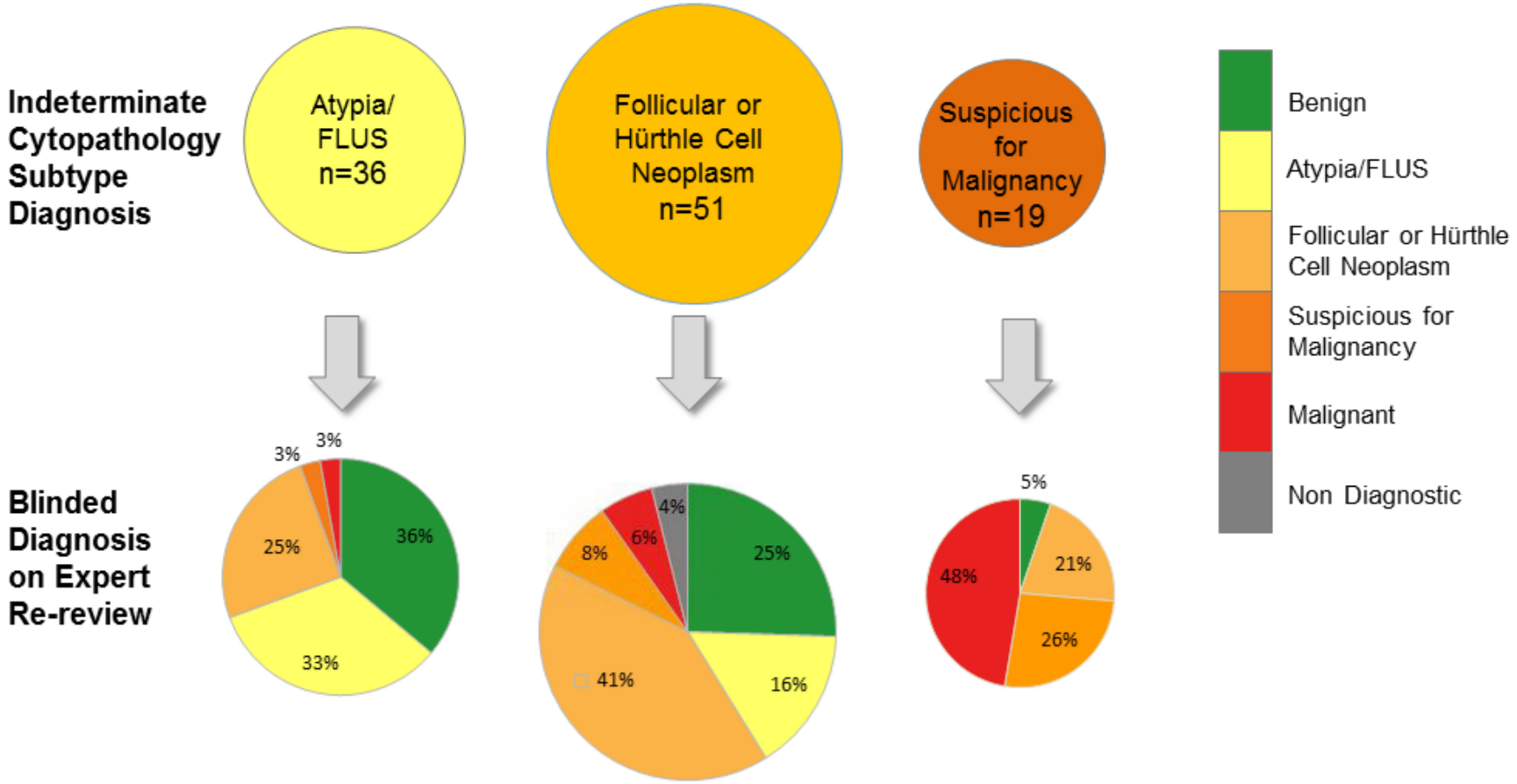
Bethesda cytopathology with % risk for thyroid cancer

I Non Diagnostic	II Benign	III AUS or FLUS	IV Follicular neoplasm	V Suspicious for Cancer	VI Cancer
rare	<5%	10-15%	30%	75%	99%
Repeat FNA	Monitor	Repeat FNA	Lobectomy	Lobe vs Total	Total

Indeterminate

Diagnosis of Cytopathology Indeterminate Subtype Not Reproducible on Expert Re-review

Using subtype diagnoses to drive clinical recommendations may not be reliable.



Haugen BR, et al. [Abstract LB-03], International Thyroid Congress, Paris, FR 2010.

The Context

Bethesda cytopathology with % risk for thyroid cancer

I Non Diagnostic	II Benign	III AUS or	IV Follicular	V Suspicious	VI Cancer
		"INDETERMINATE"			
rare	<5%	10-15%	30%	75%	99%
Repeat FNA	Monitor	Repeat FNA	Lobectomy	Lobe vs Total	Total
		Molecular Markers			

Personalized Care
Precision Medicine

- At the moment of meeting your patient
- Affirmation of benign thyroid nodules
- Molecular markers for cancer diagnosis
- Molecular markers for cancer prognosis
- Molecular markers for targeted therapies
- Genetics and Hereditary Syndromes

“Will this change what I do?

