Thyroid Disease

Presenter: Dr. Milta Little
Disclosure Statement: I have nothing to disclose.

Objectives: By the end of the session, participants will be able to…

- Describe age-related changes in thyroid function
- Define subclinical hypothyroid and distinguish the syndrome in older versus younger adults
- Describe the diagnosis and management of common thyroid diseases in older adults

Expected Outcomes (Desired change in practice):

- Reduce low-value care when managing thyroid disorders
- Implement changes to medications and diet to improve absorption of T4

Article for Review: **Thiruvengadam S and Luthra P. Thyroid disorders in elderly: a comprehensive review. Disease-a-Month 2021; 67(11):101223**

Additional articles used:

- Perkins JM and Papaleontiou. Towards de-implementation of low-value thyroid care in older adults. Current Opinion 2022; 29:483-491
- Chrysant S. The current debate over treatment of subclinical hypothyroid to prevent cardiovascular complications. Int J Clinical Practice 2020;74:e13499

Outline for Rapid Fire session

1. Case: thyroid disease

Six months ago, you joined a primary care geriatrics practice that sees patients over 65 across all settings of care. A colleague recently retired and you acquire his panel of patients. Over the next several months, you work on completing the nursing home regulatory visits and saw several new patients for their outpatient annual wellness visits. You notice that many of them were started on levothyroxine for subclinical hypothyroidism when TSH levels were >4 mIU/L. In addition, most of these patients had thyroid ultrasounds ordered annually for cancer surveillance. You have been asked by the practice medical director to cut testing and medication costs through a QI program and you decide to focus on thyroid disease management. What are the next steps you take to reduce low-value care in this practice?

2. Age-related changes in thyroid function
    a. TSH shifts higher
    b. Higher TSH and lower FT4 associated with longevity
    c. Lower TSH and higher FT4 associated with increased CV mortality risk
3. Antithyroid antibody positivity and hypothyroidism increase with age

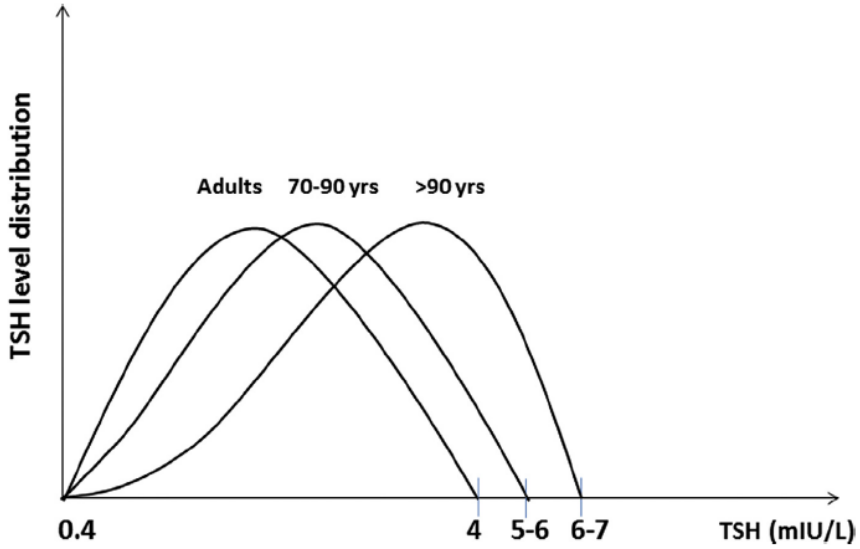

Fig. 1. Changes of serum TSH values with aging. (modified from Calsolaro et.al.[16]

