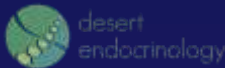


# Clinical Pearls for the Evaluation and Management of Thyroid Disorders

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Desert Endocrinology



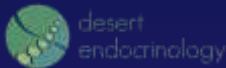
## Overview of Cases

1. Workup of Thyrotoxicosis
2. Thionamides for Treatment of Hyperthyroidism
3. Sonographic Risk of Malignancy



## Case # 1: Ana

- HPI: 42 yr old Hispanic woman with 2 months of severe fatigue, headaches. Admits to palpitations, dizziness and sweating at night. Lost 4 lbs. 2 months ago had a history of pain in the front of her neck which has diminished. Now feels like there is a lump in her throat
- PMHx
  - IGT
  - Hyperlipidemia
  - C-Section
- Medications: none



## Case # 1: Ana

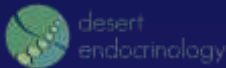
- FHx
  - Mom – DM2, HTN, CAD, MI
  - Dad – DM2, HTN
  - Brother – okay
  - Sister – uterine cancer
  - Sister – obesity
  - Sister – thyroid disease
- Social Hx
  - Married w/ 3 kids. Works in housekeeping at hotel.
  - Non-smoker, non-drinker, exercises regularly



## Case # 1: Ana

- Examination
  - Wt 152 lbs; Ht 65 inches; BMI 25.3; BP 120/71 mmHg; HR 84
  - Eyes – no lid lag, stare, exophthalmia; gaze conjugate
  - Thyroid – non-tender to palpation; ~ 2 cm thyroid nodules palpable on right and on left
  - No clinical distress, no tremors, no rashes
- Laboratory (from 4 weeks ago)
 

– TSH 0.03	– Free T3 7.4	– Hgb 11.4
– Free T4 3.5	– ESR 92	– HbA1c 6.5%



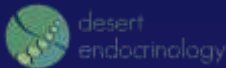
## Case # 1: Ana

- Neck U/S
  - Thyroid enlarged with heterogeneous echotexture and multiple nodules bilaterally
  - Dominant nodules
    - Isthmus: 10 x 8 x 3 mm
    - Right lobe: 16 x 15 x 7 mm & 17 x 15 x 12 mm
    - Left lobe: 18 x 18 x 14 mm



## Differential Diagnosis

- Toxic Multinodular Goiter
- Subacute Thyroiditis w/ nodules
- Graves Disease w/ nodules
- Thyroid Cancer w/ thyrotoxicosis



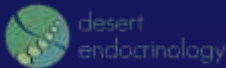
## What is the **BEST** test to order next?

- A. Thyroid Antibodies (TPO Ab, Tg Ab, TSI)
- B. Thyroid Uptake & Scan
- C. FNA biopsy of thyroid
- D. Color Doppler sonography



## Thyroid Antibodies

- Useful for identifying autoimmune thyroid disease
  - Hashitoxicosis
  - Graves
- Usually low in subacute thyroid disease



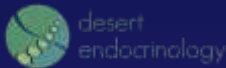
## FNA Biopsy

- Usually not necessary for hot nodules unless sonographically suspicious
  - FNA of hot nodules may have higher incidence suspicious cytology



## Color Doppler Sonography

- In subacute thyroiditis the thyroid may be normal in size or enlarged but is usually hypoechoic. Color doppler usually shows low flow during the thyrotoxic phase
- Graves hyperthyroidism usually shows diffuse increase in flow on color doppler
- Toxic Nodule show focal increased flow in the nodule on color doppler



## Thyroid Uptake & Scan

- Recommended for evaluation of thyroid nodules with low TSH
  - Hot Nodule – virtually eliminates risk of malignancy
  - Low Uptake – suggestive of subacute thyroiditis



## Case # 1: Ana

- The patient was given beta blockers and sent to the lab for repeat labs and thyroid uptake and scan
- I<sup>123</sup> Thyroid Uptake & Scan
  - 6 hour: 20.1% (5-15%)
  - 24 hour: 38.9% (15-30%)
  - Thyroid is diffusely labelled with no hot or cold nodules or focal abnormalities



