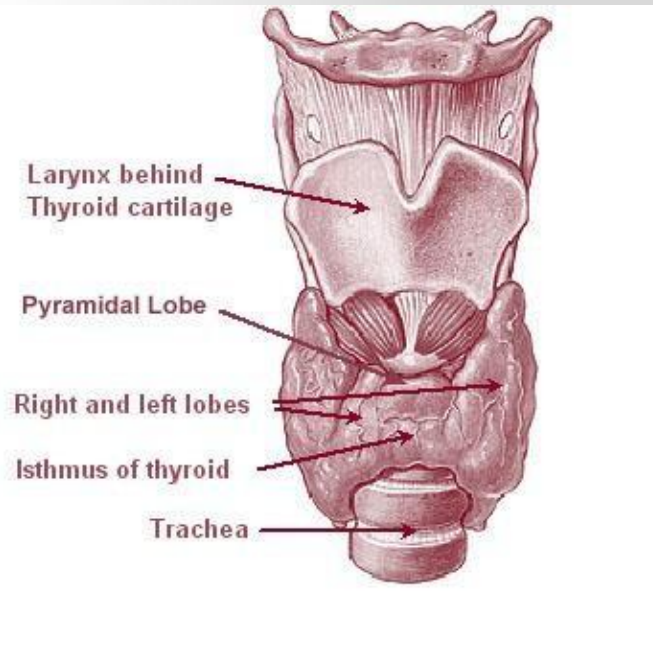


Thyroid Gland

Jason Ryan, MD, MPH

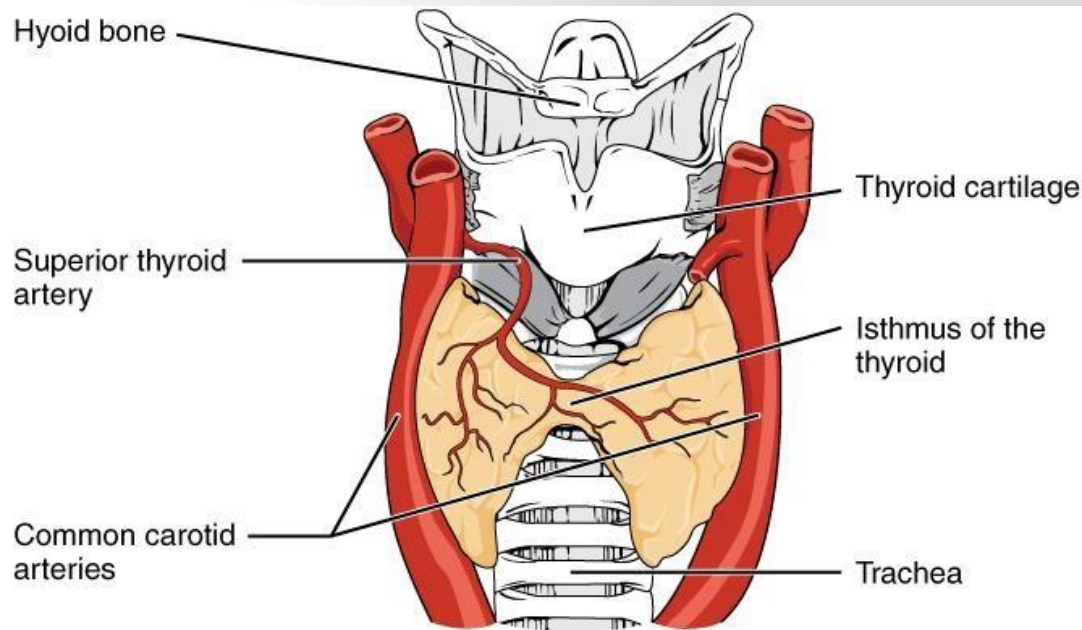
Thyroid Anatomy

- Two lobes (left, right)
- Isthmus: thin band of tissue between lobes
- Sometimes pyramidal lobe above isthmus



