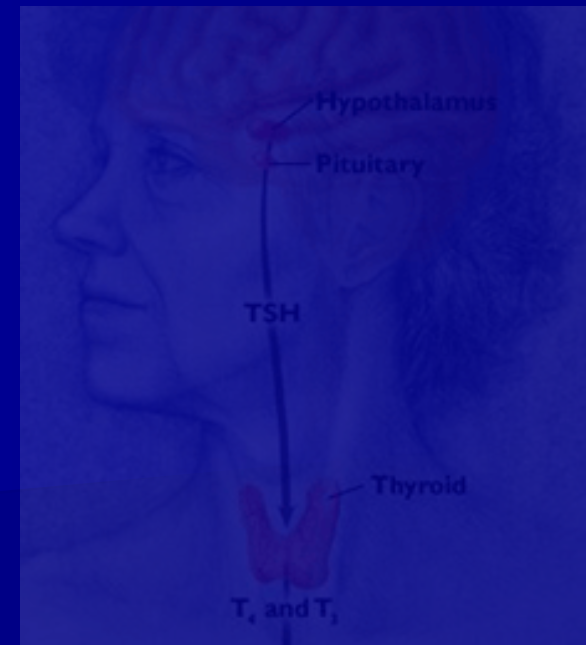


Thyroid Dysfunction in the Elderly

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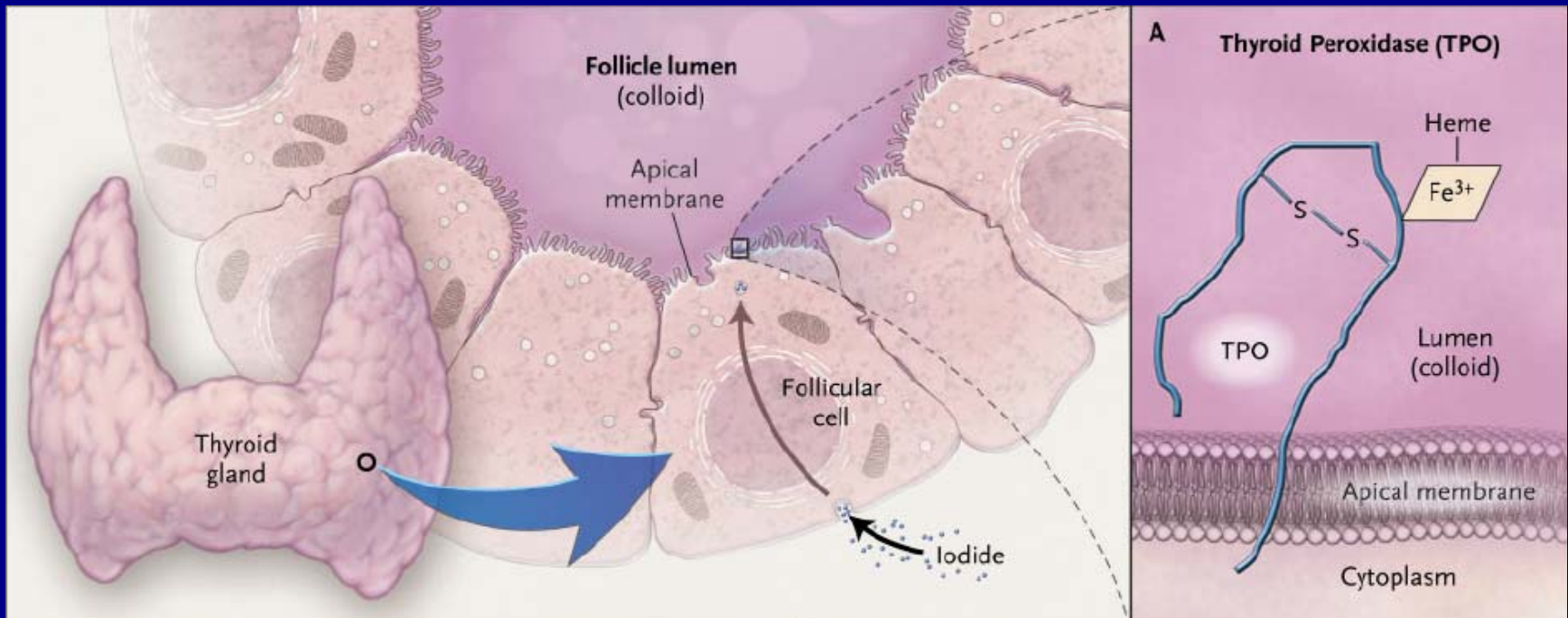
Outline