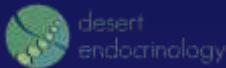
## Case # 1: Ana

- Labs after 6 weeks
  - TSH 7.79
  - Free T4 0.6
  - Free T3 2.0
  - TPO 25 (0-8.9)
  - Tg Ab < 1
  - ESR 9
  - Hgb 14.2
  - Glucose 110



## Case # 1: Ana

- Follow-Up
  - Neck pain had resolved
  - Feeling tired and cold
  - Palpitations resolved
- Plan
  - Monitoring of thyroid chemistry
  - Repeat thyroid u/s later with consideration of FNA biopsy of nodules depending on sonographic risk



## Case # 1: Ana

- Clinical Pearls
  - High ESR – highly suspicious for subacute thyroiditis (SAT)
  - Neck pain – usually a good indicator for SAT but may also be seen in autoimmune thyroid disease or nodular thyroid disease
  - Degree of elevation of Free T4 and Free T3 was higher than usually expected with SAT
  - Normal Uptake/Scan
    - May be seen during the recovery phase of SAT depending on the timing of the scan relative to onset of symptoms





# Thionamide Therapy for Thyrotoxicosis



## Case # 2: Leslie

63 yr old woman presents with hyperthyroidism seeking second opinion

HPI:

- 3-4 months of severe insomnia, hot flashes, palpitations and anxiety
- TFTs became abnormal over the course of a few months and she was diagnosed with hyperthyroidism
- Started on methimazole 5 mg/day x but after 2 wks c/o edema, brain fog, worsening fatigue, and weight gain
- Changed to PTU 50 mg BID and symptoms have persisted and are worsening for the last 3-4 wks



## Case # 2: Leslie

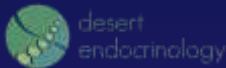
Meds: PTU 50 mg BID  
 Losartan/HCTZ 100/25 mg QD

PMHx: post-menopausal, HTN, hyperlipidemia, tongue cancer (no RoRx), arthritis

SHx: hip replacement, tongue surgery

FHx:  
 Dad – PD, neuropathy, lipids, HTN  
 Mom – PD, lipids  
 Brother – prostate cancer

Exam: Wt 135 Pulse 62 BP 133/80  
 Normal thyroid, no tenderness or nodules; otherwise neg



## Case # 2: Leslie

- Laboratory (prior to thionamides)
  - TSH 0.81 → 0.09 → < 0.01
  - Free T4 1.34 → 1.40 → 1.34 (0.8 – 1.8)
  - Free T3 ? → 2.5 → 3.0 (2.3 – 4.2)
  - TPO ? → 329 → 623
  - Tg antibodies < 1
  - TSI 117
  - TBII 34 (< 17)



## Case # 2: Leslie

- Diagnostic Imaging (prior to Rx)
  - Neck Ultrasound – heterogeneous thyroid
  - I<sup>123</sup> Thyroid Uptake & Scan
    - Diffuse labelling
    - 6 hr uptake 11.4% (5-15%)
    - 24 hr uptake 27.1% (15-35%)



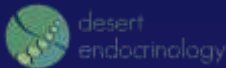
## What would you recommend while waiting for repeat labs?

- A. Increase PTU and start a beta blocker
- B. Continue PTU at same dose and start a beta blocker
- C. Discontinue PTU and restart methimazole
- D. Discontinue PTU
- E. Add beta blocker and order RAI ablation



## Case # 2: Leslie

- Clinical Course
  - PTU was discontinued and repeat thyroid function tests were ordered
    - TSH 0.26
    - Free T4 0.8
    - Free T3 2.0
  - Marked clinical improvement after stopping PTU
  - Stable clinical course with ongoing monitoring
    - Free thyroid hormone levels remain normal
    - TSH remains low but detectable



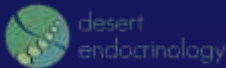
## Thionamide-Induced Hypothyroidism

- One of the most common complications of thionamide therapy
- Clinical picture is confusing
  - Symptoms
  - Laboratory
- Requires
  - good clinical judgment
  - High index of suspicion
  - Proactive adjustment of dose