Thyroid Anatomy

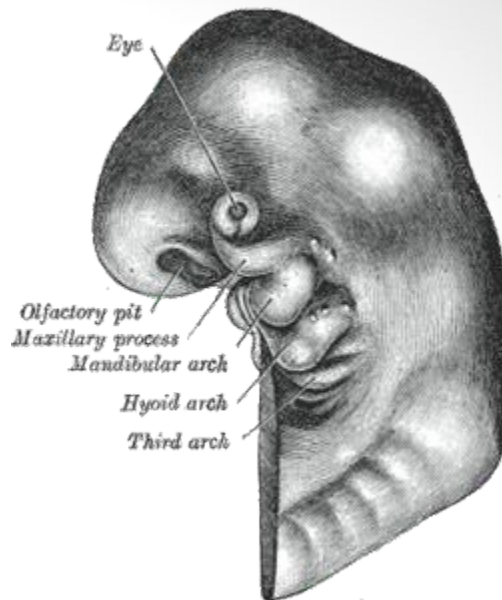
- Blood supply: superior and inferior thyroid arteries
- Superior thyroid: 1st branch external carotid artery
- Inferior thyroid: Thyrocervical trunk (off subclavian)



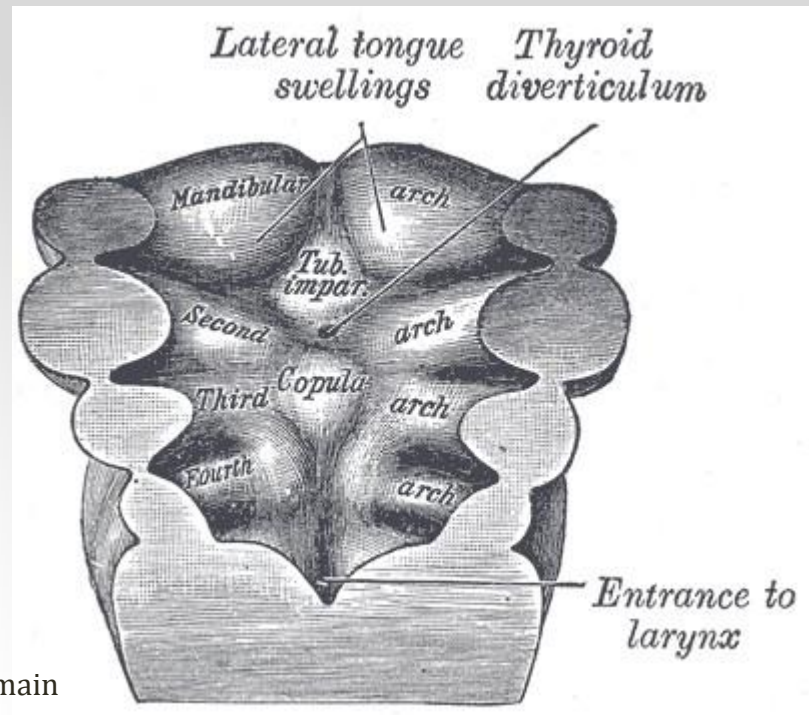
Thyroid Embryology

- Forms from floor of pharynx (epithelial cells)