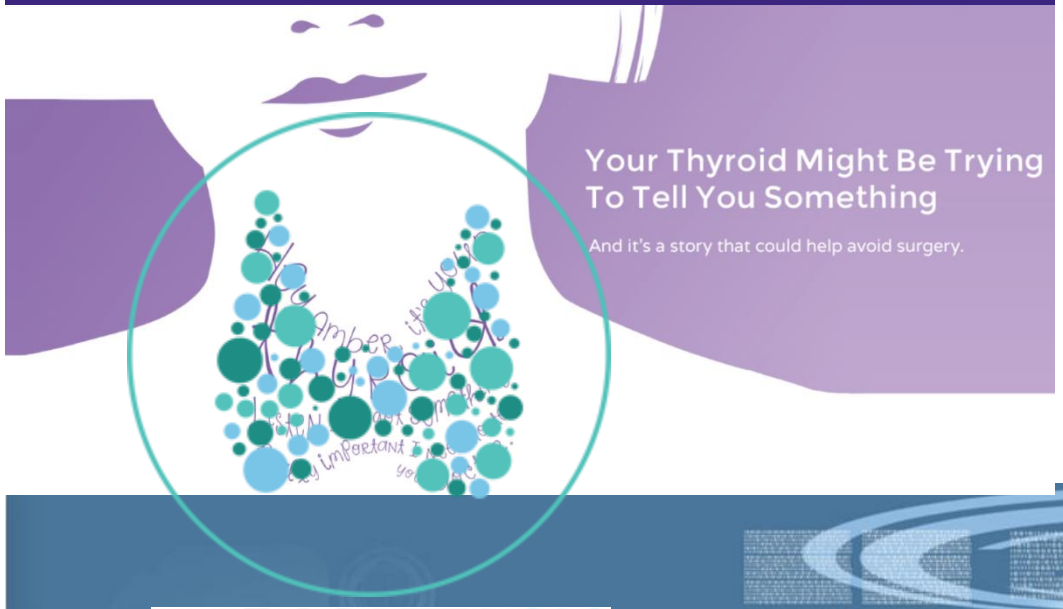
CBLPATH

A Sonic Healthcare Company

ThyroSeq® v.2 Next Generation Sequencing

Afirma®

Thyroid FNA Analysis



ThyGenX® THYROID ONCOGENE PANEL + ThyraMIR™ THYROID miRNA CLASSIFIER

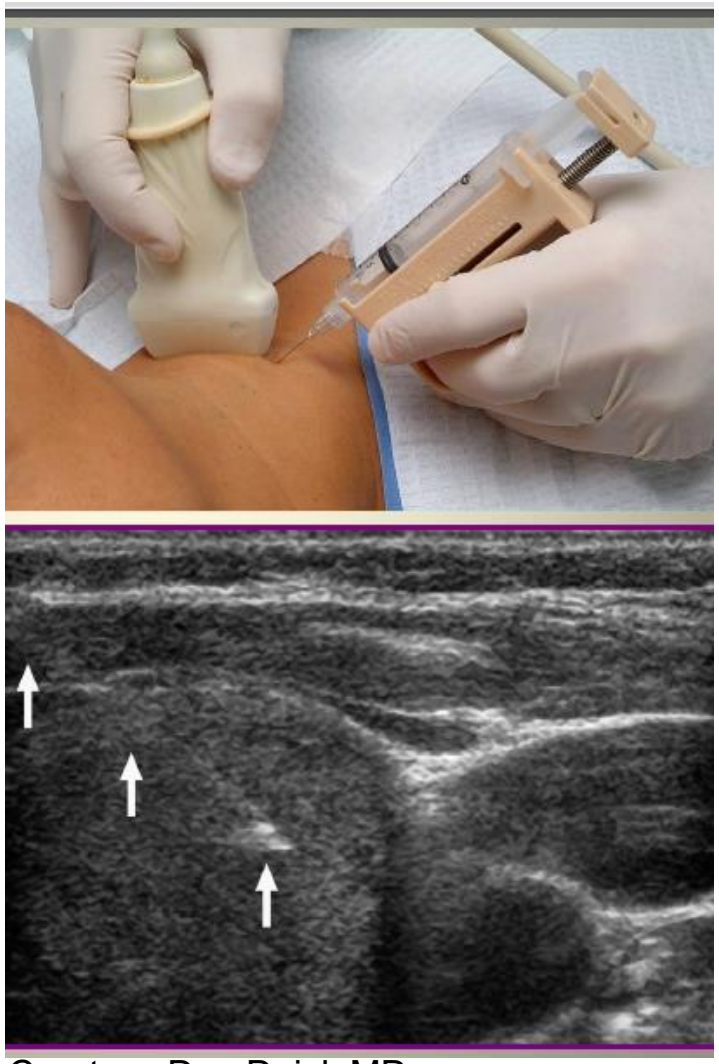
INTERPACE™ DIAGNOSTICS

GUIDING TREATMENT. DELIVERING INNOVATION.

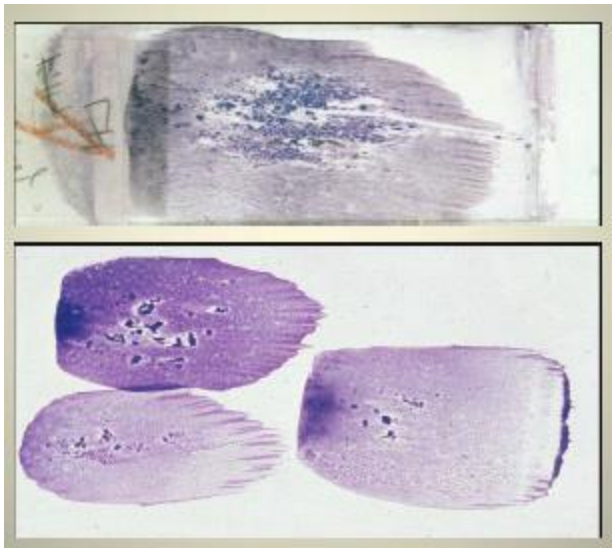
Advancing patient care through molecular diagnostic testing

ROSETTAGX REVEAL™

MOLECULAR MARKERS: DETECTION in FNA TISSUE and SLIDES



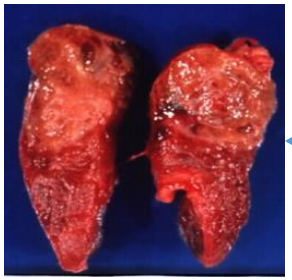
Courtesy Dan Duick MD

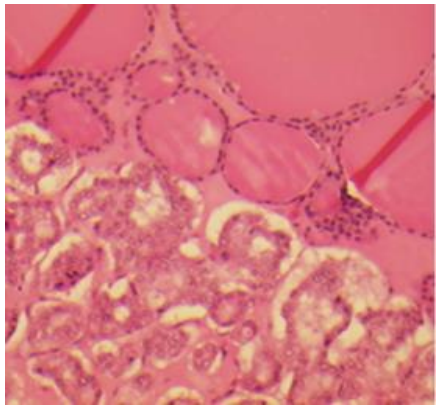


Supplies to submit patient samples for Afirma Thyroid FNA Analysis

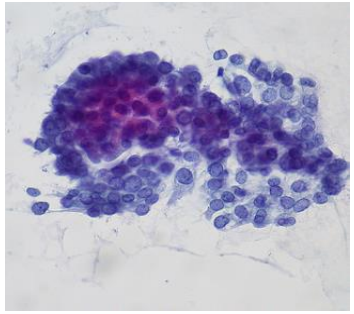
Molecular Cytology
Setting a New Standard in Diagnosis