## Methimazole (MMI)

- Preferred agent
  - Don't use during first trimester of pregnancy due to risk of aplasia cutis
  - Less hepatotoxicity vs. PTU
  - Agranulocytosis 0.1-0.5%
  - Once daily dosing
    - Half-life: 4-6 hours



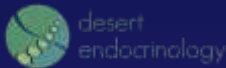
## Methimazole

- Dosing
  - Starting dose
    - 10-15 mg once daily
    - 20-30 mg in divided doses for severe hyperthyroidism
    - Doses > 30 mg/day increase risk of agranulocytosis
  - Maintenance dosing
    - 2.5-5 mg daily



## Propylthiouracil (PTU)

- Preferred agent
  - 1<sup>st</sup> trimester of pregnancy
  - Life-threatening thyroid storm
    - Decreases T4 to T3 conversion
  - Reactions to MMI in patients not candidates for RAI or surgery



## Propylthiouracil (PTU)

- Dosing
  - BID to TID dosing
    - Half-life 75 minutes
  - Starting Dose
    - 100-150 mg BID
  - Maintenance Dose
    - 50-100 mg BID



## Propylthiouracil (PTU)

- Cautions
  - Typical risks of thionamide therapy
  - Higher risk of agranulocytosis than MMI
  - Higher risk of hepatotoxicity than MMI



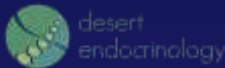
## Pitfalls of Therapy

- Under-estimating potency
- Monitoring Therapy
- Titration of Dose



## Underestimating Potency

- Low-moderate dose recommended unless severe hyperthyroidism
- MMI > 30 mg/day is rarely needed
- Over-treatment increases risk of iatrogenic hypothyroidism
  - Extra caution with Hashitoxicosis



## Monitoring Therapy

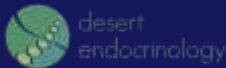
- TSH may be misleading
  - Suppression of thyrotroph lasting several months due to prior hyperthyroidism
- Measure Free T4 and Free T3
  - T3 Only thyrotoxicosis
  - Differential response to therapy
- Frequent clinical f/u
  - Q4-6 weeks with initial therapy





## Titration of Dose

- Higher doses are required to attain control of hyperthyroidism than to maintain control of hyperthyroidism
  - Down-titrate dose
    - Lower 1/3 reference range
    - Tempo of decline in Free T4 and Free T3

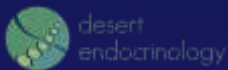


## Hashitoxicosis

- Lymphocytic thyroiditis can occasionally cause thyrotoxicosis in the early phase
  - Usually transient
  - Usually followed by hypothyroidism
  - High risk for thionamide-induced hypothyroidism



# Sonographic Risk of Malignancy in Thyroid Nodules



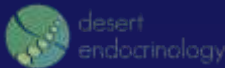
**"Have no fear of perfection—  
you'll never reach it."**

Salvador Dalí



## Case # 3: Edith

- 67 year old woman presents with enlarged thyroid discovered on routine exam
- PMHx
  - HTN, glaucoma, surgery for skin cancer x 3 on face
- FHx
  - Mom: MS, stroke, HTN
  - Dad: HTN, skin cancer, CAD, stroke, dementia
  - Sister: breast cancer
  - Brother: MS
  - Brother & Sister: skin cancer



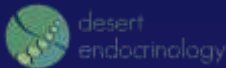
## Case # 3: Edith

- Social Hx
  - Married with 2 children
  - Retired Psychotherapist
  - Non-smoker, occasional alcohol use, regular exercise
- Medications: amlodipine
- Examination
  - Wt 137 lbs; Ht 67 inches; BP 146/80 mm Hg; HR 69
  - Thyroid non-tender with ~ 1 cm nodules palpable bilaterally; no lymphadenopathy
  - Exam otherwise unremarkable



## Case # 3: Edith

- Laboratory
  - TSH 1.07
  - TPO Ab 1
  - Free T4 1.2
  - Tg Ab < 1
- Neck U/S performed
  - Homogenous thyroid gland with 3 nodules present
  - FNA is planned for nodules with suspicious sonographic features
  - Which nodules should be biopsied?



