

Thyroid Disease: Nodules and Thyroid Dysfunction 2014

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Case 1

- 28 year old woman sees OB for routine visit
- ROS:
 - Negative except for occasional dysphonia
- PE: BP 122/78, HR 72 BPM, 5' 5", 120 lbs.
- Thyroid Exam: 2.5 cm smooth nodule left
 - Moves easily with swallowing
 - 1 cm left SCM lymph node palpable

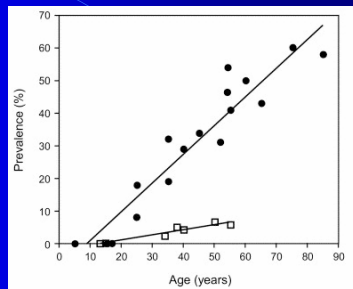
Goiters and Nodules



- **Goiter** definition: enlargement of thyroid gland, causes swelling in the neck
 - Endemic goiter; enlargement a response to a lack of iodine
 - Sporadic goiter; hyperplastic or neoplastic overgrowth
 - Toxic nodular goiter; autonomous thyroid hormone production
 - Exophthalmic goiter (Graves' disease) associated with hyperthyroidism
- **Thyroid Nodule**: area of different contour or consistency on palpation with differing echotexture on sonographic examination

Thyroid Nodule Prevalence

- By age 30, ~20% of the population has a thyroid nodule (women>men)
- Likely hood of malignancy is higher in the extremes of age (<20 years, >70 years)
- Lifetime likelihood of a nodule is ~ 60%



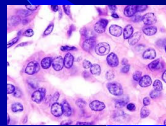
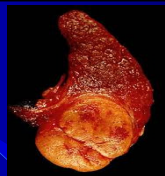
● Detected by ultrasound/autopsy
□ Detected by palpation

Mazzaferri EL, NEJM. 1993;328:553-559.

Thyroid Cancer - 2014

By the numbers (estimated)

- 62,980 new cases
- 3x more common in women
 - 47,790 women; 15,190 men
- More lethal in men
 - Deaths: 1060 women, 830 men



Incidence peaks earlier in women (diagnosed in 4th-5th decades) than in men (diagnosed in 6th-7th decades)

Siegel R et al. 2014 CA Cancer J Clin. 64:9-24

Thyroid Cancer Risk: Multinodular (MNG) versus Single Nodule (SN) Goiter

Study or Subgroup	MNG		SN		Weight	Odds Ratio		M-H, Random, 95% CI
	Events	Total	Events	Total		M-H, Random, 95% CI	Odds Ratio	
Abu-Eshy, S 1995	14	172	16	105	4.9%	0.49	[0.23, 1.06]	
Belfiore, A 1992	47	1152	211	4485	15.3%	0.86	[0.62, 1.19]	
Deandrea, M 2002	12	174	15	246	4.6%	1.14	[0.52, 2.50]	
Edino, S 2010	24	160	1	13	0.8%	2.12	[0.26, 17.05]	
Franklin, J 1993	1	72	19	321	0.8%	0.22	[0.03, 1.70]	
Fratesi, M 2006	119	804	175	1181	18.8%	1.00	[0.78, 1.29]	
Khairy, G 2004	16	124	24	172	5.9%	0.91	[0.46, 1.80]	
Marqusee, E 2000	8	90	4	60	2.0%	1.37	[0.39, 4.75]	
Matesa, N 2005	15	289	6	117	3.2%	1.01	[0.38, 2.68]	
McCall, A 1986	9	69	16	96	3.8%	0.75	[0.31, 1.81]	
Papini, E 2002	13	207	18	195	5.1%	0.66	[0.31, 1.38]	
Rago, T 2010	411	19923	446	13549	25.1%	0.62	[0.54, 0.71]	
Sachmechi, I 2000	9	92	4	50	2.1%	1.25	[0.36, 4.27]	
Taneri, F 2005	35	237	24	133	7.7%	0.79	[0.45, 1.39]	
Total (95% CI)		23565		20723	100.0%	0.80	[0.67, 0.96]	
Total events	733		979					
Heterogeneity: Tau ² = 0.03; Chi ² = 19.86, df = 13 (P = 0.10); I ² = 35%								
Test for overall effect: Z = 2.37 (P = 0.02)								