Surgery → **Needle Aspirate Cytology** → **Molecular Cytology**



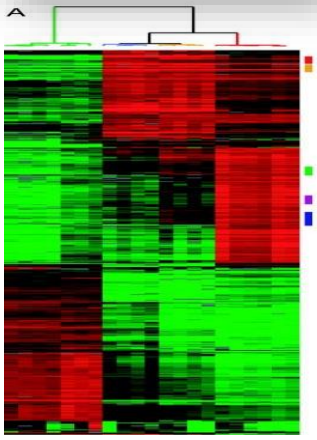


Histopathology



FNA Cytology: High Rate of Ambiguous Results

veracyte®

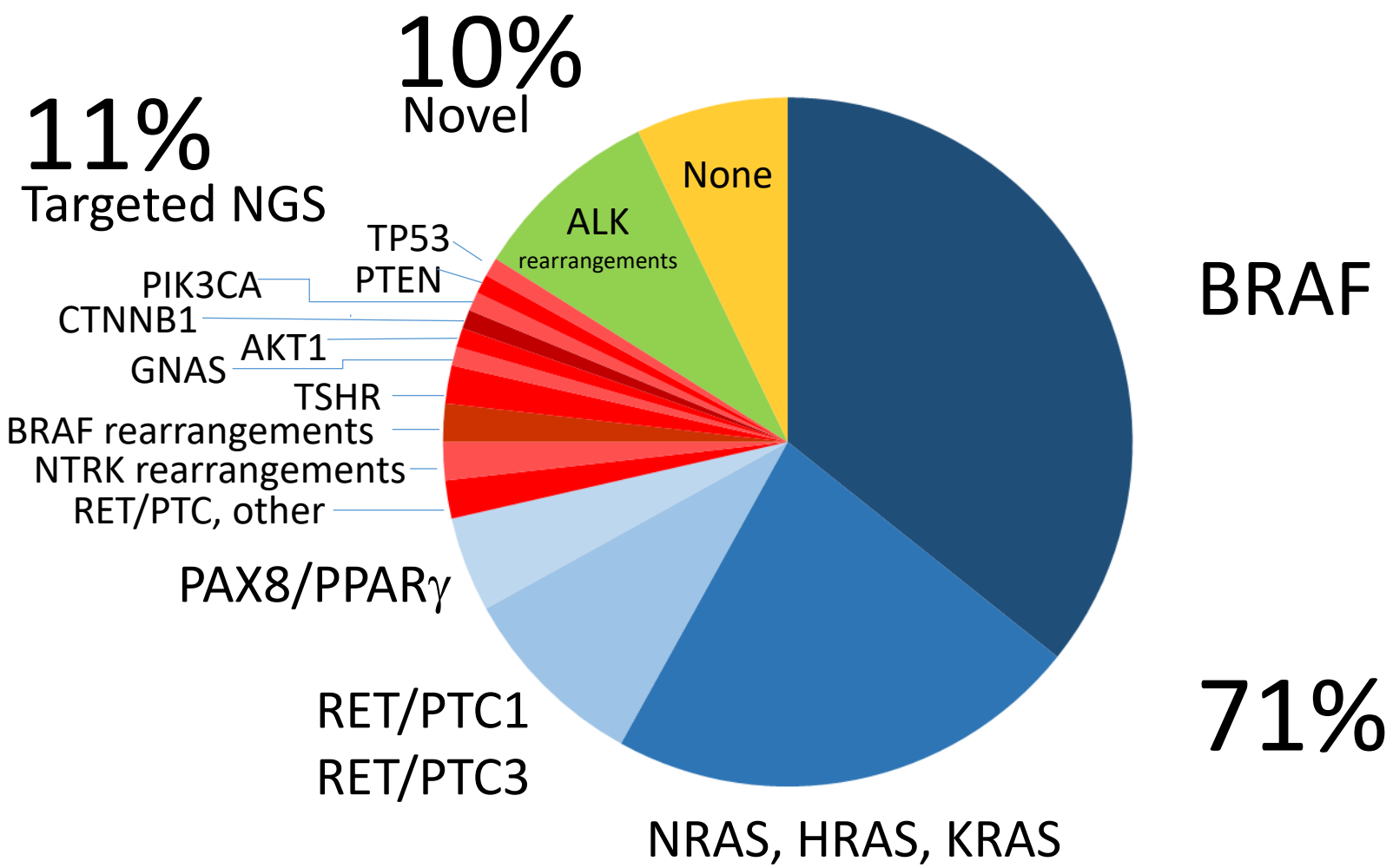


Accurate Diagnosis
Pre-operatively

1600's — 1960's - 1980's — 2012

Zajicek J. Aspiration Biopsy Cytology. Karger, Basle, 1974. (1st cytopathology monograph); Alexander et al NEJM 2012
Kaminsky DB. Aspiration Biopsy for the Community Hospital. Masson, New York, 1981. (first American guidebook)

Genetic Alterations in Thyroid Cancer



ThyroSeq (Targeted NGS for Thyroid Cancer)

Nikiforova et al JCEM
2013 Nov; 98(11):E1852-60

Afirma
Thyroid FNA Analysis

Patient Report

VG12011

Report Status: FINAL

Client ID: 6312

PATIENT [redacted] DOB: [redacted] Gender: [redacted] MRN#: [redacted]

REPORT INFORMATION

Collection Date:	03 Mar 2016	Clinic Name:	Banner University Medical Center		
Received Date:	04 Mar 2016	Submitting Clinician:	Mira Milas	Treating Clinician:	
Report Date:	15 Mar 2016	Phone #:	(602) 258-1519	Report CC:	
		Fax #:	(602) 839-0690	Afirma Req #:	BA138592

CLINICAL HISTORY

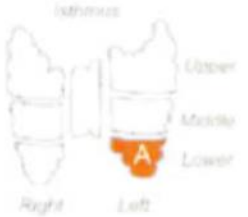
2 cm cyst that was PET (+)

REQUISITION COMMENTS

Comments: (unusual) but warranted, FNA--> no other around in concern

RESULTS SUMMARY

Nodule	Size	Location	Cytopathology	Afirma Gene Expression Classifier	Afirma MTC	Afirma BRAF
A	2 cm	Lower Left	Indeterminate	Suspicious	Neg.	N/A



RESULT DETAILS

NODULE A Size: 2 cm Location: Lower Left

Cytopathology Diagnosis: **Indeterminate - Atypia of Undetermined Significance** (AUS - Bethesda Category III)

Diagnostic Comments: These features are best classified as atypia of undetermined significance.

Microscopic Description: The cytologic preparations are sparsely cellular and predominantly contain Hurthle cells in a background of blood, few macrophages, and scant colloid. Cell block shows similar findings.

Afirma GEC Result: **Suspicious**

Afirma MTC Result: **Negative**

Afirma MTC Comments: A gene expression signature for medullary thyroid carcinoma (MTC) was not identified. A negative Afirma MTC result does not significantly change the risk of malignancy (ROM) of the Afirma GEC Suspicious result.