24-28 Day Old Embryo



Wikipedia/Public Domain

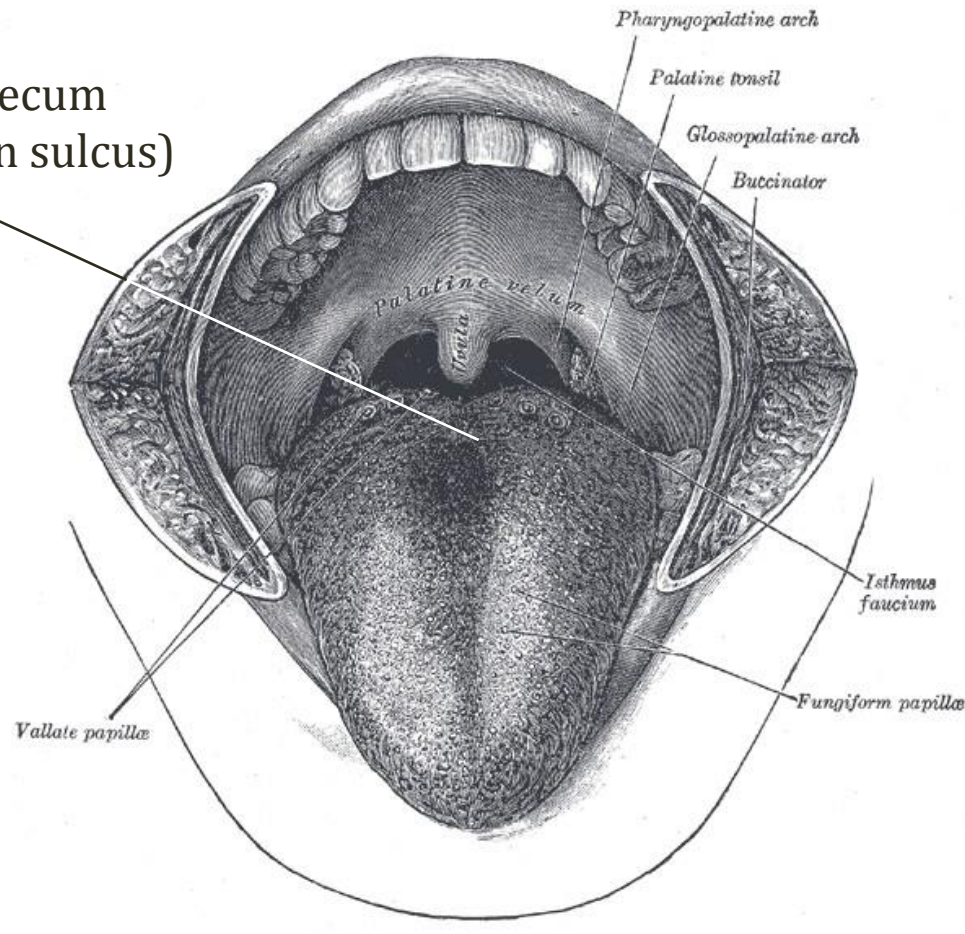


Thyroid Embryology

- Descends into neck
- Initially maintains connection to tongue
 - **Thyroglossal duct**
 - Disappears later in development
- Two remnants of duct in child/adult
 - Foramen cecum in tongue
 - Pyramidal lobe of thyroid

Foramen Cecum

Foramen Cecum
(end of median sulcus)



Thyroglossal Duct Cyst

- Persistent remnant of thyroglossal duct
- **Midline neck mass**; usually painless
- Usually discovered in childhood
- Classically, move up with swallowing or tongue protrusion
- May contain thyroid cells



