Thyroid Disorders in Older Adults

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Learning Objective

- To recognize the signs and symptoms of thyroid disease in the elderly
- Increase our understanding of the different tools used to diagnose hypothyroidism, hyperthyroidism and thyroid nodules in the elderly
- Increase our ability to implement treatments for hypothyroidism, hyperthyroidism and thyroid nodules in the elderly

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Case Scenario

- 70 years-old female admitted to the ICU with CHF exacerbation
- Diagnosed with A fib, HR 58, BP 95/60
- Pt underwent a cardiac cath showing “clean” coronaries 1 month prior
- What would you expect to find in the PE?
- What labs would you order?

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Case Scenario

- Pt has irregular heart beat, bilateral crackles on lung exam and 2+ pedal edema
- Diffuse goiter
- Lab shows a normal CMP, TSH 0.4, FT4 2,
- US shows diffusely enlarged thyroid with a 1.1 cm nodule
- What are the next steps?

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Thyroid Disorders in Older Adults
Clinical Presentation and Diagnosis

- Atypical, nonspecific, often geriatric syndrome
  - ↓ Cognition, falls, ↓ function
- Multiple co-morbidities
  - Mask or alter presentation, or mimic thyroid disease
- Nonspecific symptoms attributed to “old age”
- Diagnosis may be challenging
  - Rely on thyroid function tests (TFTs)
  - TFTs misleading with non-thyroidal illness

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Clinical Evaluation of Thyroid Disease

- Function
  - Hyperthyroid, hypothyroid or euthyroid
  - Clinical, TSH and free T_4
  - Non-thyroidal illness (sick euthyroid)
- Anatomy
  - Normal
  - Goiter (enlargement) – diffuse or multinodular?
  - Solitary nodule – benign or malignant?
- Age and comorbidities – modify presentation and management

