PRACTICAL THYROID MANAGEMENT

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Financial disclosure

- I am a paid speaker for Boehringer Ingelheim Pharmaceuticals for Jardiance

About me

- Married with 4 kids
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Overview

- Goal: practical approach for thyroid probs for PCP
- Discuss
  - Hypothyroidism
  - Hyperthyroidism
  - Thyroid nodules
  - Thyroid CA
- Management keys and common pitfalls

Hypothyroidism

- Etiologies
  - Hashimoto's (*>70-90% etiology- based on various studies)*
  - Postsurgical vs post ablative
  - Idiopathic
  - Others
- MC Sxs
  - Fatigue
  - Weight gain
  - Cold intolerance
  - Dry skin
  - Constipation

Hypothyroidism

- Which labs
  - TSH and FT_4 only
    - Rarely require FT_3
  - Avoid: TT_4,, T_4 index, T_3 index
  - +/- TPO or TG Abs (Hashimoto's Abs)
    - (+) test tells etiology only
    - by far MC etiology for hypothyroidism
    - may be helpful in pts struggling w/ fertility (*some a/w infertility and period irregularity)*
    - Do not need to refer for pos TPO Abs

Hypothyroidism

- Interpretation (more art than science)
  - TSH (.4-4.5)
  - FT_4 (.8-1.8)
  - field goal analogy
- FT_4 more likely accurate
  - Examples of falsely low TSH
    - Pregnancy
    - Weight loss
    - Pituitary d/o
    - Lab assay abnormality (falsely low or falsely high)
- Story of 70 YO on 250 mcg LT_4 w/ tremors/palpitations, but high TSH

Hypothyroidism

- Management
  - Levothyroxine (or other generic LT_4 Rx's)
    - Cheap & easy
    - ATA guidelines for the treatment of hypothyroidism (2014)
      - "We concluded that levothyroxine should remain the standard of care for treating hypothyroidism. We found no consistently strong evidence for the superiority of alternative preparations (e.g., levothyroxine–liothyronine combination therapy, or thyroid extract therapy, or others) over monotherapy with levothyroxine, in improving health outcomes."
  - Synthroid (brand name LT_4)
    - More $, consistent dosing, gluten free
  - Tirosint (water based filler)
    - Most $, maximal absorption
    - Tirosint solution: ~increased absorption independent of pH
    - Celiac, pts w/ GERD on PPI, malabsorptive d/o, hx bariatric sx
  - LT_4 Rx w/ ~1 wk halflife
  - LT_3 Rx (Cytomel/liothyronine): onset ~2-3 hrs, ~2 day halflife

Hypothyroidism

- Management
  - Once starting on Rx
    - Goal mid nl range TFTs (field goal analogy)
      - "Thyroid hormone therapy should be initiated as an initial full replacement or as partial replacement with gradual increments in the dose titrated upward using serum thyrotropin as the goal." (ATA guidelines for hypothyroidism)
    - Set clear expectations for pts
      - "not all fatigue is d/t thyroid"
    - Repeat TFTs Q 2-3 mo (not earlier)
      - My approach- TSH & FT_4 both→ improved accuracy of dosing

Hypothyroidism management

- My principles for management:
  - if increasing or decreasing dosage, go 1 step at a time
    - Example: FT_4 from 1.0-1.2 after LT_4 from 88 – 100 mcg→ may increase to 112 mcg LT_4
  - use only 1 dosage strength at a time
    - Ex: do not use 88 and 100 mcg and alternate dosage- just use 100 mcg 6.5 weekly
  - Titrate to optimal TFTs and sxs
    - Example: FT_4 from 1.4-1.6 after increase to 112 mcg- pt now w/ slight palpitations
      - May lower to 112 mcg 6.5 pills weekly (slightly lower FT_4, lower sxs, but keep FT_4 at mid nl range goal)