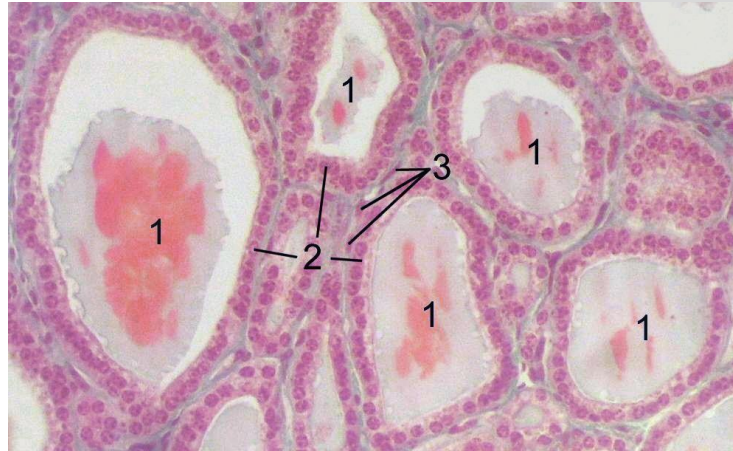
Klaus D. Peter, Gummersbach, Germany

Ectopic Thyroid

- Functioning thyroid tissue outside of gland
- Most common location is **base of tongue**
- Presents as a mass in the tongue
 - Commonly detected during increased demand for hormones
 - Puberty and pregnancy
- May be the only functioning thyroid tissue
 - May under-produce thyroid hormone □ **hypothyroidism**
 - ↑ TSH □ growth of ectopic tissue

Thyroid Histology

- Thyroid gland contains “follicles”
- Filled with colloid (protein material)
- Single layer of epithelial cells lines each follicle
 - “Follicular cells”
- Hormone synthesized by follicular cells



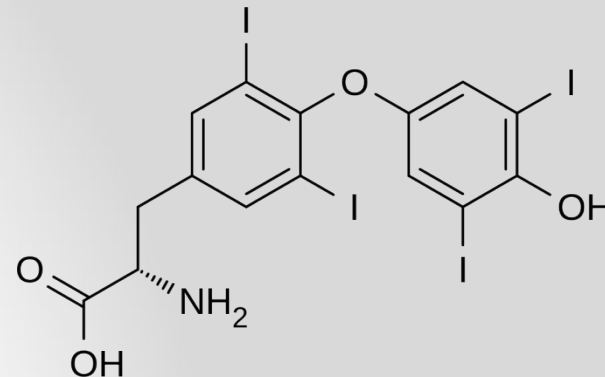
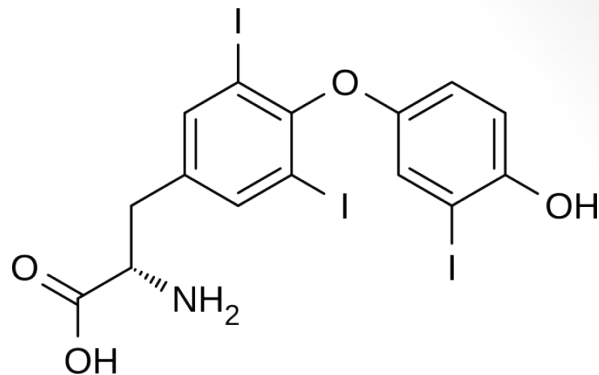
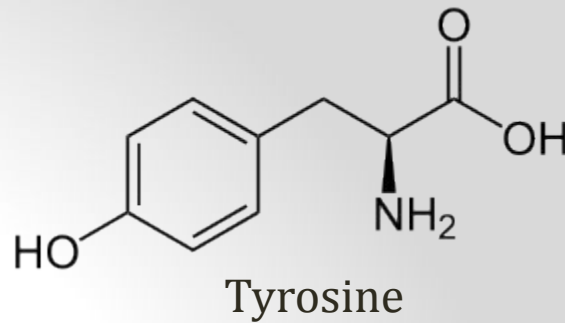
[Uwe Gille/Wikipedia](#)

Thyroid Hormones

- Contain the element **iodine**
- **Iodized salt**
 - Table salt (NaCl) mixed with small minute amount of iodine
 - Done in many countries to prevent iodine deficiency
 - Added to salt in US in 1924