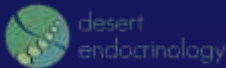
## Nodule Sonography

- Size in 3 dimensions
- Composition (solid/cystic/spongiform)
- Echogenicity
- Margins
- Calcifications
- Tall v. Wide
- Vascularity



## FNA Nodule is

- Recommended
  - < 1 cm if high risk sonography
  - > 1 cm if intermediate risk sonography
  - > 1.5 cm if low risk sonography
- Considered
  - > 2 cm with very low risk sonography
- Unnecessary
  - Purely cystic nodules



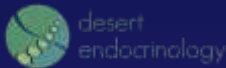
## Suspicious Sonographic Features

- Microcalcifications
- Nodule hypoechogenicity
- Irregular margins
- Taller than wide on transverse view
- Internal vascularity
- Solid



## Benign Sonographic Features

- Spongiform nodules
  - aggregation of microcystic components > 50% of volume
- Purely cystic nodules



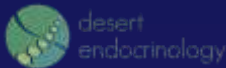
## High Suspicion Sonography

- 70-90% risk of malignancy
- Hypoechoic solid & hypoechoic complex with one or more of following
  - Irregular margins
  - Microcalcifications
  - Taller than wide on transverse
  - Disrupted rim calcifications
  - Extrathyroidal extension



## Intermediate Suspicion Sonography

- 10-20% risk of malignancy
- Hypoechoic solid nodule with
  - Smooth regular margin
  - No microcalcifications
  - No extrathyroidal extensions
  - Not taller than wide



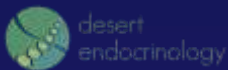
## Low Suspicion Sonography

- 5-10% risk of malignancy
- Partially cystic solid nodule with eccentric uniformly solid areas and
  - Smooth regular margin
  - No microcalcifications
  - No extrathyroidal extensions
  - Not taller than wide



## Very Low Suspicion Sonography

- < 3% risk of malignancy
- Spongiform or partially cystic nodules without any features of high/intermediate or low risk nodules

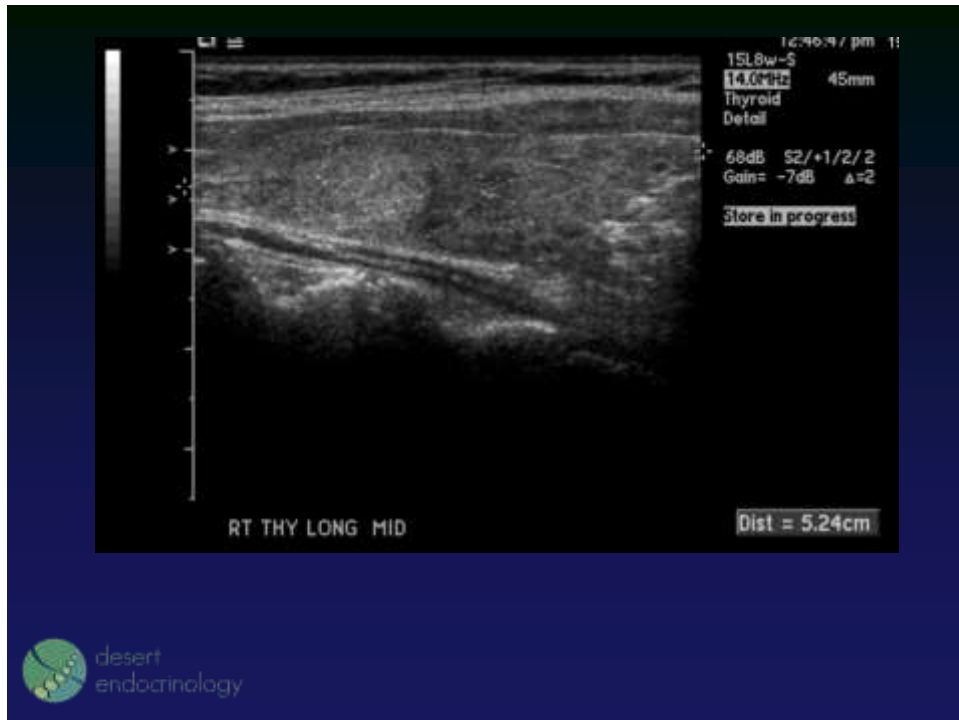


## Right Upper Lobe Nodule







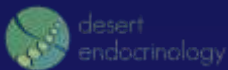


Would you biopsy this nodule?