- Normal thyroid physiology, regulation and action
- Changes in thyroid function with aging
- Unique features of thyroid disease in the elderly
- Medications
- Nonthyroidal illness

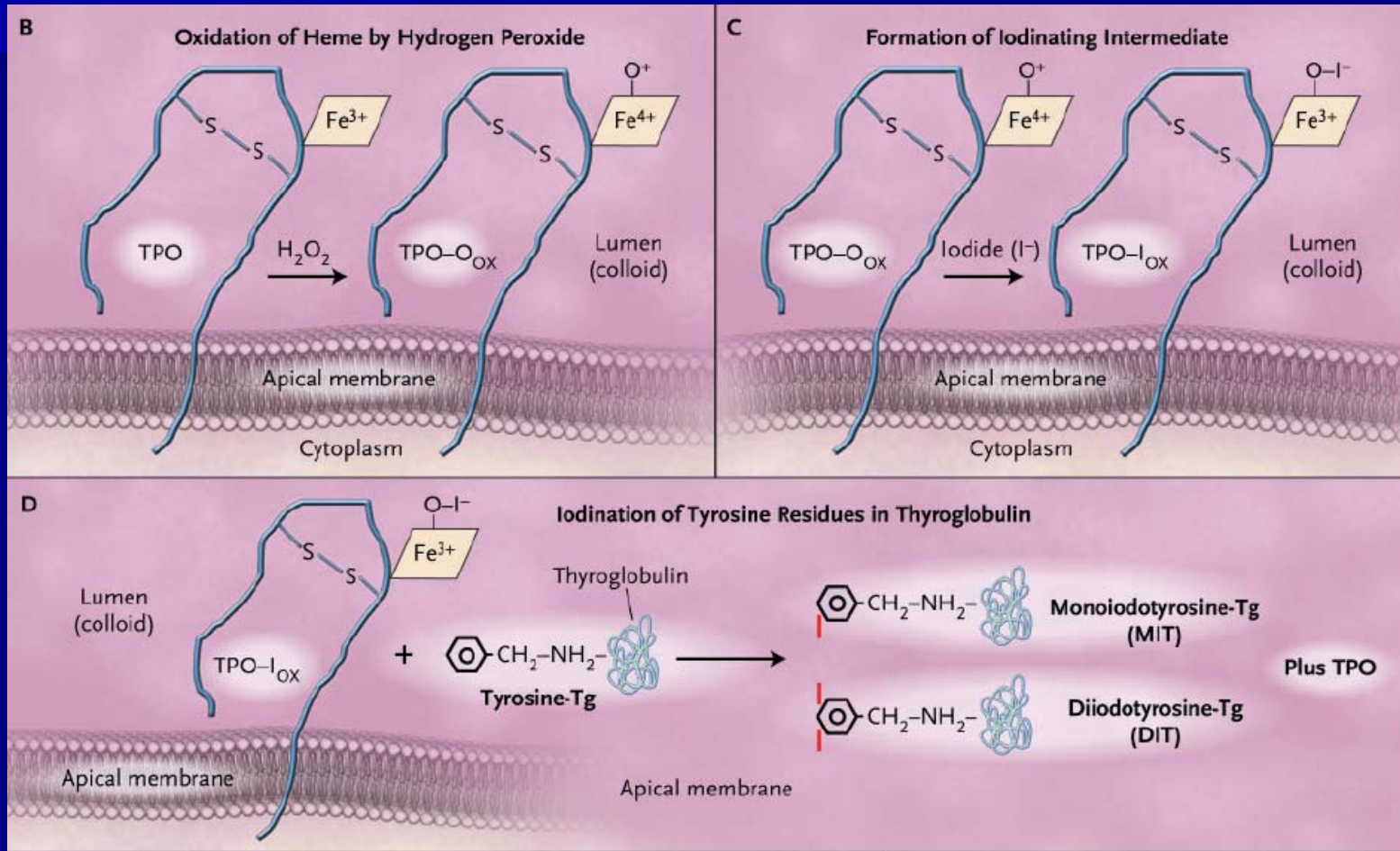
Normal Physiology of the Thyroid

- Its main function is to secrete appropriate amounts of tetraiodothyronine (T4) and triiodothyronine (T3)
- Most (80%) of T3 is produced by extrathyroidal deiodination of T4
- T3 interacts with nuclear T3 receptors in multiple target tissue and subsequently affect promoter regions of genes that are positively or negatively regulated by thyroid hormone