Thyroid Hormones

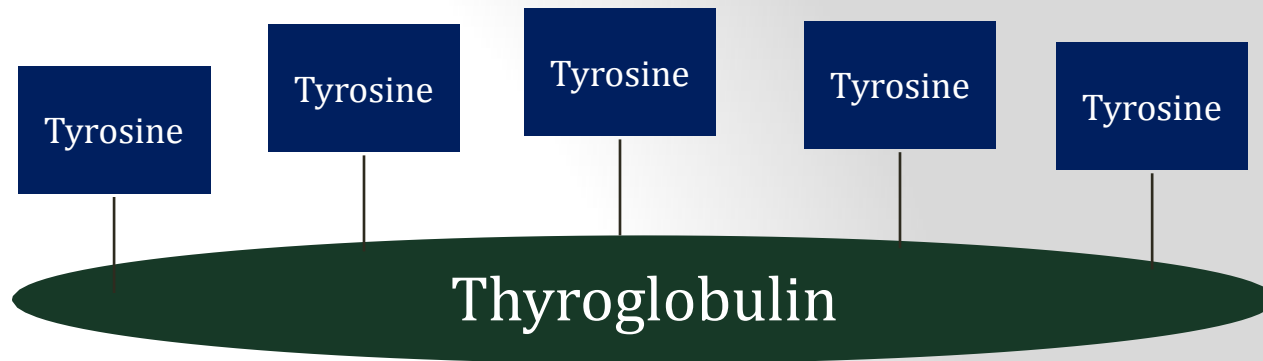
- Two hormones: T₃ and T₄
- Synthesized from tyrosine and iodine



Thyroglobuli

n

- Large protein
- Produced by thyroid follicular cells
- Contains numerous tyrosine molecules