Hypothyroidism

- What about desiccated thyroid hormone
  - Human ratio ~14/1 T_4/T_3
  - Pigs ~4/1 T_4/T_3
  - Desiccated thyroid hormone examples
    - Naturethroid, Armour thyroid, NP thyroid
  - LT_4 Rx= all T_4
  - Desiccated thyroid Rx: ~4/1 ratio of T_4/T_3 (pig thyroid extract)
- ATA guidelines for the treatment of hypothyroidism- section regarding desiccated thyroid extracts: "We recommend that levothyroxine be considered as routine care for patients with primary hypothyroidism, in preference to use of thyroid extracts. Although there is preliminary evidence from a short-duration study that some patients may prefer treatment using thyroid extracts, high-quality controlled long-term outcome data are lacking to document superiority of this treatment compared to levothyroxine therapy. Furthermore, there are potential safety concerns related to the use of thyroid extracts, such as the presence of supraphysiologic serum triiodothyronine levels and a paucity of long-term safety outcome data."

Hypothyroidism management

- My approach:
  - T_4 Rx predominantly, occasional LT_3 if low/nl FT_3 w/ nl FT_4
  - If using LT_4 + LT_3- check TSH, FT_4 and FT_3
  - If using LT_4 only- check TSH and FT_4 only
  - If using desiccated thyroid hormone
    - Set clear expectations for pt
    - Check TSH, FT_4, FT_3
- If pts cannot convert T_4/T_3- can add T_3 back individually (*liothyronine)*
  - check TSH, FT_4, FT_3

Thyroid Rx absorption

- Empty stomach:
  - Take Rx 1 hr before breakfast, or 3 hrs after dinner
  - 3-4 hrs away from Ca, Fe, Vit D, PO estrogen
- If missing dosage of LT4- can double next day
  - Remember 1 wk halflife
  - Routinely recommend weekly pillbox

Hypothyroidism- special circumstances

- Pregnancy:
  - require ~30-50% more thyroid Rx in pregnancy
  - Trimester specific TSH goals (*ATA guidelines for thyroid disease in pregnancy)*
    - 0.1–2.5 mIU/L for the first trimester,
    - 0.2–3.0 mIU/L for the second trimester
    - 0.3–3.0 mIU/L for the third trimester,
  - If morning sickness- can take LT_4 in evening (3 hrs after dinner)
- Malabsorptive d/o, bariatric surgeries, celiac
  - Likely need higher dosage
  - Consider tirosint for maximal absorption
- Thyroid CA:
  - Keep TFTs upper nl range to lower risk of recurrence
  - Goal TSH .1-.4 if active CA vs .4-2 if in remission

Hyperthyroidism

- Sxs:
  - Palpitations
  - Tremors
  - Wt loss
  - Diaphoresis
  - Exophthalmia (graves eye disease)
- Etiologies:
  - Graves (autoimmune)
  - Acute thyroiditis
  - Autonomous nodule
  - Postpartum thyroiditis
  - Gestational Hyperthyrotoxicosis

Hyperthyroidism

- Which labs?
  - TSH, FT_4, FT_3
  - Graves Abs labs: TSI (thyroid stimulating immunoglobulin), TRAb (thyrotropin R Abs)
  - Avoid: TPO, TG Abs (Hashimoto's), thyroid antibody panel (usually TPO, TG Abs)
- Interpretation
  - TSH ↓, FT_4 or FT_3 moderately/very ↑ = usu graves vs autonomous nodule
  - TSH ↓ w/ nl FT_4 and FT_3= usu acute thyroiditis vs wt loss vs pituitary disease
    - If TSH low, review hx, repeat TFTs in 2-3 mo- if FT_4/FT_3 nl, may be resolving thyroiditis
  - Key: if unsure and pt asxs, repeat labs 2-3 mo later