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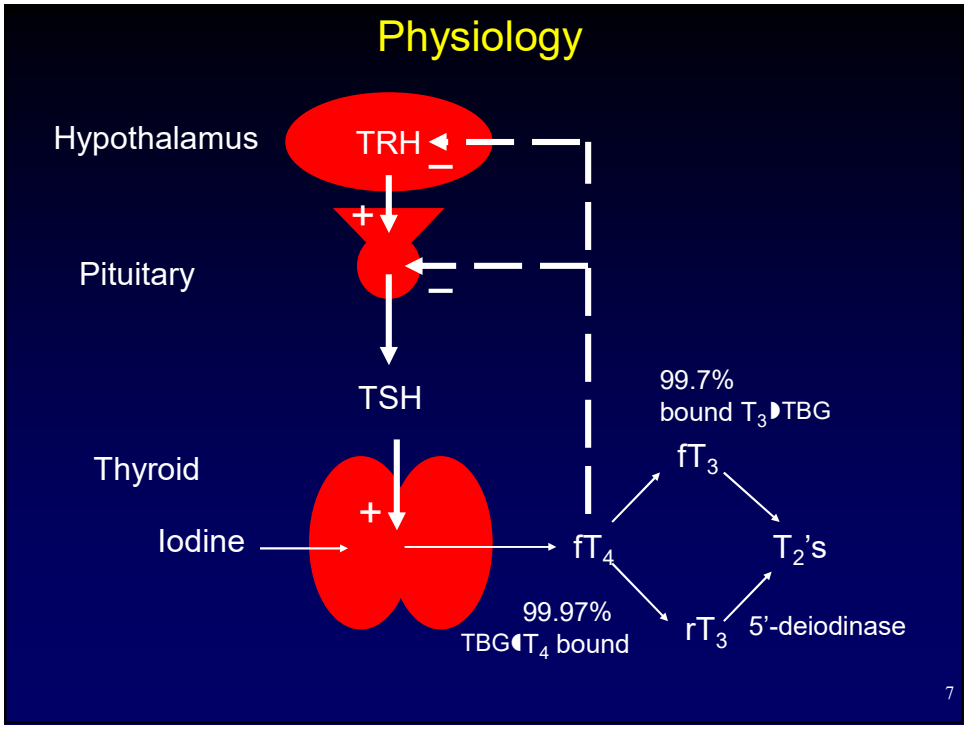
Physiology
Hypothalamus
TRH
+
–
Pituitary
–
TSH
99.7%
bound T3 TBG
fT3
Thyroid
+
Iodine
fT4
T2's
99.97%
TBG T4 bound
rT3
5'-deiodinase
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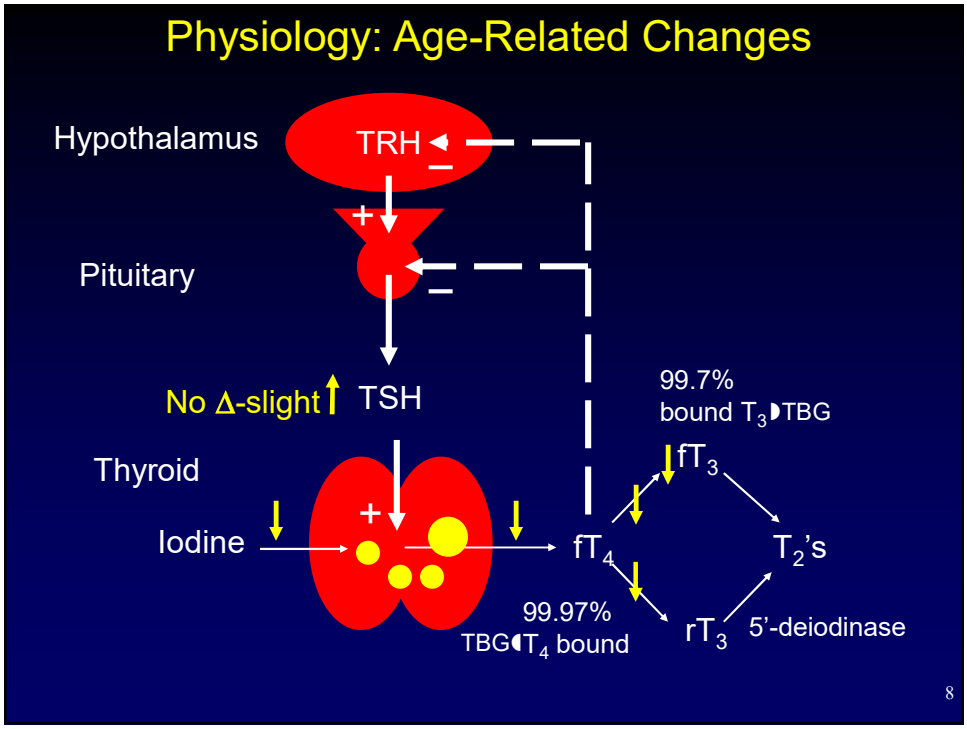
Physiology: Age-Related Changes
Hypothalamus
TRH
+
–
Pituitary
–
No Δ-slight
TSH
99.7%
bound T3 TBG
fT3
Thyroid
+
Iodine
fT4
T2's
99.97%
TBG T4 bound
rT3
5'-deiodinase
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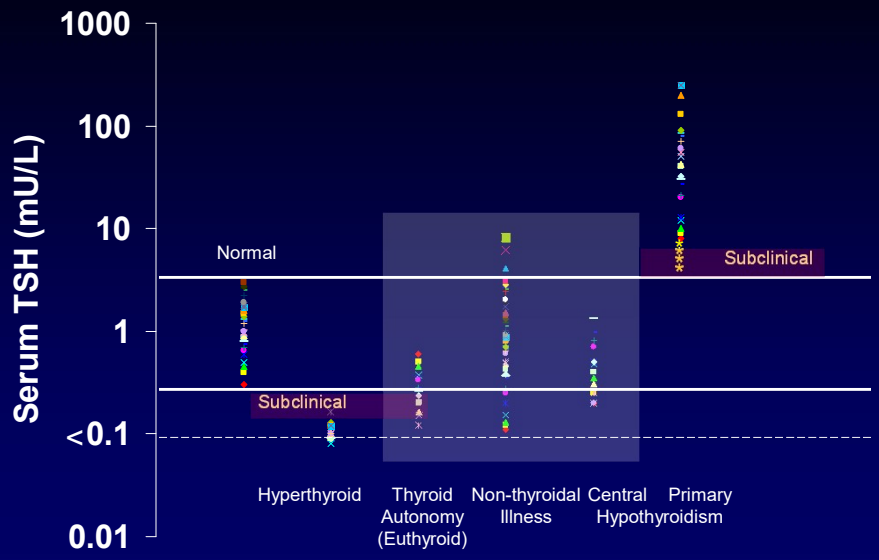
TSH in Thyroid and Non-thyroidal Disease