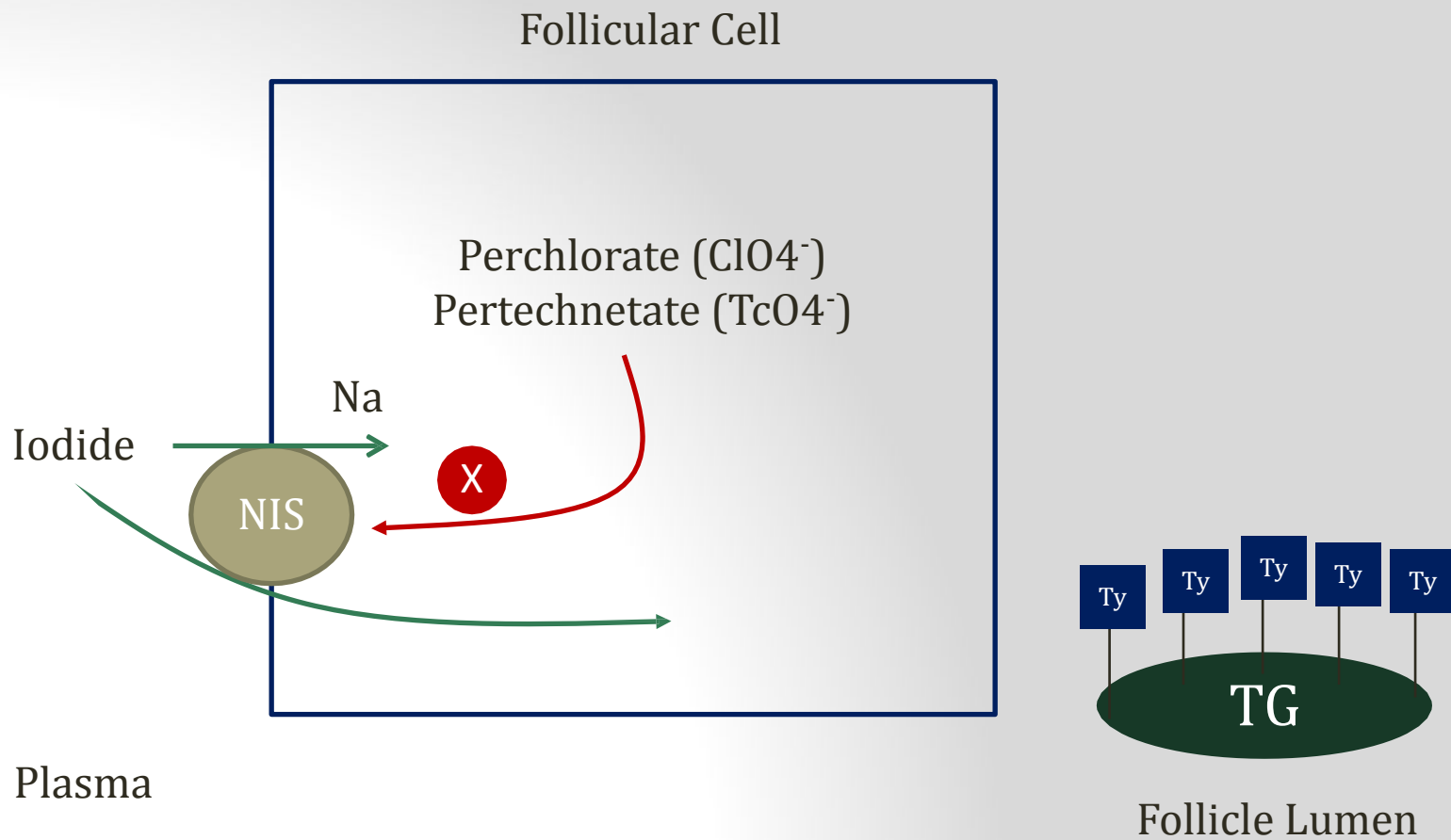


Iodin

e

- **Iodine** = I (chemical element, atomic number 53)
- **Iodide** = iodine bound to another atom
 - “Iodide salt” with negative charge (I^-)
 - Potassium iodide = KI
 - Plasma iodine exists as iodide salt
- For thyroid hormone, iodide in our diet needs to be:
 - Taken up by follicular cells
 - Oxidized to I_2 (undergo “**oxidation**”)
 - Added to organic/carbon structures (“**organification**”)

NIS
Na-Iodine Symporter



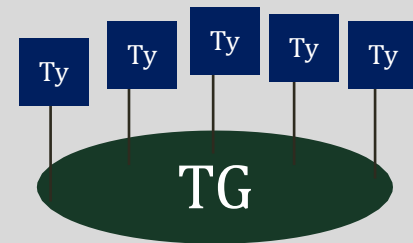
Follicular Cell

Iodide

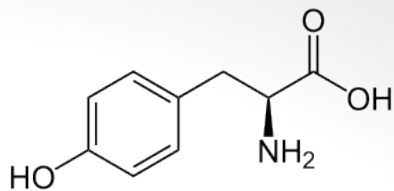
Thyroid
Peroxidase
(TPO)

I_2

Plasma



Follicle Lumen

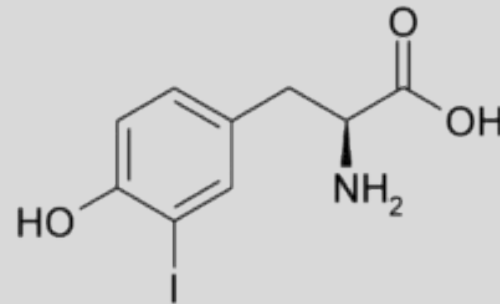


Tyrosine

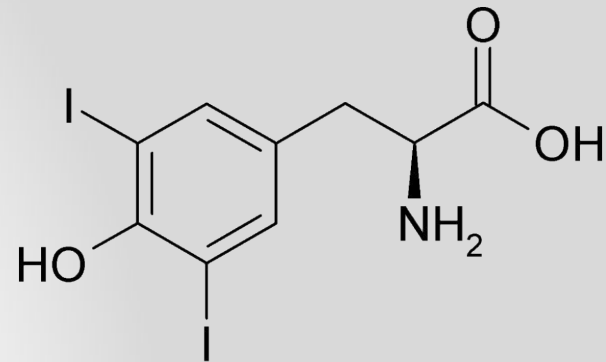
+

Iodine (I_2)