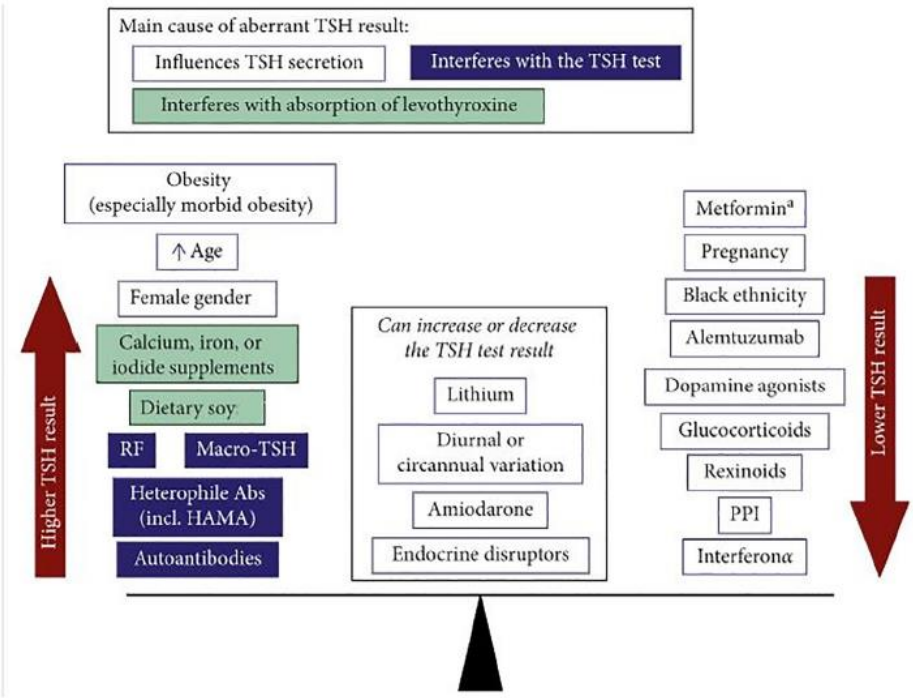

Fig. 2. Polypharmacy and other factors altering TSH levels.
(Reproduced with permission from Salman Razvi et al.[24] HAMA: human anti-mouse antibody; RF: rheumatoid factor; TSH: thyrotropin. PPI Proton pump inhibitor

4. Hypothyroidism – Primary = increased TSH with reduced FT3 and FT4; Central = normal/low TSH with low FT4
    a. Associated with increased CV events and mortality in older adults
    b. Chronic autoimmune (Hashimoto) thyroiditis is the #1 cause of hypothyroidism in the elderly in United States
    c. Worldwide, environmental iodine deficiency is the most common cause of hypothyroidism in any age group
    d. Iatrogenic causes and polypharmacy (Fig 2)
    e. Classic symptoms often lacking and may present only with neuropsychiatric symptoms, cerebellar dysfunction, macrocytic anemia, or neuropathy
    f. If TSH > 10 mIU/L, start L-thyroxine (levothyroxine) 12.5-25 mg
        i. Older adults absorb less efficiently but require 20-25% less dose/kg due to decrease in lean body mass
        ii. AGS recommends against desiccated hormone due to unpredictable pharmacokinetics and higher cardiac ADR risk
5. Subclinical hypothyroidism (ScH)
    a. Serum TSH above upper reference limit with normal FT4
    b. Classically, reference point for TSH is >4 mIU/L and treatment of ScH in younger adults may reduce future CV events
    c. In older adults (≥65), reference point changes to 7.55 mIU/L and no benefit to starting levothyroxine until TSH ≥10 mIU/L
    d. Before starting treatment, repeat TFTs in 3-6 months
6. Hyperthyroidism – Primary = decreased TSH with increased FT3 and/or FT4
    a. Primary manifestations in older adults is CV disease (a-fib, CHF), weight loss, FTT, depression, osteoporosis/fracture; 25-40% apathetic thyrotoxicosis
    b. Graves disease is the #1 cause in US older adults
        i. Mild disease often goes into spontaneous remission
        ii. Multinodular goiter and toxic nodules also increase with age
    c. Diagnosis: TSH low → FT4/FT3 high → thyrotropin receptor antibodies (TRAb) for Graves disease → radioactive iodine uptake (RAIU) for toxic adenoma or multinodular goiter
    d. Subclinical hyperthyroidism = low TSH with normal FT4 = risk assess before treatment to prevent complications
    e. Treatment

Table 7
Management of hyperthyroidism.

Symptomatic therapy	Definitive therapy
Beta-blockers Glucocorticoids	Anti-Thyroid medications- Methimazole Radioactive Iodine (RAI) ablation Surgery

- Beta-blockade if resting HR >90 or CV disease
- Glucocorticoids decrease conversion of T4 to T3
- Methimazole is preferred definitive therapy in elderly
    - Agranulocytosis, rash, liver injury, arthralgias/myalgias
    - Baseline CBC and LFT, FT4 and total T3 in 2-6 wks
    - TSH not good for monitoring early in treatment
    - Once euthyroid, decrease dose by 30-50% and repeat TFT in 4-6 wks, then q3 mo
- RAI good alternative but increases risk of ophthalmopathy and hypothyroidism
- Thyroidectomy for large goiters causing obstruction or malignancy

Table 5
Drugs interfering with thyroid function.