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Thyroid Function Tests

- TSH
  - Outpatient screening
  - Not sufficient alone in sick patients, or central hypothyroidism
  - TSH in non-thyroidal illness
    - ↓ Corticosteroids, dopamine, fasting,
    - ↑ Transiently during recovery
- Free T_4 (fT_4)
  - fT_4 equilibrium dialysis – gold standard
  - fT_4 direct – local labs
    - Unreliable when extremely high or low TBG
- Biotin interference (falsely low TSH and falsely high FT4 and T3)

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Drug interfering with Thyroid Axis

- TSH Suppression
  - Prednisone (>20 mg/day), dopamine, dobutamine, octreotide
- Hyperthyroidism
  - Iodine (Jod Basedow effect), amiodarone, lithium, “Immune-modulators” (IL2, IFNa, alemtuzumab, ipilimumab)
- Hypothyroidism
  - Iodine (Wolff-Chaikoff effect), lithium, TKI (i.e.; sunitinib), checkpoint inhibitors (i.e.; pembrolizumab, nivolumab), IFNa, IL2

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Drug interfering with Thyroid Axis

- GI absorption
  - Bile acid resins, PPIs, $CaCO_3$, Ferrous Sulfate
- TH metabolism
  - Phenobarbital, rifampin, phenytoin, and carbamazepine (↑metabolism)
  - Amiodarone, PTU, BB, prednisone (↓5’MDI)
- TBG alterations

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Thyroid Disorders in Older Adults
Screening

- Sick older – frailty, depression, ↓ cognition, chronic disability
- Well older – h/o thyroid or autoimmune disease, depression, ↓ cognition
- Asymptomatic well older – controversial
  - ATA – TSH in all adults > 35 yrs old every 5 yrs
  - USPSTF and ACP – no screening (no benefit in treating subclinical disease)

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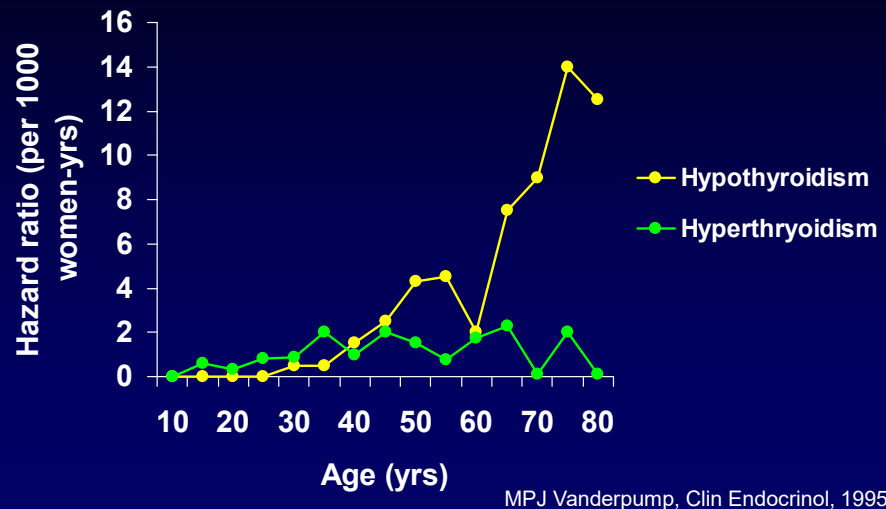
Hazard Ratio for Development of Overt Hypothyroidism and Hyperthyroidism



MPJ Vanderpump, Clin Endocrinol, 1995

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Hypothyroidism
Classic HYPOmetabolism

Symptoms	Signs
Dry skin, ↓ sweating	Coarse dry skin and hair
Cold intolerance	Cold skin
Hoarseness	Periorbital edema
Weight gain, constipation	Mild-moderate weight gain
Paresthesias, ↓ hearing	Slowed movements/reflexes
Fatigue, weakness, cramps	Bradycardia
Depressed mood	Depressed mood