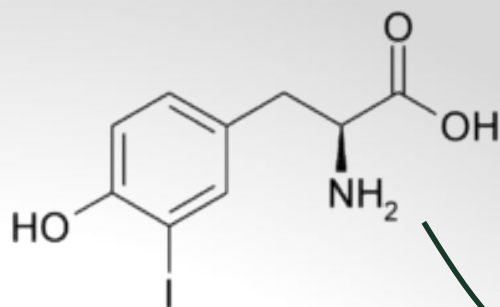
Thyroid Peroxidase
(TPO)



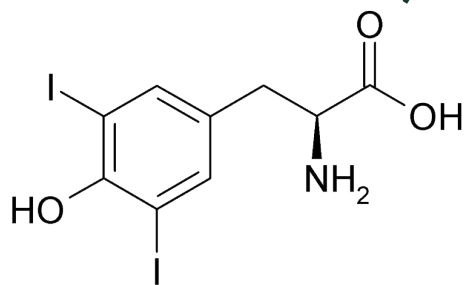
Monoiodotyrosine
(MIT)



Diiodotyrosine
(DIT)

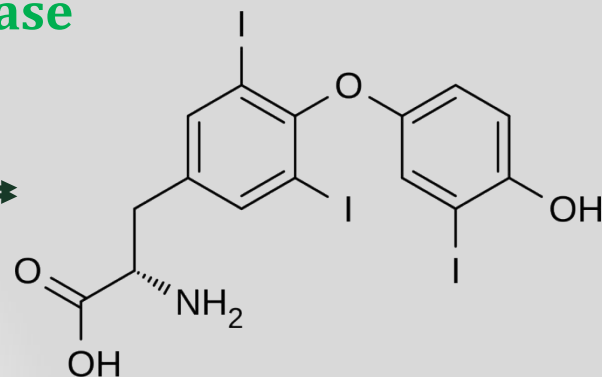


Monoiodotyrosine
(MIT)



Diiodotyrosine
(DIT)

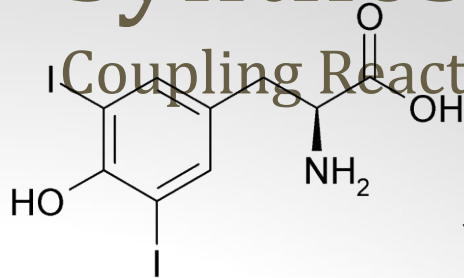
**Thyroid Peroxidase
(TPO)**



Triiodothyronine (T_3)

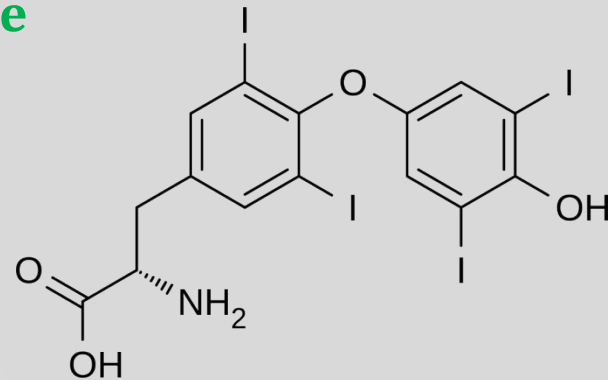
Hormone Synthesis

Coupling Reactions

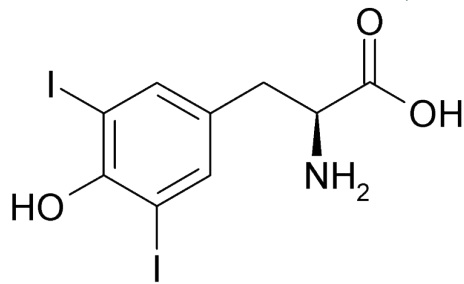


Diiodotyrosine (DIT)

Thyroid Peroxidase (TPO)



Thyroxine (T₄)