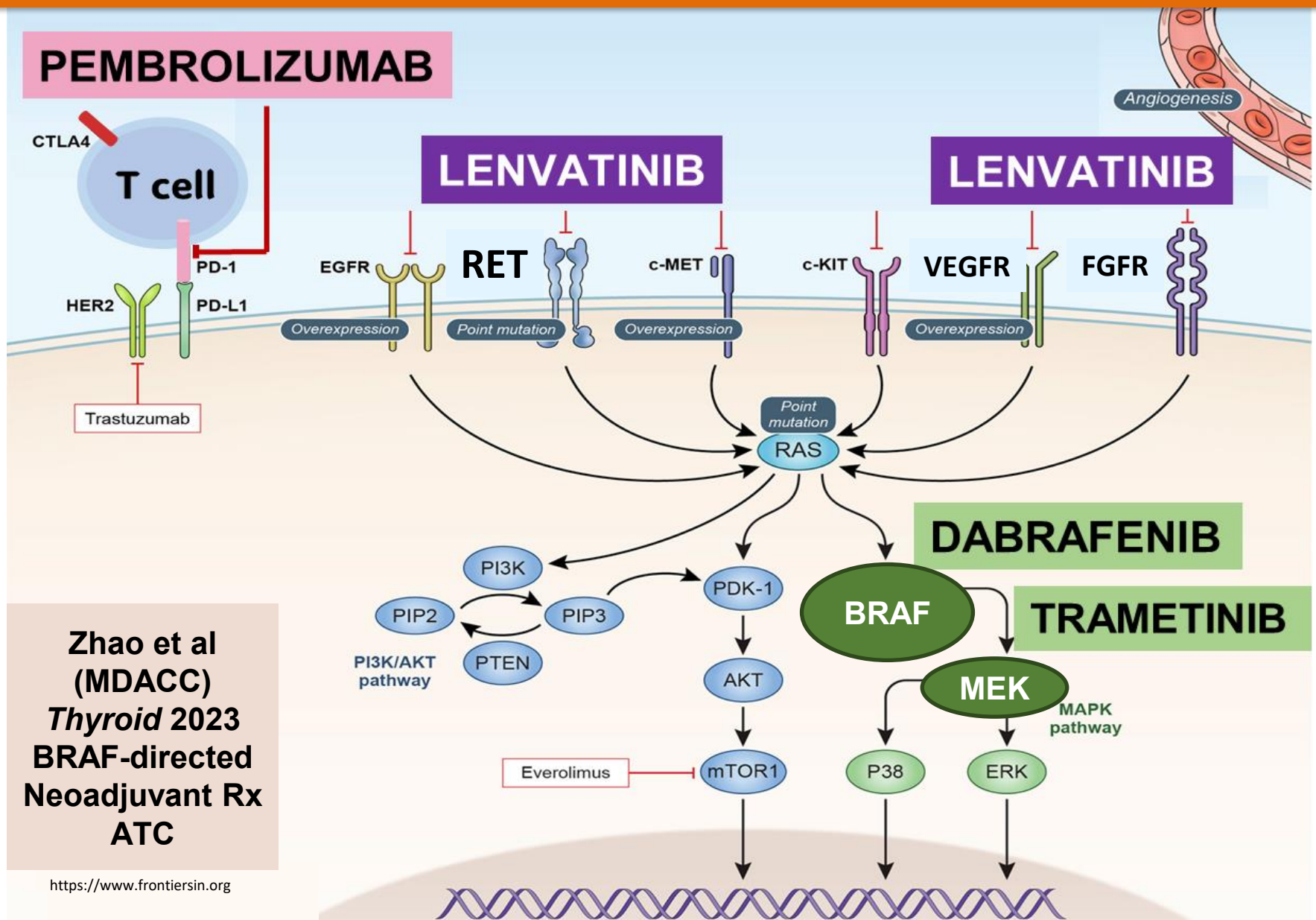
BACKGROUND INFORMATION FOR INTERPRETING AFIRMA RESULTS

A Timeline Moment

Courtesy Siperstein *et al*
Cleveland Clinic

Highlight new treatment options for thyroid nodules/thyroid cancer

NEOADJUVANT THERAPY FOR THYROID CANCER



Zhao et al (MDACC) *Thyroid* 2023 BRAF-directed Neoadjuvant Rx ATC

https://www.frontiersin.org

RESULTS: Patient with ATC alive at 2 Years

Surgically Unresectable Disease

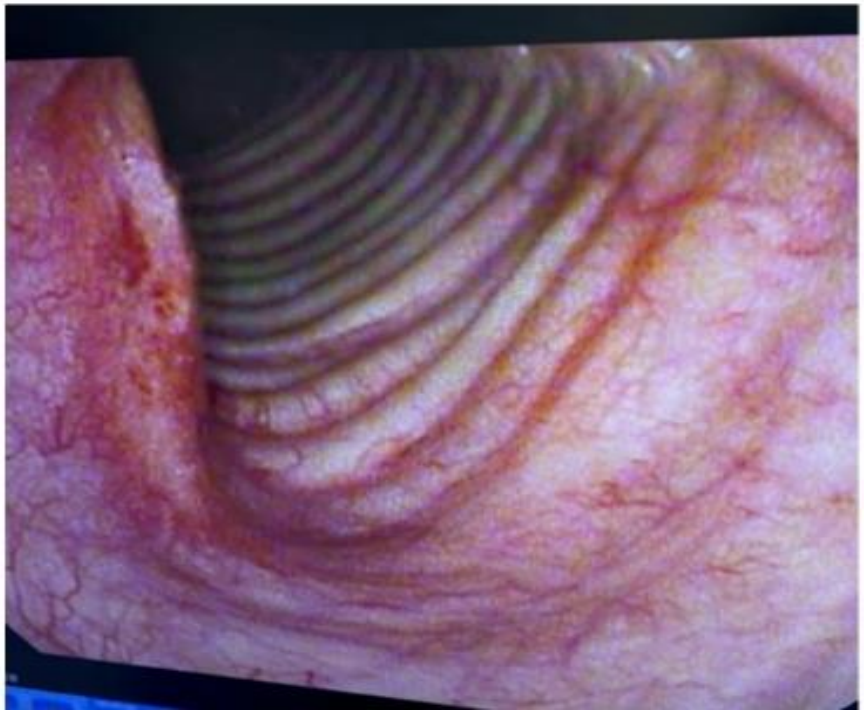
57M 12 cm ATC
BRAF/TERT
5 mo Dabrafenib/Trametinib
R1 resection (3 mm tracheal margin)
No local recurrence, PD (lung mets)

RESULTS: NEO-TKI Stopped Hemoptysis

Surgically Unresectable Disease

48M 10 cm PTC with 17/17 LN+
8+ months Dabrafenib/Trametinib
BRAF/BRCA/TERT/others
Prior R2 thyroidectomy

FEBRUARY

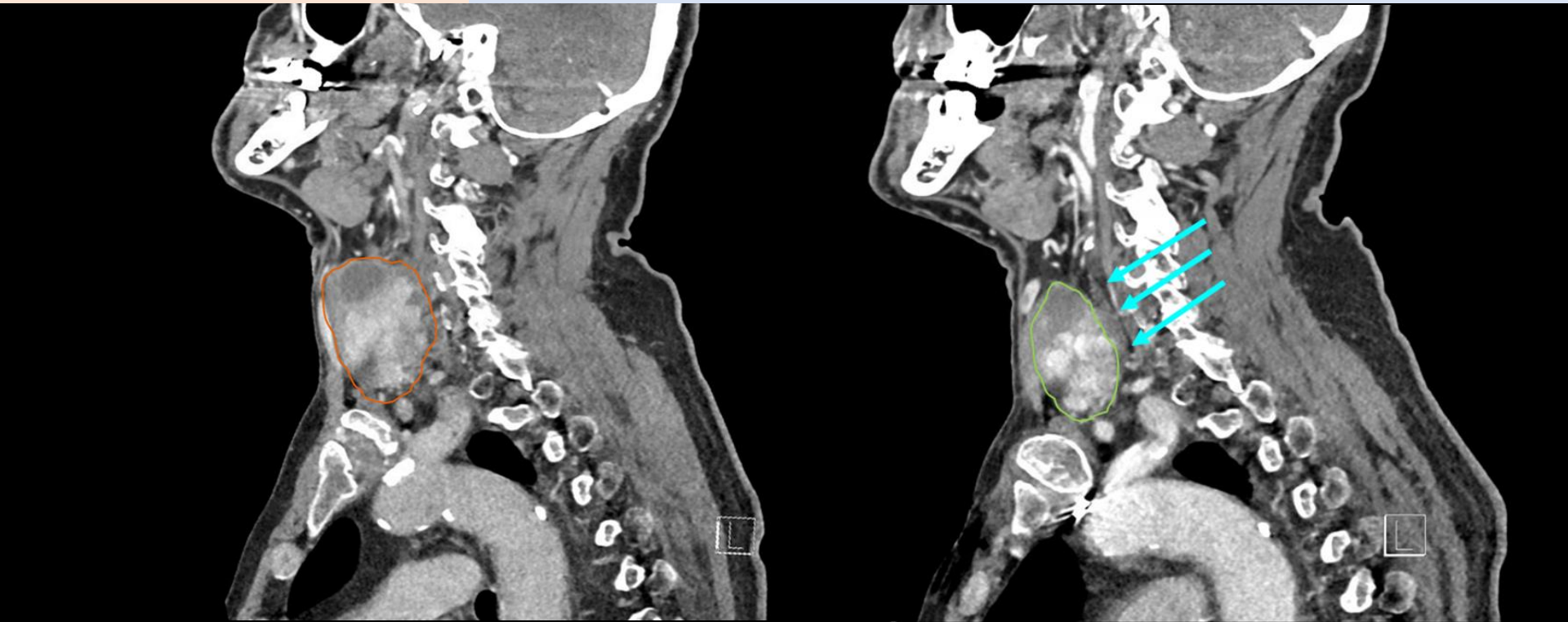


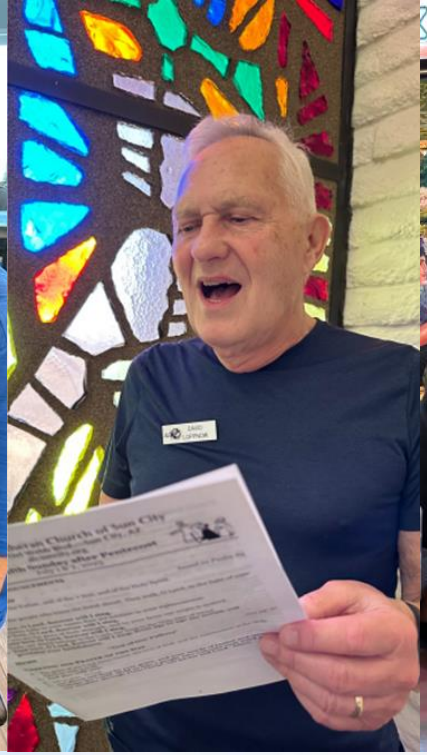
NOVEMBER

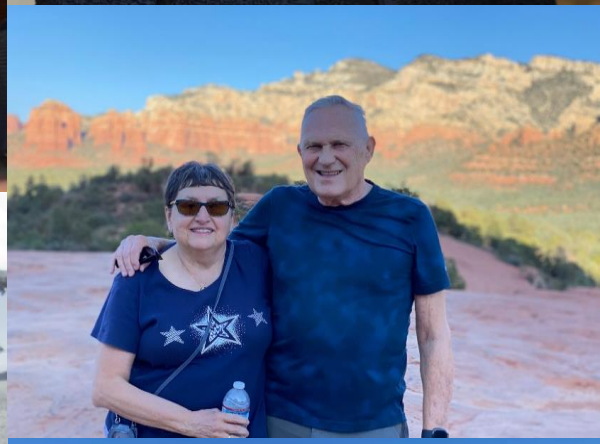
RESULTS: Avoided Laryngectomy

Resectable WITH Unacceptable Morbidities

80M 8 cm PTC BRAF
5 mo Dabrafenib/Trametinib
R0 resection
Alive, NED
Sings in Church