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Hypothyroidism in Older Adults
More Neurobehavioral and CV Manifestations

- Dry skin, hair loss, periorbital edema, cold intolerance (myxedema)
- Paresthesias (carpal tunnel), ataxia, ↓ cognition, depression, apathy, psychosis
- Myopathy, arthralgia
- Bradycardia, pericardial effusion, ↑ CHF

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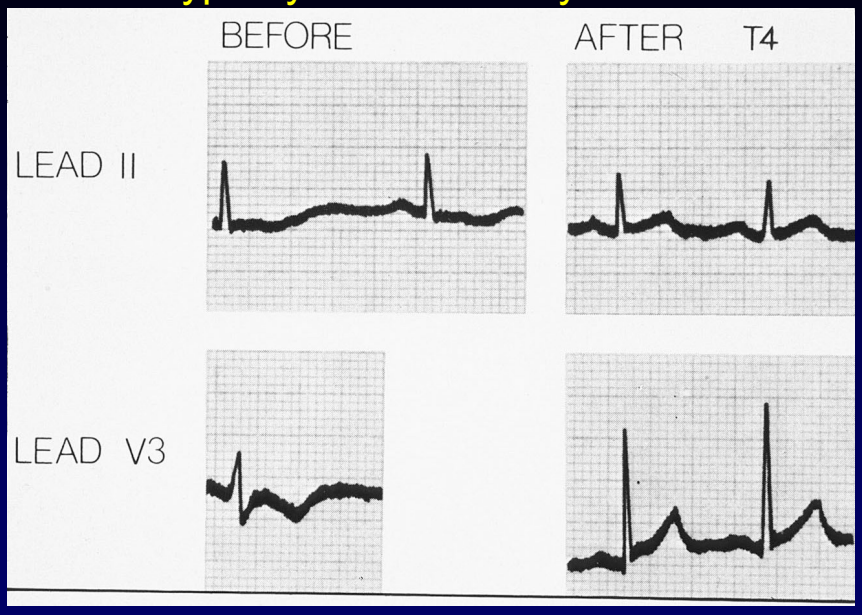
Hypothyroidism: Bradycardia



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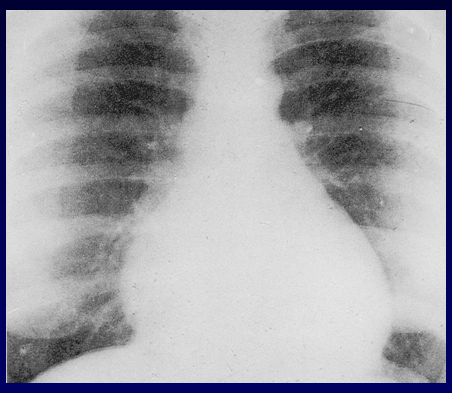
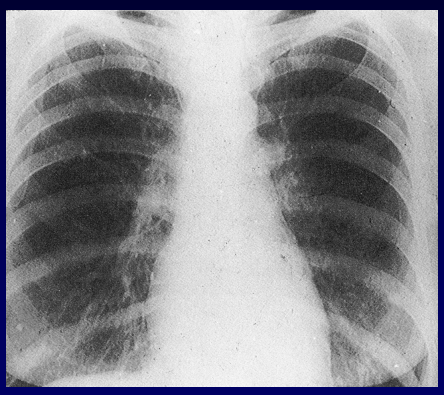
Hypothyroidism: Cardiomegaly Due to Pericardial Effusion



Untreated



After thyroid hormone replacement

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Hypothyroidism
Diagnosis

- ↓ fT_4
  - ↑ TSH - 1° hypothyroidism
  - Normal to ↓ TSH - 2° hypothyroidism
- Normal fT_4 and ↑ TSH (subclinical hypothyroidism)
- Caution – transient ↑ or ↓ TSH with non-thyroidal illness
- Anti-thyroid antibodies (Hashimoto's disease)