Squares/horizontal lines: Odds ratio/95%CI; diamonds: pooled odds ratio

Brito JP et al. Thyroid. 2013 Apr;23(4):449-55

Thyroid Cancer Risk: Multinodular vs. Single Nodule Goiter: Results

- MNGs were associated with a lower risk compared to SN (pooled odds ratio 0.8 [95% CI, 0.67-0.96]; I(2)=35%)
- A subgroup analysis suggested that this difference depends on the inclusion of studies conducted outside the United States (Outside the US the odds ratio was 0.71 [95% CI, 0.60-0.83]; I(2)=11%)
- Thyroid cancer may be less frequent in MNG compared to SN, particularly outside the U.S., perhaps due to relative iodine-deficiency in these area areas

Brito JP et al. *Thyroid*. 2013 Apr;23(4):449-55

Risk Factors for malignancy: Patient History

- Surgical Dx of thyroid cancer in contralateral lobe
- Ionizing Irradiation (XRT) as child/adolescent
- Calcitonin > 100 pg/mL
- PET positive thyroid nodule
- Low dietary iodine intake
- Thyroid cancer in first degree relative

<http://www.cancer.org/cancer/thyroidcancer/detailedguide/thyroid-cancer-risk-factors>

Risk Factors: Family History

- FHx non-medullary thyroid cancer; 1° relative
- Familial adenomatous polyposis (FAP) (≥ 12%)
- PTEN-hamartoma tumor syndromes
 - Carney complex
 - Werner & Pendred syndrome
- MEN2/FMTC RET proto-oncogene positive
 - Familial medullary thyroid cancer (MTC)
 - Multiple endocrine neoplasia type 2 (MEN 2)

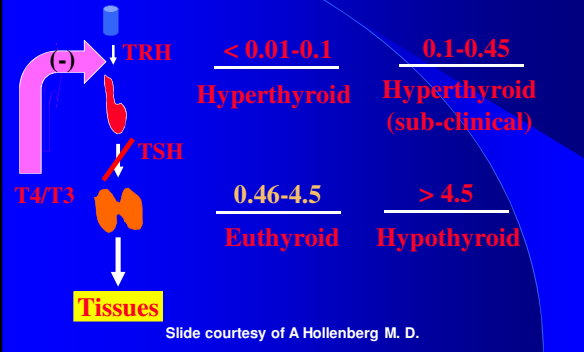
Fagin and Nikiforov 2013 *The Thyroid* pp681-702
<http://www.cancer.org/cancer/thyroidcancer/detailedguide/thyroid-cancer-risk-factors>

Thyroid Nodule Laboratory Diagnosis

- TSH

Haugen BR et al. 2014 ATA Thyroid Nodule and DTC Guidelines

WHAT DOES THE TSH LEVEL MEAN ?



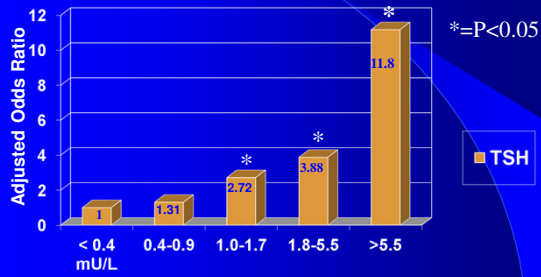
Thyroid Nodule Laboratory Diagnosis

- TSH

- Suppressed C/W thyrotoxicosis
 - Malignancy unlikely
- Elevated C/W hypothyroidism

Haugen BR et al. 2014 ATA Thyroid Nodule and DTC Guidelines

TSH Concentration & Risk of Malignancy



Boelaert, et al. *JCEM*. 2006;91(11):4295-301.

Thyroid Nodule Laboratory Diagnosis

- **TSH**
 - Suppressed C/W thyrotoxicosis
 - Malignancy unlikely
 - Elevated C/W hypothyroidism

RADIONUCLIDE SCANNING

Indication:

- Thyrotoxic nodule identification (TSH < normal)
- ^{99m}Tc (False +s), ¹³¹I (Rads) or ¹²³I (Std)

Haugen BR et al. 2014 ATA Thyroid Nodule and DTC Guidelines

Thyroid Ultrasound

Indication: normal to ↑ TSH

- Defines a distinct nodule vs. abnormal parenchyma
- Role to guide FNA (cystic, posterior)
- MNG nodule selection
- Useful in f/u of low risk patient, incidentaloma