- A. Yes
- B. No

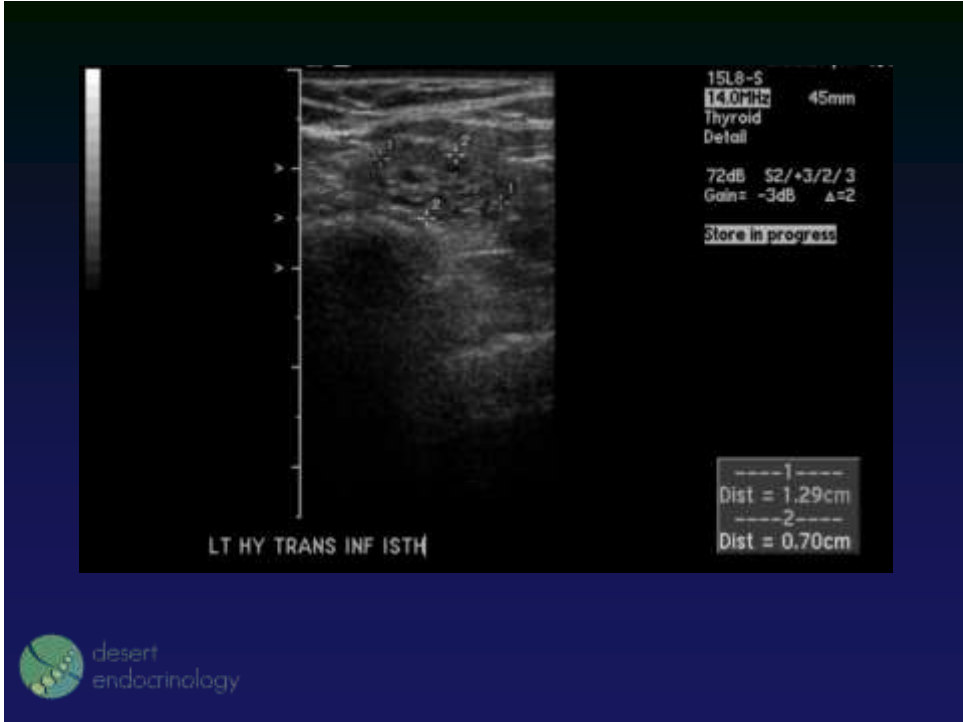
## Right Upper Lobe Nodule

- 14 x 11 x 8 mm
- echogenic
- Microcalcifications are present
- FNA was performed