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Hypothyroidism
Causes

- Primary
  - Hashimoto's disease (autoimmune) most common
  - Neck irradiation (lymphoma, head & neck CA)
  - Thyroiditis (recovery phase)
  - Surgical removal
  - Lithium, amiodarone, iodine, antithyroid drugs
- Secondary
  - Hypothalamic-pituitary disease
    - Destructive process, e.g. tumor, granulomatous dz
    - Head trauma

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Hypothyroidism in Older Adults

- Common (2-10%) – most subclinical
- Atypical, nonspecific presentation
  - Insidious, often subclinical
  - Neurobehavioral and cardiovascular
  - Myxedema (cold, puffiness)
- Falls, ↓ cognitive function, ↓ mobility
- Non-thyroidal illness affect TFTs

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Hypothyroidism in Older Adults
Treatment

- Symptoms, TSH > 10, + anti-TPO Ab – treat
- Asymptomatic and TSH 4-10 (subclinical) – monitor
- Goal – normal TSH
- T_4 (levothyroxine) fasting
  - 25-50 μg/d → ↑ 25-50 μg/d every 4-6 weeks
  - More rapid for severe
  - Requirement less (~110 μg/d)
  - Ca, alendronate, iron, PPIs, resins → ↓ absorption
  - Dilantin, carbamazepine → ↑ clearance

Peters RP, N Eng J Med 376:2556-2565, 2017; Feller M, et al, JAMA 320:1349-1359, 2018; Biondi B, et al, JAMA 322:153-160, 2019

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Hyperthyroidism
Classic HYPERmetabolism

Symptoms	Signs
Nervousness	Hyperkinesis
↑ Sweat, heat intolerance	Warm, moist hands and skin
Dyspnea, palpitations	Tachycardia, atrial fibrillation
Fatigue, weakness	Tremor, weakness
Weight loss, ↑ appetite	Weight loss
Double vision, red eye	↓ EOMs, lid retraction/lag
Hyperdefecation	Thyroid enlargement

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Hyperthyroidism in Older Adults
More Neurobehavioral and CV Manifestations

- ↓ Appetite, weight loss, nausea, constipation
- Depression, apathy, lethargy, irritability
- Proximal muscle wasting and weakness
- Peripheral neuropathy
- Palpitations, atrial fibrillation, CHF

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Graves Disease

- Autoimmune disease (TSI)
- Hyperthyroidism with diffuse goiter
- Ophthalmopathy
  - Proptosis, ↓ EOMs, chemosis
- Dermopathy
  - Pretibial myxedema, thyroid acropachy (nails)
- Elderly may not have any of these signs

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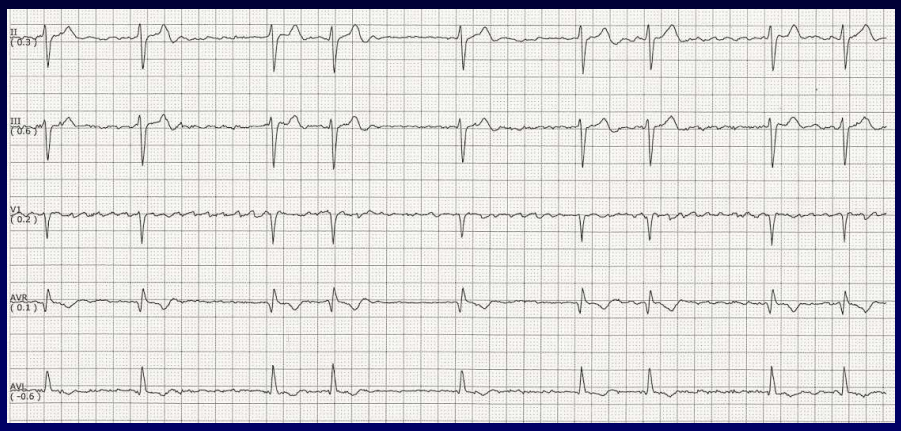
Hyperthyroidism: Atrial fibrillation

- Atrial fibrillation with a slow ventricular response may be present in older patients



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Hyperthyroidism
Diagnosis

- Undetectable or ↓↓ TSH and ↑ fT_4
  - Sometimes only ↑ T_3 (T_3 thyrotoxicosis)
- ↓ TSH and normal T_4 and T_3 (subclinical hyperthyroidism)
- TSI (Graves' disease)