Hyperthyroidism

- Dx: history remains key
  - Graves
    - personal/Fam hx autoimmunity
    - Acute onset
    - Sxs more predominant
  - Thyroiditis
    - Subacute onset
    - Preceding URI within months
    - Preceding contrast study w/ iodine
    - Usually resolves w/in 3-6 mo
  - Autonomous nodule:
    - Requires RAI uptake and scan- "hot nodule" = autonomous nodule

Hyperthyroidism- special cases

- pregnancy
  - Postpartum thyroiditis:
    - TFTs high over few months- ~resolve within 3-6 mo
    - Generally do not treat (particularly if breast feeding)- repeat TFTs in 2-3 mo
  - Gestational hyperthyrotoxicosis
    - During peak hCG (10 to 12 weeks), T4 + T3 both ↑ (~Upper nl limits), & TSH slightly ↓.
    - Very common during 1st trimester, or in pregnancies with high hCG levels
    - Usually asxs, usu do not treat
      - if sxs present in 2nd trimester, recheck TFTs

Hyperthyroidism

- What about RAI uptake and scan
  - Diagnostic modality for underlying etiology
    - Graves- high diffuse uptake
    - Autonomous nodule: focal high uptake
    - Thyroiditis: very low uptake throughout
- Order if Graves Abs neg and TFTs still high
- My approach for hyperthyroidism:
  - Order TSH, FT_4, FT_3, TSI Abs
  - very rarely require RAI uptake and scan
  - TSI Abs ~95-98% sensitivity and specificity for graves
  - If TSI Abs neg & TFTs still high- then get RAI uptake and scan

Hyperthyroidism

- When to refer vs when to wait
- My approach:
  - FT_4 or FT_3 moderately high- refer
  - TSH low, but FT_4/FT_3 nl- wait (majority will be thyroiditis)
    - repeat TFTs 2-3 months later
- Good idea to always get TSH + FT_4 + FT_3
  - Some forms of hyperthyroidism can be T_3 predominant

Hyperthyroidism management

- B-blockers for palpitations
  - My approach: propranolol 10-20 mg Q6 hrs PRN palpitations
- Anti-thyroid RX
  - Start after confirming dx (pos Abs for pos RAI uptake and scan)
    - Typical to refer these pts to endo for Rx management
  - Methimazole
    - My typical dosing 5-10 mg QD vs BID
      - 5 mg QD for mild FT_4/FT_3 elevation
      - 10 mg QD for moderate FT_4/FT_3 elevation
      - 10 mg BID for significant FT_4/FT_3 elevation
  - PTU: Use only during 1st trimester pregnancy- higher AE profile than MTZ
- if considering total thyroidectomy vs RAI ablation: rec'd endo referral first

Hyperthyroidism management

- IF using MTZ or PTU for management
  - Repeat TFTs Q 2-3 mo for dosage adjustment (just like hypothyroidism)
  - Rec'd using FT_4/FT_3 for dosing rather than TSH value
    - TSH will take months to normalize

Thyroid nodule

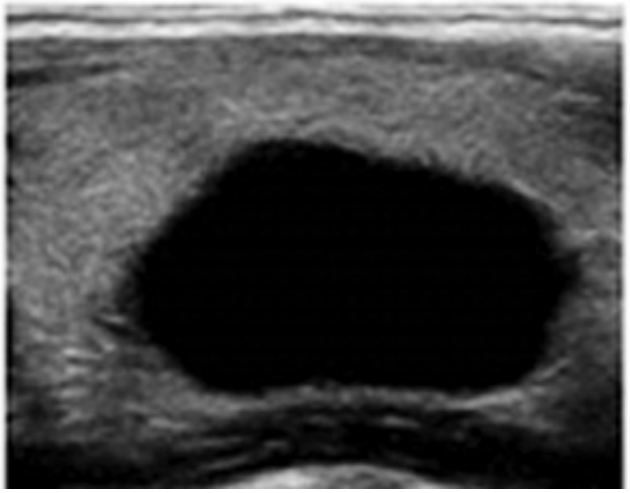
- Frequently present *(~50% by age 50 based on multiple studies)*
- Etiologies from FNA (*% below based on avg over multiple studies)*
  - Benign (*~70%)*
  - Malignant (*~1-10%)*
  - Inadequate cellularity (*~5-10%)*
  - AUS (*~10-30%)*
- No Labs needed if asxs