Thyroid hormone synthesis

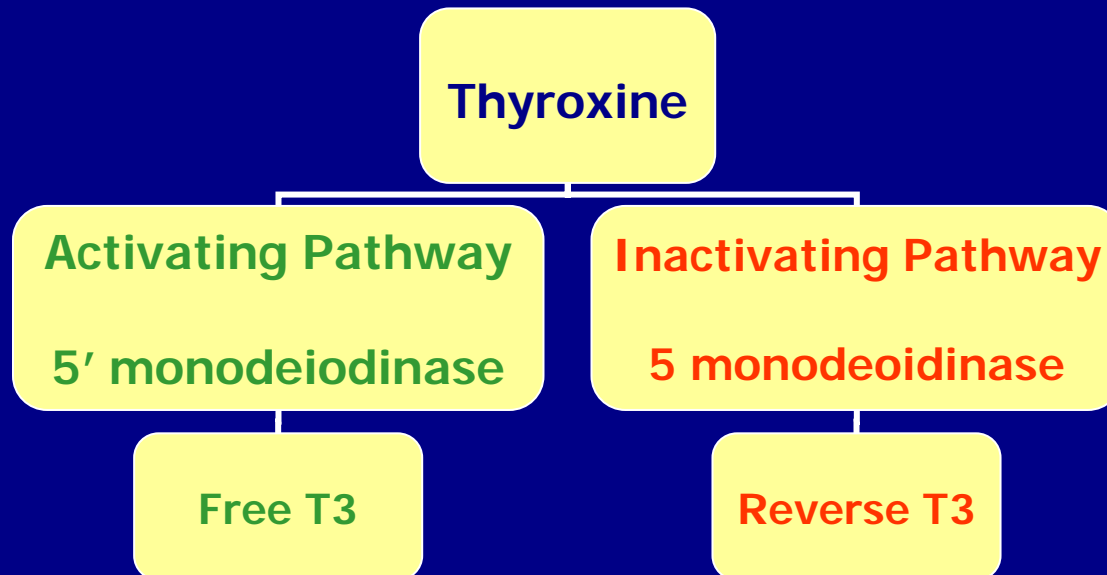


Thyroid hormone synthesis



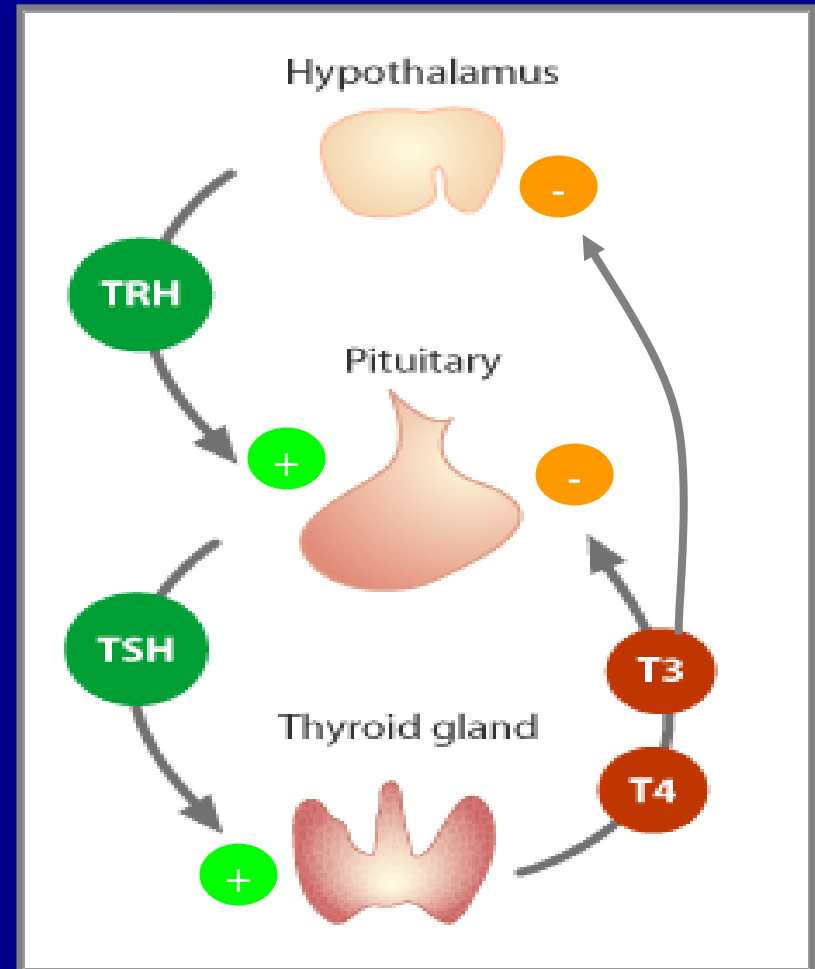
Thyroid hormone transport and metabolism