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Radioactive Iodine Uptake (RAIU)
DDx of Hyperthyroidism

- High uptake
  - Graves disease
  - Toxic multinodular goiter or adenoma
- Low to no uptake
  - Thyroiditis
  - Exogenous thyroid hormone
  - Iodine-induced

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Hyperthyroidism in Older Adults

- Not uncommon (0.5-2.0%) – most subclinical
- Atypical or subclinical presentation
  - Apathetic, depressed, hypokinetic
  - Weight loss, anorexia, constipation, weakness
  - Dyspnea, slow atrial fibrillation, CHF
- Graves disease most common (atypical)
- Toxic multinodular goiter more common
- T_3 thyrotoxicosis

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Hyperthyroidism in Older Adults
Treatment

- Symptoms and TSH < 0.1 (undetectable)
- Asymptomatic normal fT4 and TSH 0.1-0.3 (low) – subclinical hyperthyroidism
  - Atrial fibrillation
  - Heart disease
  - Osteoporosis
  - Cognitive impairment

Bondi B and Cooper DS, N Eng J Med 378:2411-2419, 2018

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Hyperthyroidism in the Elderly
Treatment of Graves Disease

- Symptomatic/prior to radioactive iodine
  - β blockers
    - Propanolol 40-120 mg/d
- Anti-thyroid drugs
    - Methimazole 5-15 mg/d
- Radioactive iodine

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Nodular Thyroid Disease

- Multinodular
  - Usually benign
  - Suspicious nodule may be cancer
- Solitary nodule – most nonpalpable
  - Most benign and cold on scan
  - Some cancer
- Cysts
  - Usually benign and cold on scan

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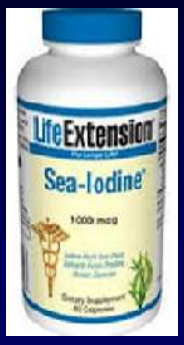
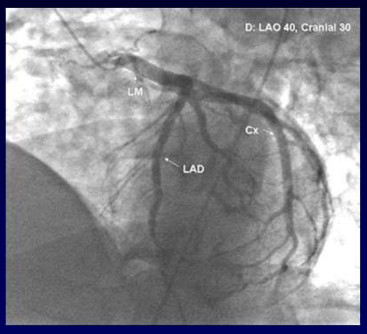
Nontoxic Multinodular Goiter: Excessive Iodine Intake or Radiocontrast May Induce Hyperthyroidism

1950 μg



1000 μg



30,000 μg

RDA ~150 μg

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Nontoxic Multinodular Goiter
Management

- Issues
  - Local compressive symptoms
  - Cosmetic
  - ↑ Risk iodine-induced hyperthyroidism
  - Low risk of malignancy
- Treatment
  - No treatment
  - TSH suppression with T_4 NOT RECOMMENDED
    - Poor partial response
    - ↑ Risk of symptomatic hyperthyroidism
  - Surgery

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Solitary Thyroid Nodule

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Solitary Thyroid Nodule

- Common (prevalence ~5%)
  - Palpable in ~7% women and 2% men
  - ↑ Prevalence with neck irradiation and in elderly
  - ~50% at autopsy
  - Greater incidental detection with ultrasound
- Majority benign ~85%
  - ~15% malignant (most clinically suspicious)

Durante C, et al, JAMA 319:914-924, 2018

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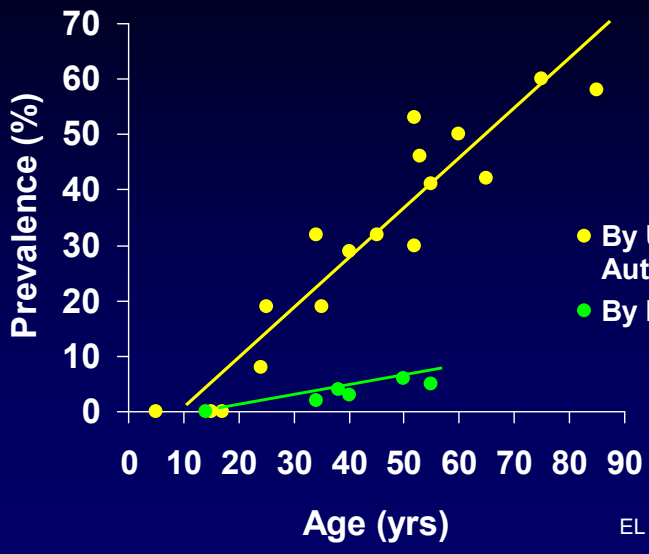
Prevalence of Thyroid Nodules