Thyroid nodule

- When to biopsy vs observe vs refer
  - Very low risk: observe (<1-3% risk of CA)
  - low risk- consider FNA if nodules >1.5 cm
  - Intermediate vs high risk- FNA vs refer

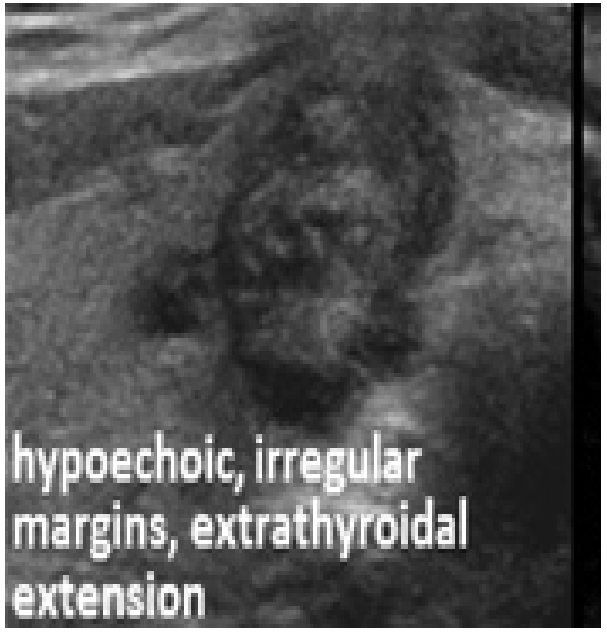
Thyroid nodule

- Examples of very low risk nodules- *<1-3% risk of CA-* do not need FNA
  - Anechoic (cystic)- regardless of size- do not FNA (pic on R)
  - Spongiform (pic on L)
  - (all US *Images via ATA guidelines for assessment of thyroid nodules 2015*)