- Only 0.04% of T4 and 0.4% of T3 are unbound
- Major binding protein
 - Thyroxine binding globulin 70%
 - Transthyretin 10%
 - Albumin 15%
- Deiodination in target tissue



Regulation of Thyroid function

- Hypothalamic TRH stimulates thyrotrophic cells in anterior pituitary to produce TSH
- TSH promotes thyroid gland growth and hormone secretion
- TSH is regulated by T3 levels within thyrotrophic cells



Thyroid hormone action

- Promotes normal fetal and childhood growth and development
- Regulates heart rate, myocardial contractility and cardiac output
- Maintains ventilatory responses to hypoxia and hypercapnia in the brainstem
- Modulates body energy expenditure, heat generation and weight
- Lipid and carbohydrate metabolism
- Stimulates bone turnover and increases bone resorption and bone formation
- Affects gastrointestinal motility and renal water clearance

Age related changes

- Each organ system function declines at different rates
- 75% of the elderly have at least one disease
- Thyroid disease will manifest itself with symptoms derived from the most compromised system
- The existence of other disease and the use of multiple medications will mask or mimic the presentation of thyroid disease

Age related changes in thyroid function

- Overall thyroid function tests T4, TSH and T3 do not change with aging

Prevalence of Thyroid Disease

- Prevalence is twice that of younger population
- Hypothyroidism 2-7%
- Subclinical hypothyroidism 6-13%
- Progression to overt hypothyroidism is 2-5% per year
- Hyperthyroidism 2%

Hypothyroidism in the Elderly

- Most commonly due to Chronic autoimmune thyroiditis, radioactive iodine ablation, thyroid surgery, iodine deficiency.
- Other possible causes in the elderly amiodarone, lithium
- The risk of developing overt hypothyroidism increases with age in the presence of anti-thyroid Abs or elevated TSH
- Female: Male ratio 10:1

Unique features of hypothyroidism in the Elderly

- May easily overlook hypothyroidism
- 50% complain of fatigue and weakness
- Weight gain is usually not more than 10-20 lbs
- More likely to present with cardiovascular or neuropsychiatric symptoms

Clinical Presentation

■ Cardiovascular:

- bradycardia
- Diminished cardiac output
- Low voltage QRS
- Diastolic hypertension
- Increased LDL
- Pericardial effusion

■ Neuropsychiatric:

- Lethargy, fatigue, sleep disturbance
- Poor concentration, cognitive impairment
- Depression
- Myxedema madness (confusion, paranoia) in severe disease

■ Pulmonary

- Sleep apnea
- Exquisite sensitivity to sedative medications

Clinical Presentation

- Signs:
 - Puffy face
 - Hoarseness of voice
 - Coarse hair, hair loss
 - Edema
 - Dry skin
 - Macroglossia
 - Atrophic thyroid gland
 - Delayed relaxation phase of deep tendon reflexes

FACIAL SIGNS OF MYXEDEMA

Characteristic myxedematous signs in adults include dry, flaky, inelastic skin; puffy face; and upper eyelid droop.



Diagnosis

- Clinical presentation
- Biochemical assessment:
 - Elevated TSH
 - Low Free T4
 - Central hypothyroidism should be considered if low FT4 and normal TSH

Treatment

- Levothyroxine:
 - Initiation of low dose levothyroxine 25-50 mcg/ day
 - Increase by 12.5-25 mcg every 1-2 weeks until an approximate dose of 1 mcg/kg/day
 - Ensure proper administration of levothyroxine
 - Target TSH 1.0-3.0 mIU/L
 - Adjustment of other medications as hypothyroidism is corrected
 - Avoid over treatment




Drugs influencing thyroid hormone requirements

- Affecting exogenous T4 absorption
 - Bile acid sequestrants
 - Ferrous Sulfate
 - Calcium/ MVI
 - PPI
 - Bisphosphonates
- Drugs that increase TBG concentration
 - Oral estrogens
 - Tamoxifen
 - Methadone
 - Mitotane, Fluorouracil
- Drugs affecting T4 metabolism
 - Phenobarbital
 - Rifampin
 - Phenytoin
 - Carbamazepine

Subclinical Hypothyroidism

- A lab diagnosis: High TSH with normal Free T4
- Asymptomatic or vague symptoms : fatigue, sleep disturbance, cognitive impairment, depression
- Same causes as overt hypothyroidism: most commonly autoimmune thyroiditis.
- Prevalence in women > 60 years old is 20%
- Progression to over hypothyroidism 2-5% per year