EL Mazzaferri, NEJM, 1993

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Solitary Thyroid Nodule
↑ Risk of Cancer

- Male, child or elderly
- History of neck irradiation
- Family history of medullary thyroid cancer/MEN
- Recent ↑ size, large (> 4 cm)
- Rock hard
- Hoarseness, fixed, dysphagia, dyspnea
- Lymphadenopathy, distant metastasis

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Solitary Thyroid Nodule
Management

- Surgery if suspicious for cancer
- Fine needle aspiration biopsy (FNAB) US-guided
  - Nodule ≥ 1 cm and suspicious US
  - Nodule ≥ 1.5-2.0 cm and not suspicious US

2015 ATA Guidelines. BR Haugen, et al, Thyroid 26:1-133, 2016

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Nodular Thyroid Disease in the Elderly

- Multinodular goiter very common (60-90%)
  - ↑ Autonomy → ↑ risk of hyperthyroidism
  - Resistant to T_4 suppression
  - ↑ Iodine-induced hyperthyroidism
- Solitary nodules also very common
  - ↑ Mortality with well-differentiated thyroid carcinoma
  - ↑ Lymphoma and anaplastic thyroid carcinoma
  - ↑ Hyperthyroidism with TSH suppression

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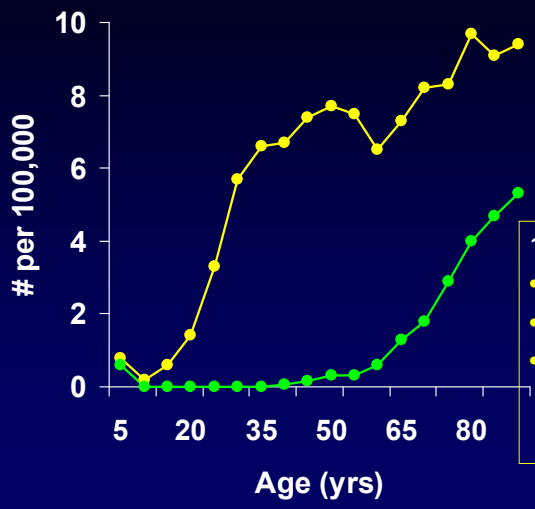
Increased Incidence and Death Rate of Thyroid Cancer with Aging



1974-2013
- Incidence ↑ 3.6%/year
- Mortality ↑ 1.1%/year
- Advanced papillary thyroid cancer mortality ↑ 2.9%/year

JL Young Jr, NCI Pub NIH81-2330, 1981;
Lim H, et al, JAMA 317:1338-1348, 2017

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Thyroid Disorders in Older Adults
Take Homes

- Common – hypothyroidism > hyperthyroidism
- Subclinical > overt disease
- Clinically atypical, confounded by co-morbidities, attributed to “old age”, geriatric syndrome
- Measure fT_4 and TSH in non-healthy
- TFTs misleading in non-thyroidal illness
- Thyroid replacement dose lower
- Co-morbidities may compromise therapy, worsened by inappropriate treatment, predispose to drug interaction and poor compliance
- Well-differentiated thyroid cancer prognosis worse

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Case Scenario

- 70 years-old female admitted to the ICU with CHF exacerbation
- Diagnosed with A fib, HR 58, BP 95/60
- Pt underwent a cardiac cath showing “clean” coronaries 1 month prior
- Pt has irregular heart beat, bilateral crackles on lung exam and 2+ pedal edema
- Diffuse goiter
- Lab shows a normal CMP, TSH 0.4, FT4 2,
- US shows diffusely enlarged thyroid with a 1.1 cm nodule

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Case Scenario

- No scan or FNA were performed
- TSI was negative
- Pt was diagnosed with hyperthyroidism and treated with MMI and BB after fluid repletion
- Her symptoms improved over the ensuing days

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