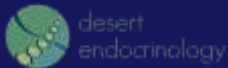
## Left Mid Thyroid Nodule





## Would you biopsy this nodule?

- A. Yes
- B. No



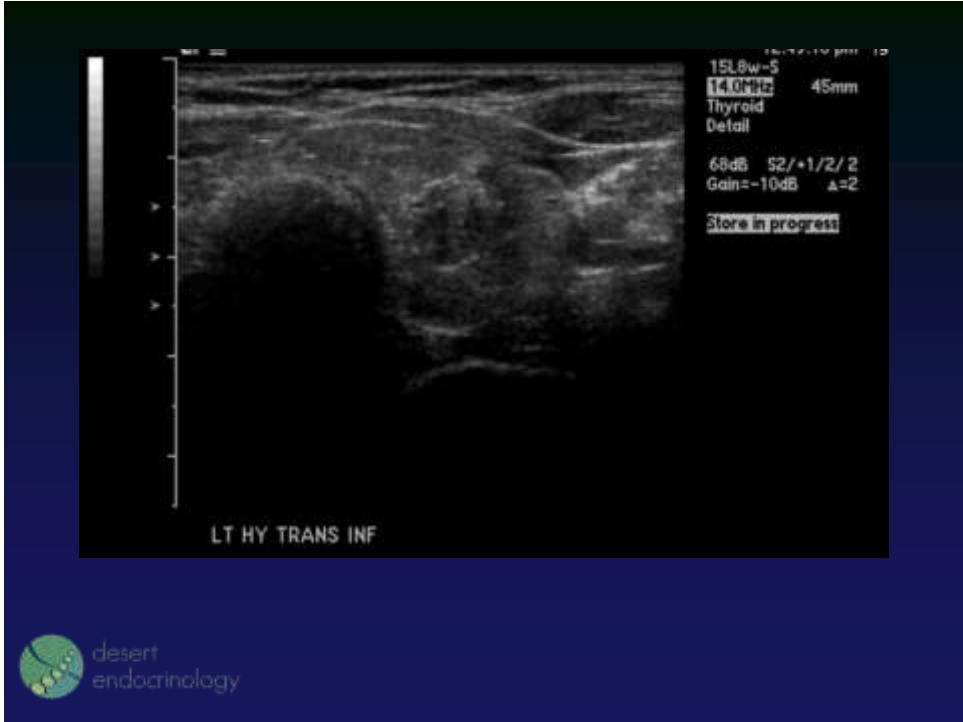
## Left Mid Thyroid Nodule

- 12 x 13 x 7 mm
- Spongiform appearance
- FNA was not performed



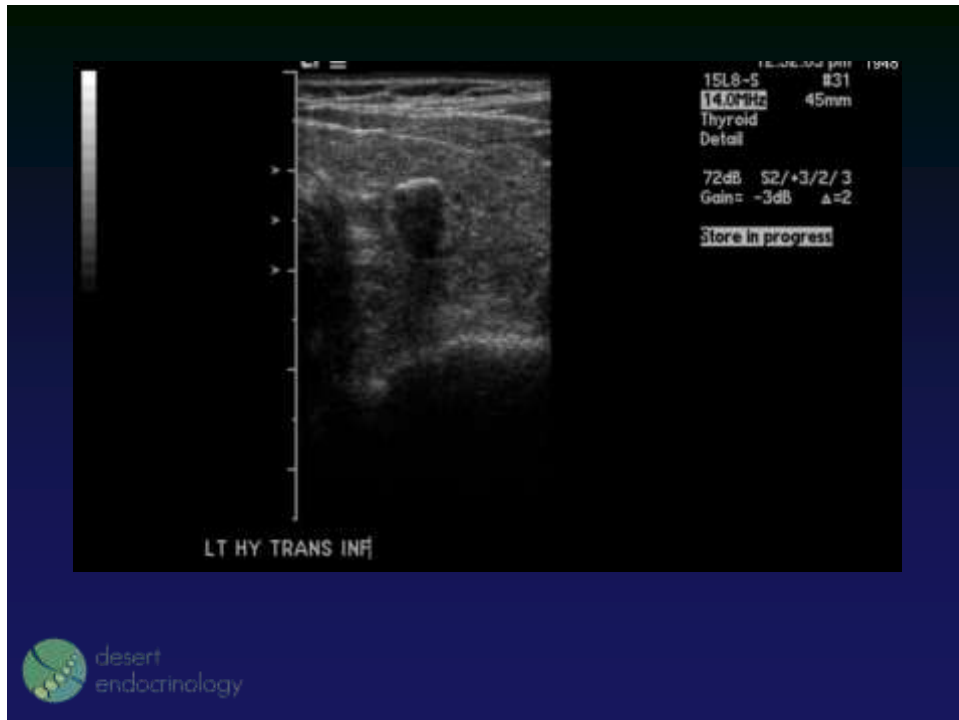
# Left Inferior Thyroid Nodule









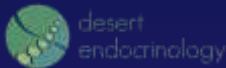


Would you biopsy this nodule?

- A. Yes
- B. No

## Left Inferior Thyroid Nodule

- 11 x 10 x 9 mm
- rim calcification with focal disruptions
- FNA was performed



## Case # 3: Edith

- FNA biopsies showed
  - Watery colloid
  - Bland looking follicular cells without cytological atypia and round, regularly space nuclei
  - No nuclear grooves or pseudo-inclusions
- **Bethesda Category II: Benign Colloid Nodules**



# Thank You

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