Subclinical Hypothyroidism

- To treat or not to treat ?
- Cardiovascular risk?
 - Rotterdam study : increased risk of aortic atherosclerosis and MI in women
 - Increased total cholesterol and LDL, decreased HDL
 - Treatment of subclinical hypothyroidism associated with improvement in surrogate markers of cardiovascular disease
- TSH values between 4.5 -10 mIU/L  controversial
- Treatment strongly recommended for:
 - TSH >10 mIU/L
 - Symptoms or signs
 - Family history of thyroid disease
 - hyperlipidemia

Hyperthyroidism in the Elderly

- Prevalence of suppressed TSH 2%
- Prevalence of Grave's disease decreases but remains most common cause of hyperthyroidism
- There is an increased prevalence of Multinodular goiter and toxic nodules

Clinical Presentation in the Elderly

- Presentation reflects most vulnerable systems
- Nonspecific symptoms
 - Anorexia
 - Weight loss and loss of appetite
 - Constipation
- Cardiovascular:
 - atrial fibrillation
 - Dyspnea
 - Angina
 - CHF and MI
- “Apathetic thyrotoxicosis”
- Muscle weakness and proximal muscle wasting

Diagnosis

- Low TSH (some pitfalls)
- High Free T4 and/or Free T3
- I-123 thyroid scan
 - evaluate cause of hyperthyroidism
 - To determine dose of radioactive iodine to be used for treatment in the future

Treatment

- Symptom control with beta blocking agents
- Referral to endocrinologist
 - Anti-thyroid drugs
 - Radioactive iodine
 - Surgery
- Post treatment monitoring and adjustment of other medication doses

Antithyroid Medications

- Side effects:
 - Allergic reaction : minor rash in 5% of patients
 - Rare
 - Agranulocytosis 0.5%
 - Hepatic toxicity 0.1%
 - Acute arthritis
 - Vasculitis

Subclinical Hyperthyroidism

- Low or undetectable TSH level in the face of a normal Free T4 and T3 level
- Causes: Grave's , MNG, autonomous solitary nodule, thyroiditis
- Cardiovascular effects:
 - Increased frequency of premature atrial & ventricular beats
 - Increased frequency of atrial fibrillation
- Treatment recommended if TSH < 0.1 mIU/L or the patient has cardiovascular disease

Factors affecting thyroid evaluation

- Overt thyroid disease present in 9% of hospitalized elderly patients
- Hospitalized patients:
 - Medications
 - Radiocontrast studies
 - Non-Thyroidal Illness (Euthyroid sick syndrome)

Medications and Thyroid Function

- Drugs affecting thyroid function tests
- Drugs causing thyroid dysfunction

Drugs affecting thyroid function tests

- Low TSH can be caused by use of:
 - Dopamine
 - Octreotide
 - Glucocorticoids

Drugs causing thyroid dysfunction

- Lithium Carbonate
- Cytokines:
 - Interferon alfa: positive antithyroperoxidase antibodies in 20%
 - Interleukin-2 : painless thyroiditis in 20%
- Iodine containing medication
 - Radiographic contrast (coronary angiography, computed tomography)
 - Amiodarone

Iodine containing medications

- Normal thyroid gland
 - Transient decrease T3 and T4 secretion and increase in TSH
- Euthyroid with Chronic Autoimmune thyroiditis
 - Persistent hypothyroidism
- Euthyroid with thyroid autonomy (multinodular goiter)
 - Persistent hyperthyroidism

Amiodarone

- Iodine content is 75mg per tablet
- Elimination half life is 100 days
- Transient effects (may last for several months)
 - Inhibits T4 to T3 conversion
 - Increases rT3 and decreases T3
 - Increase TSH
- Destructive thyroiditis
- May cause hypothyroidism in 5-25%
- May cause hyperthyroidism in 2-10%
- Obtain thyroid function tests before initiation of therapy and periodically afterwards

Non-Thyroidal Illness in the Elderly

- Also referred to as euthyroid sick syndrome, or low T3 syndrome
- Adaptive changes in acute illness to conserve energy expenditure by reducing metabolic rate
- Low T3, Low T4, High reverse T3
- Can occur in 75% of hospitalized patients
- Magnitude of changes depends on severity of illness
- Low T3 is an independent predictor of survival
- TSH can be low during acute illness and may increase as high as 20 mIU/L during recovery phase

Summary

- Knowledge of the physiology of the hypothalamic pituitary thyroid axis, the common drug interactions and effects, the multiple coexistent illnesses, and the subtle presentation of thyroid disease is essential for the clinicians evaluation and management of thyroid disease in the elderly patient