	Hypothyroidism	Hyperthyroidism
Drugs Affecting Hypothalamic–Pituitary Control of the Thyroid	Synthetic retinoid bexarotene Mitotane Immune checkpoint inhibitors *Suppress TSH without clinical hypothyroidism:* Glucocorticoids Dopamine agonists Somatostatin Metformin	
Drugs Affecting Thyroid Hormone Synthesis or Release	Amiodarone Lithium	Iodine excess (Jod–Basedow phenomenon) Radioactive Iodine contrast Amiodarone Topical povidone–iodine Over-the-counter preparations expectorants, vaginal douches, and kelp, Lithium
Drugs That Enhance Thyroid Autoimmunity	Immune check point inhibitors	Immune check point inhibitors *(Initially causes painless thyroiditis with hyperthyroidism followed by hypothyroidism)*
Drugs Causing Direct Thyroid Damage	Amiodarone Tyrosine kinase inhibitors (Sunitinib)	Amiodarone
Drugs Affecting Protein Binding of Thyroid Hormone	Oral estrogen and selective estrogen-receptor modulators Methadone Heroin Mitotane Fluorouracil	Antiepileptic agents (phenytoin and carbamazepine) Nonsteroidal anti-inflammatory drugs High-dose furosemide Heparin
Drugs Affecting Thyroid Hormone Activation, Metabolism, and Excretion	Amiodarone Dexamethasone (and other glucocorticoids) Propranolol Phenobarbital, phenytoin, carbamazepine Rifampin Sorafenib Bile acid sequestrants (Cholestyramine, colestipol, and colesevelam)	
Drugs Affecting Absorption of Thyroid Hormone Preparations	Proton-pump inhibitors Ferrous sulfate Calcium carbonate Aluminum hydroxide Sucralfate Bile acid sequestrants Raloxifene Biotin	Biotin

7. Thyroid nodules and cancer
    a. On routine US, ~50% of older adults have a thyroid nodule
    b. 4-6.5% of all nodules are cancer (up to 15% in high risk groups)
    c. Papillary carcinoma is #1 cause
    d. Routine US in people with thyroid disease not recommended unless palpable
    e. PET not routinely recommended

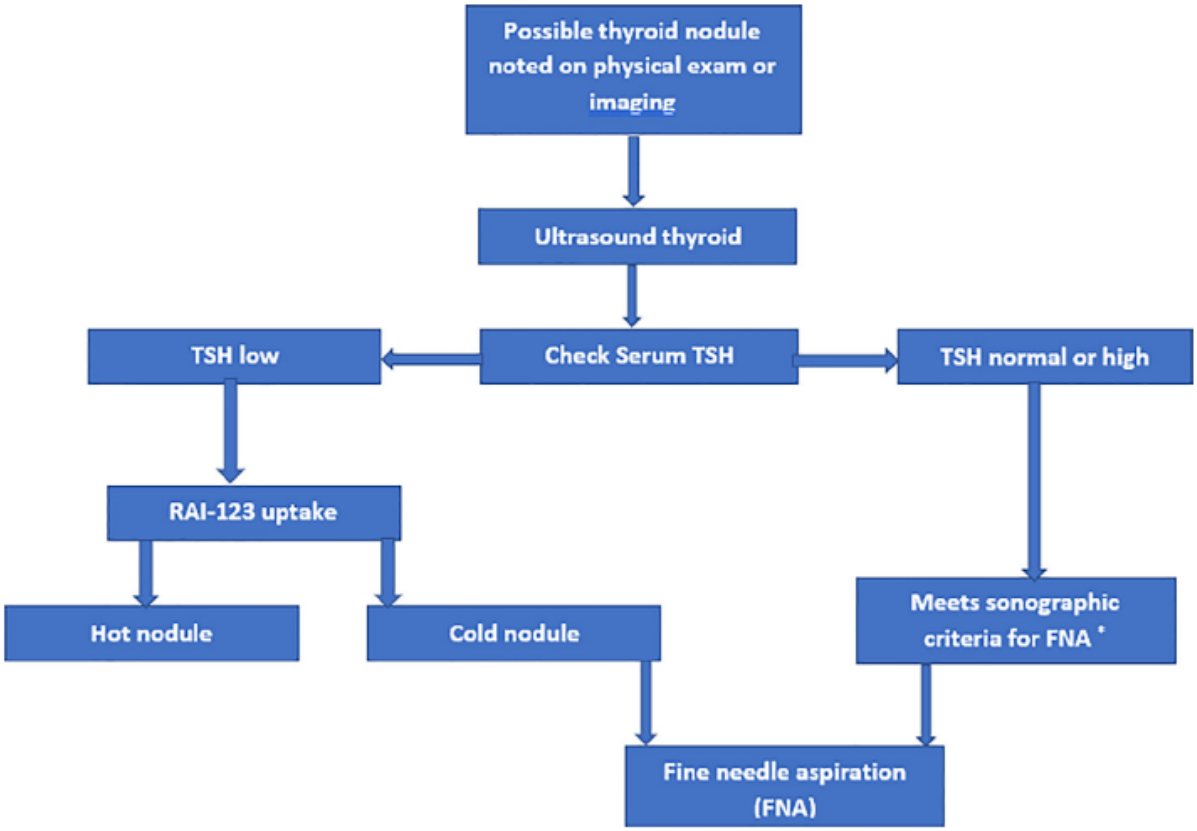

Fig. 3. General principles in evaluation of a Thyroid Nodule.
Hot nodule: Autonomous, hyperfunctioning thyroid follicular tissue producing thyroid hormone excess.
Cold nodule: Nodules without autonomous production of thyroid hormone
(Adapted from American College of Endocrinology Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules-2016).[102]