● MRI / CT SCANNING

- Offer little in pre-operative diagnosis
- Contrast administration may delay Dx &/or Rx

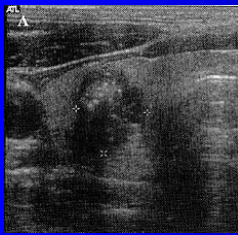
Haugen BR et al. 2014 ATA Thyroid Nodule and DTC Guidelines

Analysis of US Predictors

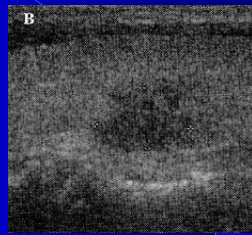
Characteristic	Sensitivity	Specificity
• Microcalcification	44%	89%
• Hypoechoic	81%	53%
• Solid	86%	18%
• Absence of Halo	66%	54%
• Intranodal vascularity	62%	77%
• Poorly defined margin	55%	79%
• Taller than Wide	48%	92%

Haugen BR et al. 2014 ATA Thyroid Nodule and DTC Guidelines

Papillary Thyroid Cancer Appearance on U/S



58 male, 10 mm mass
+ microcalcifications



39 female, 9 mm mass
+ irregular margins

Tae et al. Thyroid 2007 17:461-466

Ultrasound Pattern = Risk

- **High Suspicion** = 70-90% Cancer Risk
 - Hypoechoic, microcalcs, irregular border
 - Hypoechoic, microlobulated margin
 - Hypoechoic, irreg margin, Taller than wide
 - Hypoechoic, irreg margin, X-thyroid Extension
 - Irregular margins, suspicious Lymph nodes
- **Intermediate suspicion** = 10-20% Risk
 - Hypoechoic with regular margins

Haugen BR et al. 2014 ATA Thyroid Nodule and DTC Guidelines

Malignancy Prediction: Bethesda System

Category	Malignant risk	What next?
• Non-Diagnostic	1-4+ %	Re-do (U/S)
• Benign	0-3%	Clinical F/U
• Atypical	5-15%	Re-do (U/S)
• Follicular Neoplasm	15-30%	Lobectomy
• Suspect malignancy	60-75%	Total Tx
• Malignant	97-99%	Total Tx

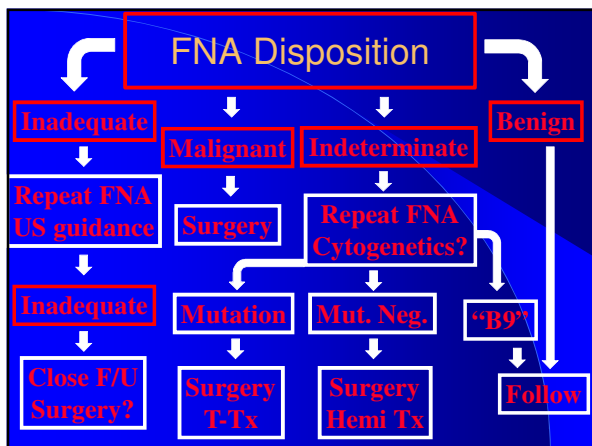
Indeterminate

FNA = fine needle aspiration

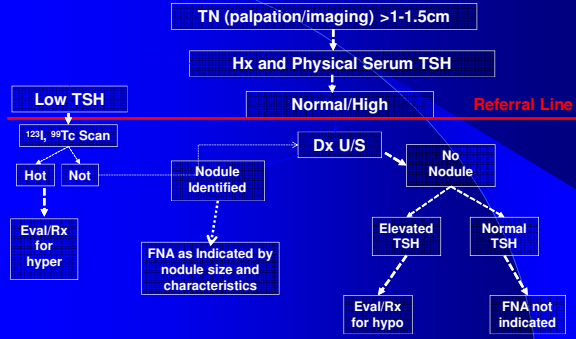
Cibas ES et al. Am J Clin Path.2009(132):658-65

Indeterminate: What Next?

- Mutation Panel
 - BRAF, RET, RAS, RET/PTC, PAX8/PPAR γ
 - High Positive Predictive value (80-90%)
- Multigene classifier: identify benign nodule
 - High Negative predictive value (94-95%)
- TSH Receptor mRNA in circulation
 - High Positive Predictive value (96%)



Thyroid Nodule Work-up



Adapted from Cooper, et al. *Thyroid*. 2006;16(2):1-33.