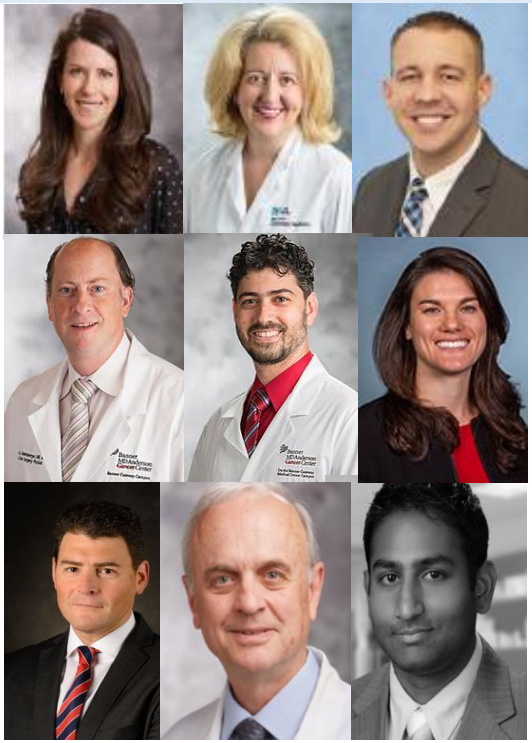





Pink Jeep Tours
74

College of Medicine - Phoenix

NEO-TKI Multidisciplinary Care 2024

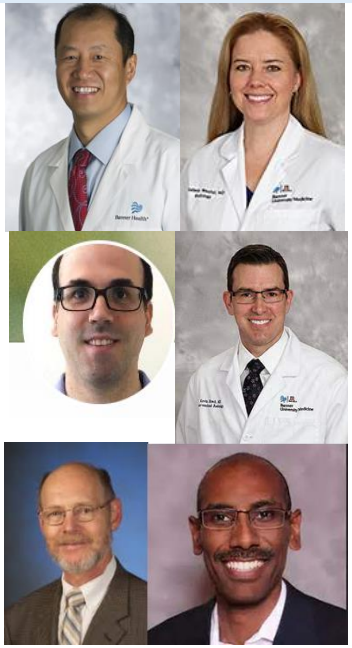


SURGERY
METZGER
MILAS
NELSON
SHELLENBERGER
TOMEH
DICKERSON

KUPFERMAN
MILLER
SUGUMARAN

ENDOCRINOLOGY
NASR
ALSAYED
AHMED

SHETH
NARULA
VINALES
HARMAN



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HEBERT

RADIOLOGY
WESTFALL
HIRSCH

BMG/VA ENDO

PATHOLOGY
EISEN
NOVOA-TAKARA
MAJEED
IBRAHIM
MOSTAFA

CLINICAL TEAMS & LSWs
BRINDLE
DIAZ-CATALAN

THE UNIVERSITY OF ARIZONA


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Thank You

Breast
Thyroid
Kidney
Intestine
Endometrium

Hereditary Cancer Syndromes

- Hereditary Breast & Ovarian Cancer Syndrome
- Hereditary Non-polyposis Colorectal Cancer Syndrome (Lynch Syndrome)
- Familial Adenomatous Polyposis (FAP)
- Cowden Syndrome
- Li-Fraumeni Syndrome
- Von Hippel-Lindau Disease
- Multiple Endocrine Neoplasias

Hereditary Cancer Syndromes

- Hereditary Breast & Ovarian Cancer Syndrome
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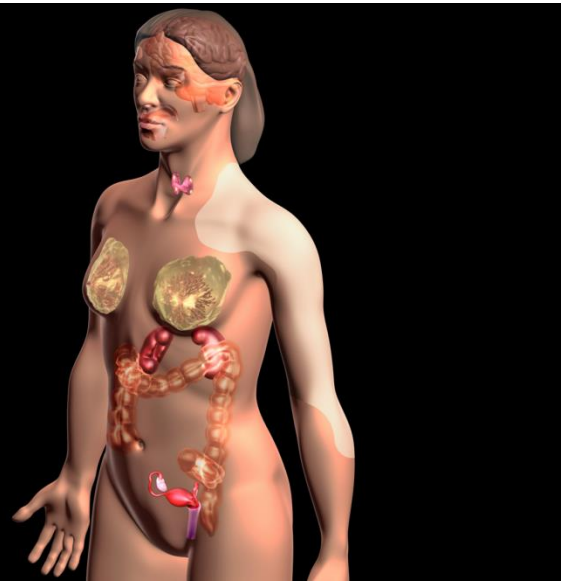
- ***Familial Adenomatous Polyposis (FAP)***
- ***Cowden Syndrome***
- ***Li-Fraumeni Syndrome***
- Von Hippel-Lindau Disease
- ***Multiple Endocrine Neoplasias***

Cowden Syndrome (CS)

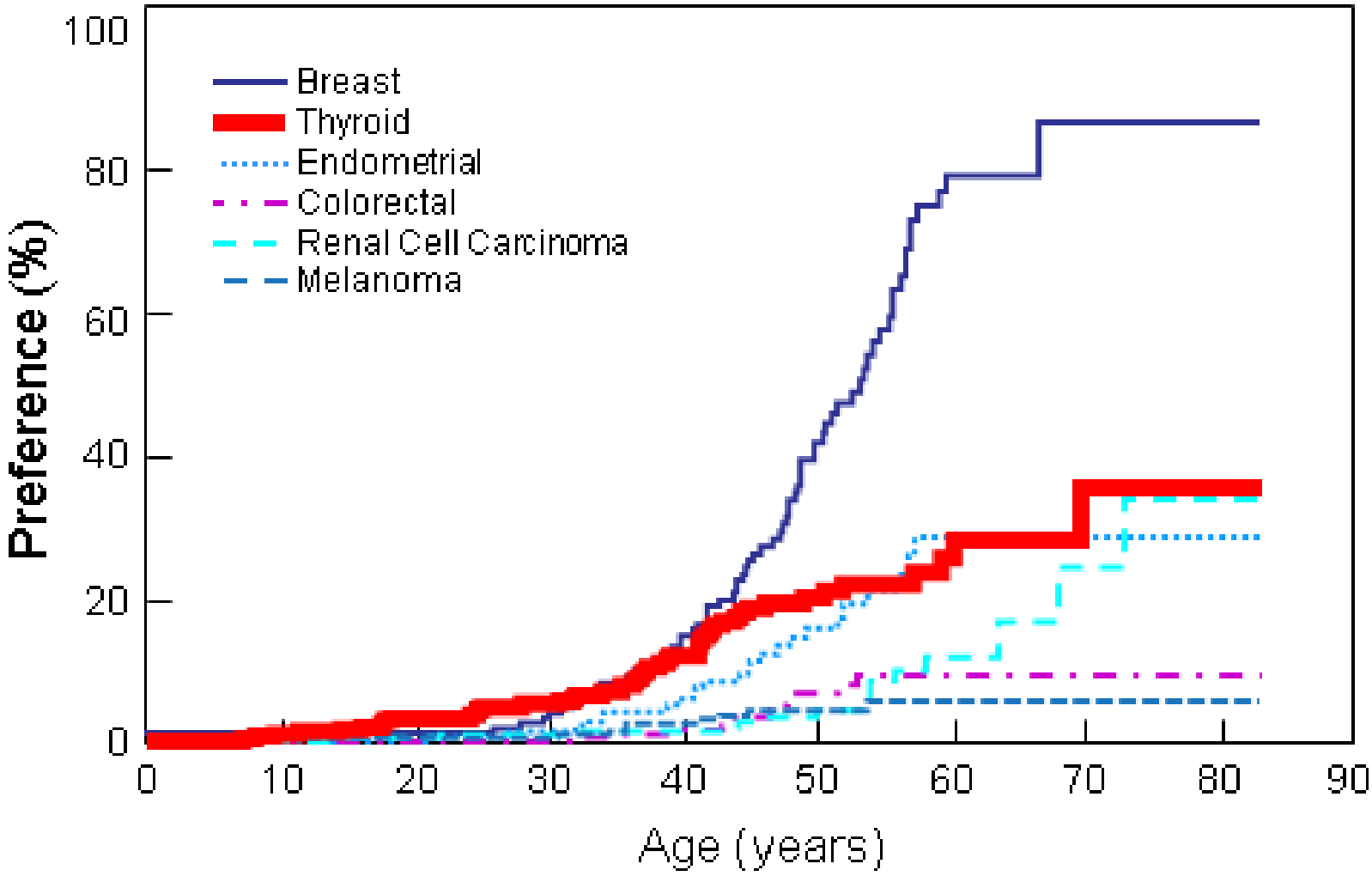
- Characterized by benign hamartomas
- Increased risk of malignant transformation