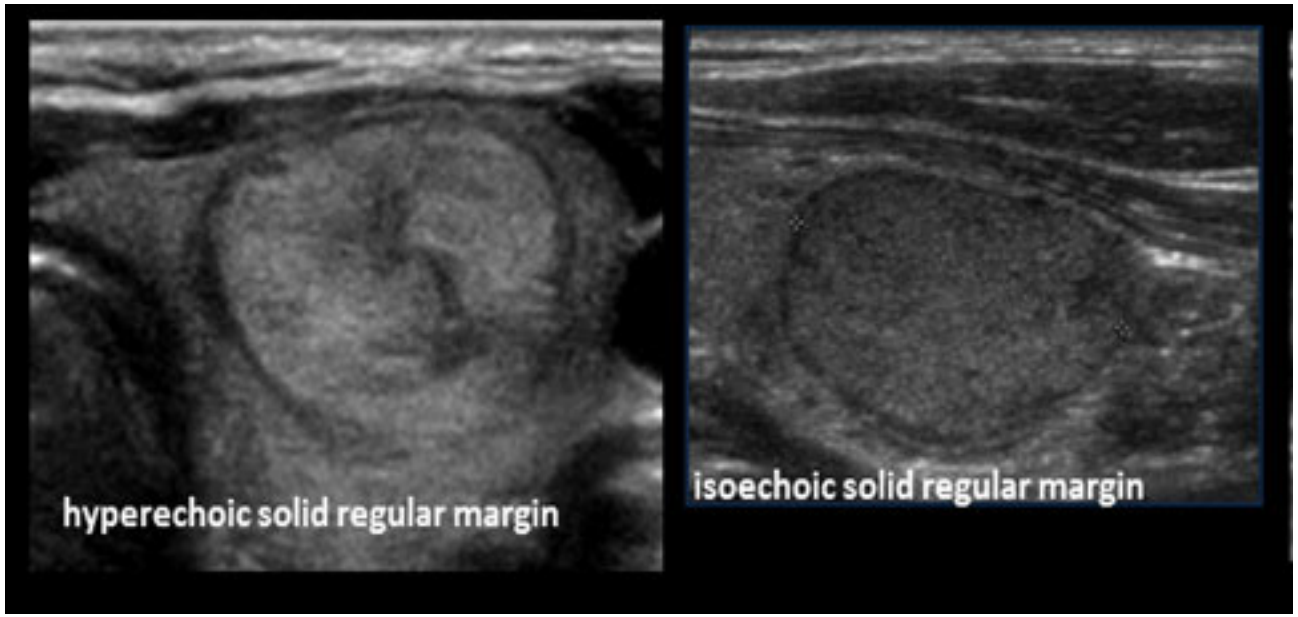
Thyroid nodule

- Examples of high risk nodules- (~70-90% risk of CA)
  - Calcifications, large, hypoechoic, irregular borders, extrathyroidal extension, etc



Thyroid nodule

- Examples of low risk nodules- ~5-10% risk CA- consider bx if >1.5 cm
  - solid, iso/hyperechoic



Thyroid nodule

- FNA w/ AUS (*atypia of undetermined significance- an indeterminate read)*
  - Different than inadequate cellularity
  - Options for management
    - Observe
    - Repeat FNA
    - Cytogenetic study
      - Examples: ThyraMIR, AFFIRMA
      - Gene classifiers- use genetic material to classify relative risk of CA

Thyroid nodule

- Long-term management
  - ATA guidelines: Q 1-2 yr US surveillance (*low to intermediate risk nodules)*
  - if stable in size/characteristics- may continue monitoring
  - Always can refer to endo if unsure of progression
  - If pts w/ dyspnea/dysphagia, or considering total thyroidectomy- refer to endo
- Note on GLP1 use
  - GLP1s are contraindicated in personal or fam hx of medullary thyroid CA (MTC)
    - MTC very rare, familial
  - Pts w/ thyroid nodules CAN be on GLP1s

Thyroid Cancer

- Etiologies
  - Differentiated thyroid CA (*papillary and follicular)*
  - Medullary Thyroid CA (*rare, a/w MEN syndromes)*
  - Anaplastic (*very rare, high mortality rate)*
- If (+) FNA for DTC- refer to endo
  - Endo can assist in finding surgeon, planning for short/long term surveillance
- If (+) FNA for MTC or anaplastic- urgent endo referral
- If pos hx of thyroid CA in remote past- may not need endo referral (*pt preference)*

Thyroid Cancer

- DTC cases
  - Majority w/ low mortality rate
  - Rarely metastasize beyond cervical LNs
- Surveillance
  - Thyroid US yearly
  - TG, TG Abs yearly (*tumor markers)*-
  - Generally do not require CT/PET scans
- Note: Fam hx of MEN syndromes
  - a/w Pancreatic, parathyroid, pituitary masses, rarely MTC, pheochromocytomas
  - Refer all these to endo for surveillance

Summary

- Hypothyroidism
  - TSH & FT_4
  - goal mid nl range (*splitting the uprights)*
  - optimize absorption
  - small dosage adjustments
- Hyperthyroidism
  - TSH, FT_4, FT_3- do not rely on TSH only
  - TSI or TRAb Abs for graves
  - Rarely require RAI uptake and scan
  - Refer for graves or autonomous nodules

Summary

- Thyroid nodules
  - Majority benign
  - Not all require FNA
  - Refer if worrisome, large, high risk, abnl FNA
  - GLP1s ok if no MTC
- Thyroid CA
  - Majority non-aggressive (DTC)
  - Referral if new or longstanding w/ worrisome features
  - May not require referral if stable and longstanding

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