Breast
Thyroid
Kidney
Intestine
Endometrium



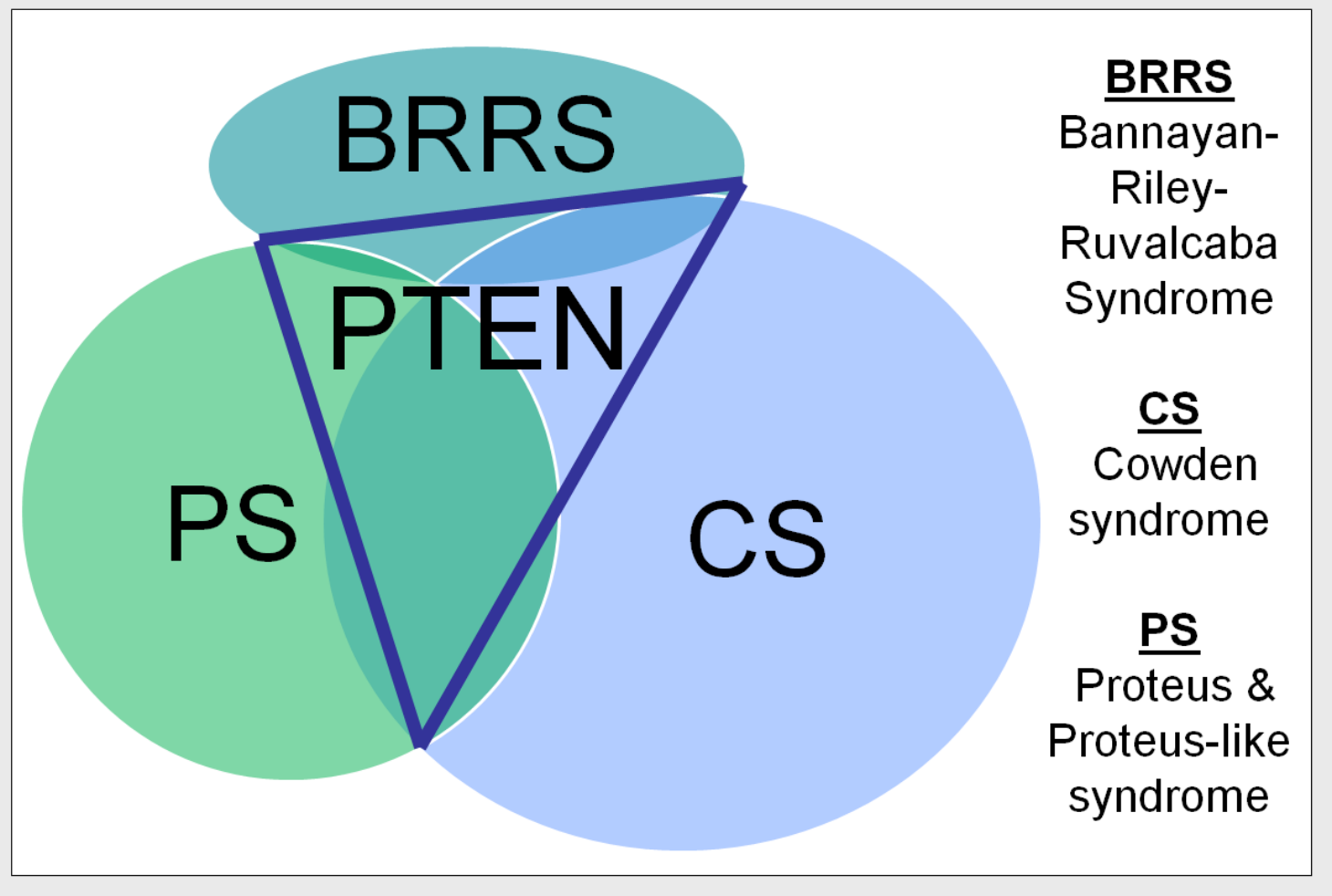
- Dominantly inherited germline mutation
  - tumor suppressor *PTEN*
  - *PTEN* mut+ is ultimate diagnostic confirmation

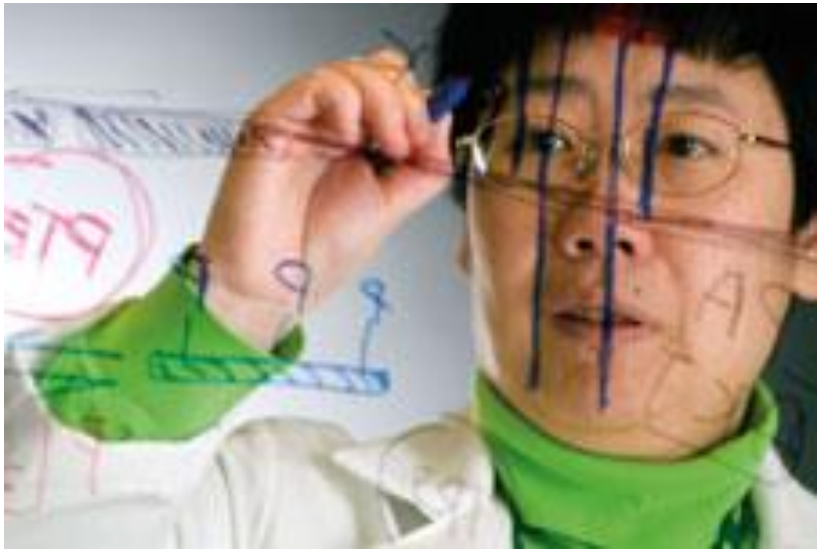
Of CS-associated cancers, thyroid cancer has the earliest onset and 2nd highest lifetime risk (35%)



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

PTEN Hamartoma Tumor Syndrome: PHTS





Charis Eng MD, PhD
Genomic Medicine Institute
Cleveland Clinic

PTEN

SDH (B-D)

KLLN

(RASAL1)

Nelen, M.R., G.W. Padberg, E.A. Peeters, A.Y. Lin, B. van den Helm, R.R. Frants, V. Coulon, A.M. Goldstein, M.M. van Reen, D.F. Easton, R.A. Eeles, S. Hodgsen, J.J. Mulvihill, V.A. Murday, M.A. Tucker, E.C. Mariman, T.M. Starink, B.A. Ponder, H.H. Ropers, H. Kremer, M. Longy, and C. Eng, Localization of the gene for Cowden disease to chromosome 10q22-23. Nat. Genet., 1996. 13(1): p. 114-6.

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**

CASE STUDIES

Cowden's Disease

A Possible New Symptom Complex with Multiple System Involvement

KENNETH M. LLOYD, II, M.D., and MACEY DENNIS, M.D.

Youngstown, Ohio

IN RECENT YEARS an accelerated interest has been directed toward a better understanding of the rare, familial, developmental diseases. The purpose of this communication is to define an unusual symptom complex which previously has not been described. Because of the multiplicity of findings, and the ill-defined classification for this disease, it shall be referred to as "Cowden's disease," the family name of the propositus. The clinical findings include: an adenoid facies; hypoplasia of the mandible and maxilla; a high-arch palate; hypoplasia of the soft palate and uvula; microstomia; papillomatosis of the lips and oral pharynx; scrotal tongue; multiple thyroid adenomas; bilateral virginal hypertrophy of the breasts with advanced fibrocystic disease and early malignant degeneration; pectus excavatum; scoliosis; space-occupying lesions in the liver and bone; abnormalities of the central nervous system; and a history of *forme fruste* of the syndrome in other members of the family.

CASE REPORT

A 20-year-old female was admitted to the Youngstown Hospital Association on March 14, 1962, because of a lesion on her right breast.

The patient had enjoyed good health until 2 months prior to admission when she developed a small, draining, ulcerative area on the inferior lateral surface of the right breast following minor trauma. This failed to heal in the subsequent months.

The patient had had difficulty with her breasts since her menarche at the age of 12 years, when the breasts had rapidly and progressively enlarged to an abnormal degree with the development of multiple, occasionally tender nodules of varying size. The skin overlying the breasts became increasingly discolored with frequent ulceration and drainage. Healing of these ulcerations was always retarded, but usually complete within a few weeks. A biopsy of a nodule in the left breast was done at the age of 16, and it was reported as showing fibrocystic disease of the breast. Bilateral simple mastectomy was recommended at the time but was refused. Hormone therapy was of no therapeutic benefit and was discontinued 2 years prior to the present admission.

PAST HISTORY

The patient had had her thymus irradiated at the age of 2. She had had all her teeth extracted at the age of 16 because of advanced decay and malocclusion.

FAMILY HISTORY

The patient's mother, age 55, has a large goiter and a marked emotional stutter. A sister, who died accidentally at the age of 20, had a high-arched palate, difficulty with articulation, a pectus excavatum, a large thyroid tumor, mild mental retardation, and numerous small firm skin tumors of an unknown nature. Her remaining sibling, a 24-year-old female, appears to be normal with none of the physical characteristics of her sisters.

Two maternal aunts died of carcinoma of the breast. One maternal aunt died in a state mental institution at the age of 35 of post-encephalitic parkinsonism. She was described as having had

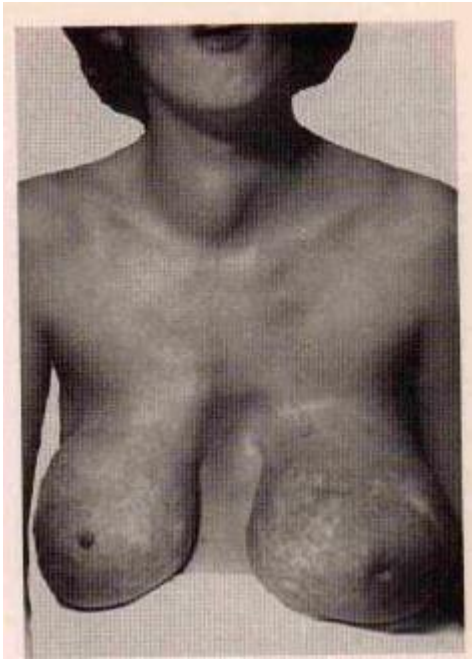
Received September 28, 1962: accepted for publication October 3, 1962.

From the Department of Medicine, Youngstown Hospital Association, Youngstown, Ohio.

Requests for reprints should be addressed to Kenneth M. Lloyd, II, M.D., Henry Ford Hospital, Box 166, Detroit 2, Michigan.

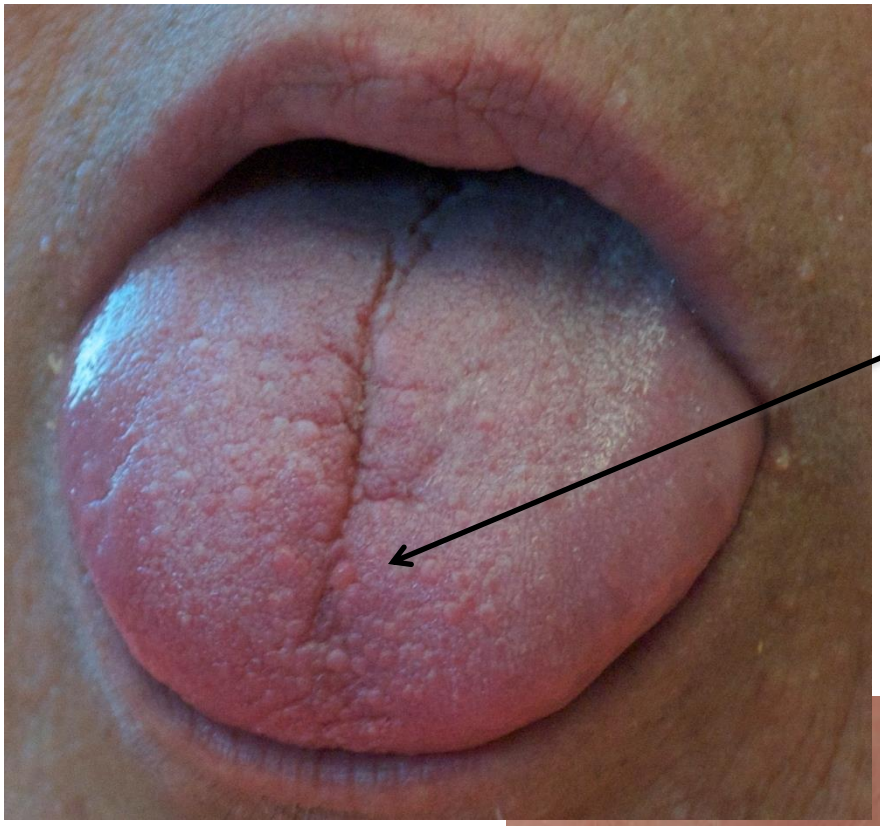
Rachel Cowden Youngstown, Ohio 1960

Lloyd and Dennis
Ann Intern Med
963;58:136-42.

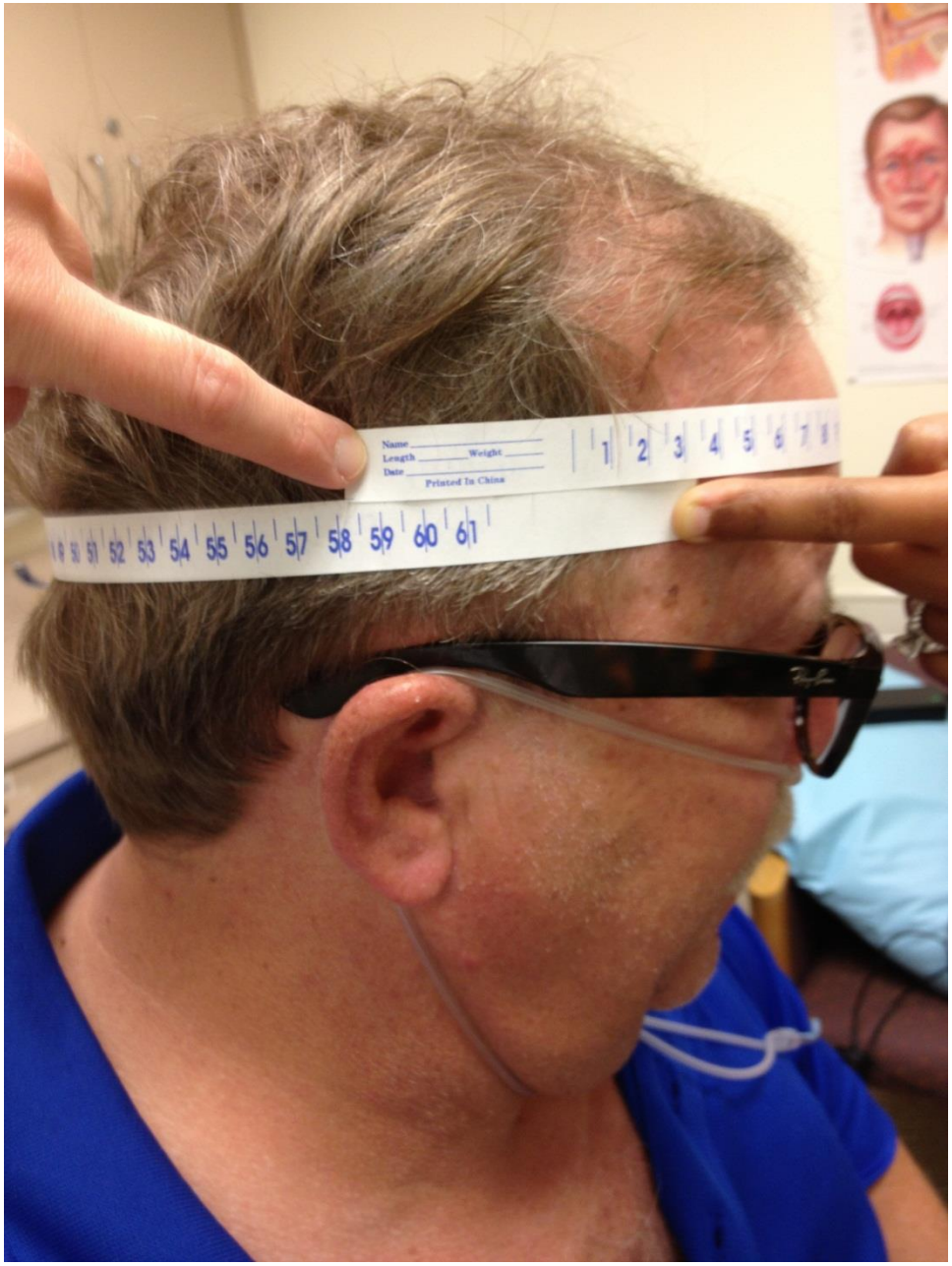


Trichilemmoma

Papillomas



Acral keratoses

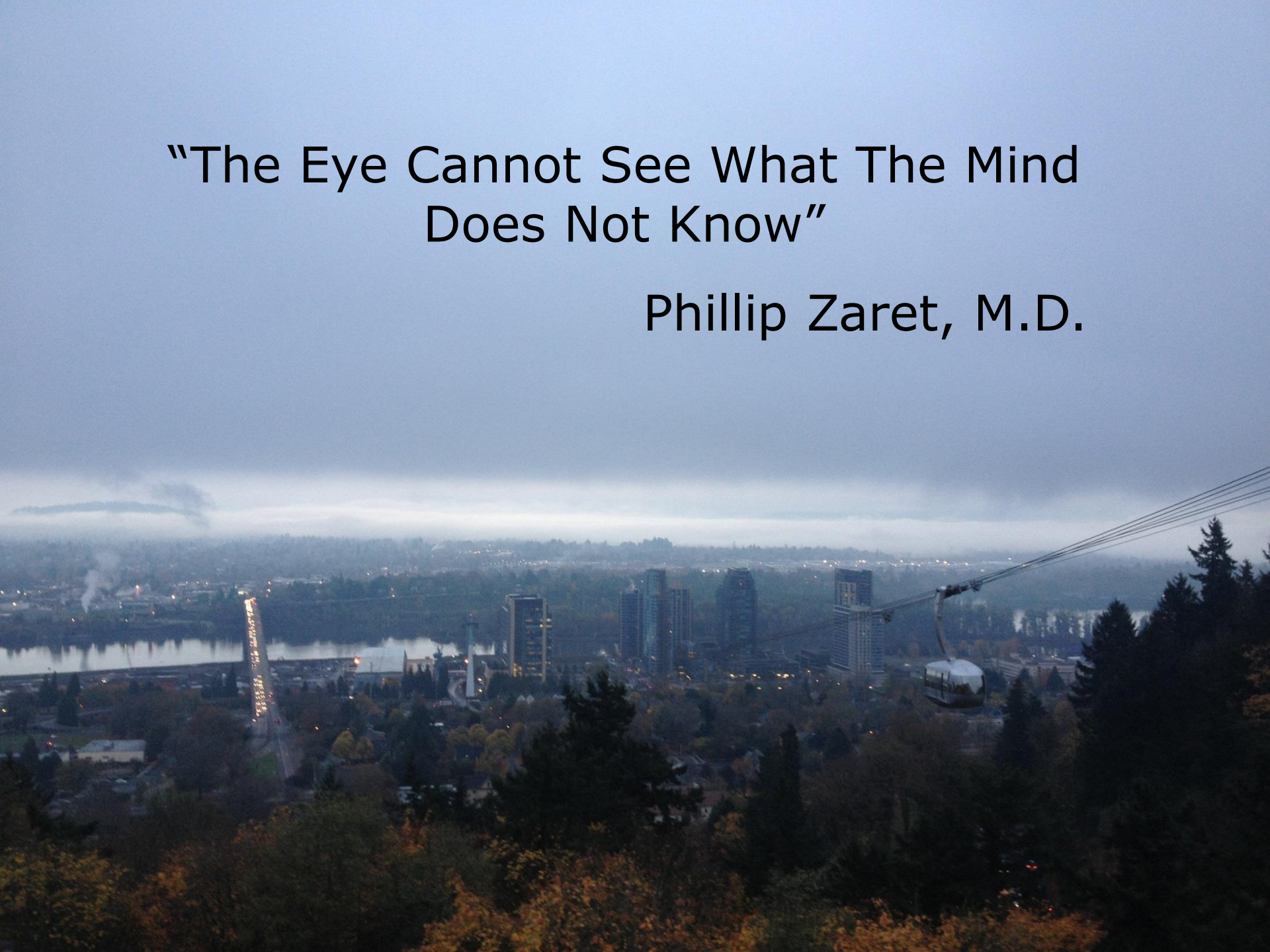


Macrocephaly

Men: 58.0 cm
Women: 57.3 cm

occipitofrontal circumference
>2 standard deviations
over the population mean

97.5th percentile


"The Eye Cannot See What The Mind Does Not Know"
Phillip Zaret, M.D.

http://www.lerner.ccf.org/gmi/ccscore/

Risk Calculator for Estimating a Patient's Risk for PTEN Mutation

Welcome to the Cleveland Clinic risk assessment tool for estimation of a person's risk of having a *PTEN* mutation. Clinical syndromes often associated with this gene mutation include Cowden syndrome (CS) and Bannayan-Riley-Ruvalcaba syndrome (BRRS). This tool was designed for use by healthcare professionals. If you are not a healthcare professional, you are encouraged to discuss the results with your doctor or a genetics healthcare provider. Detailed information on the Cleveland Clinic adult score and pediatric criteria is available

Tan et al *Am J Hum Gen* 2011