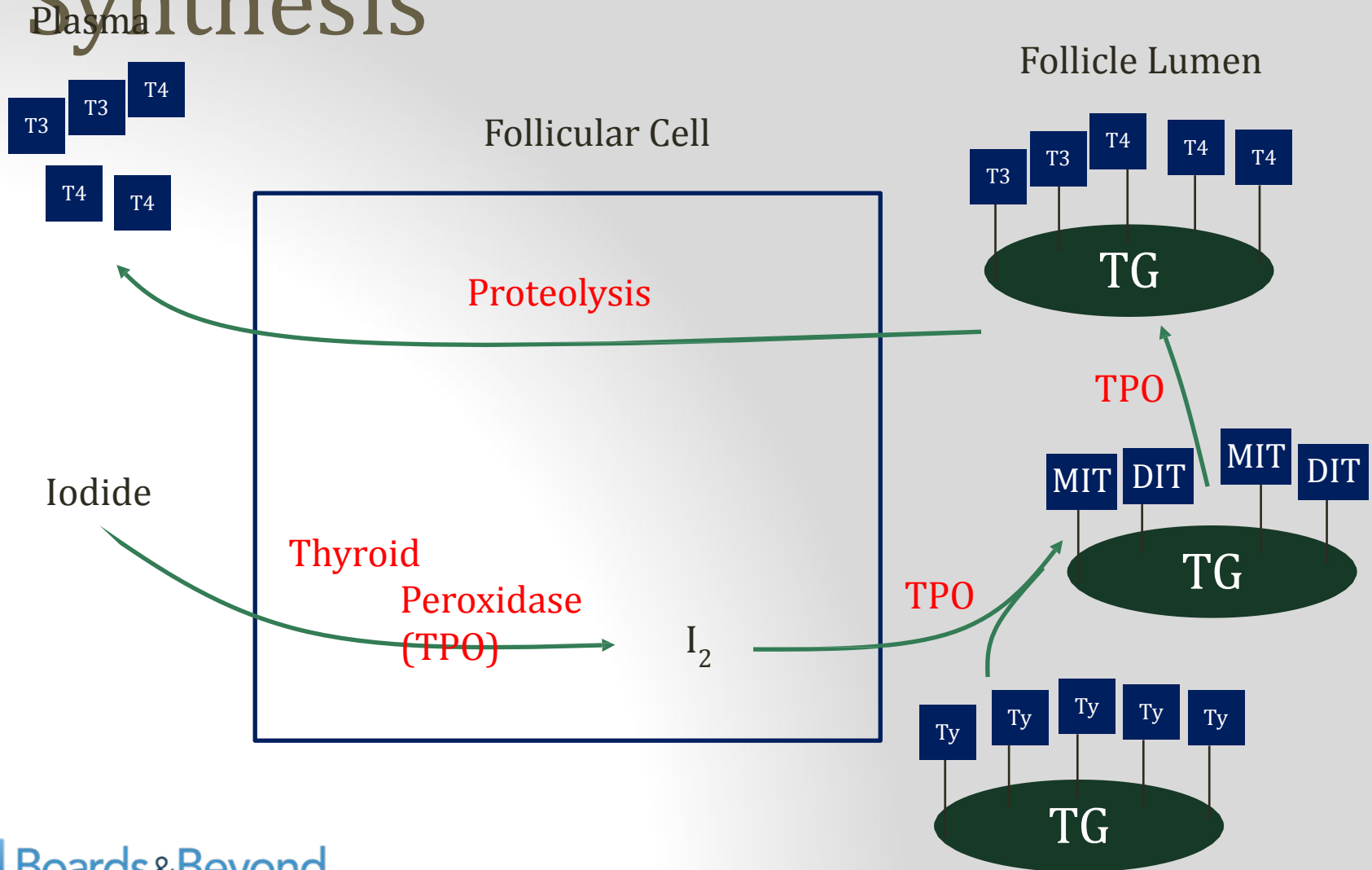
Diiodotyrosine (DIT)

TP

Thyroid Peroxidase

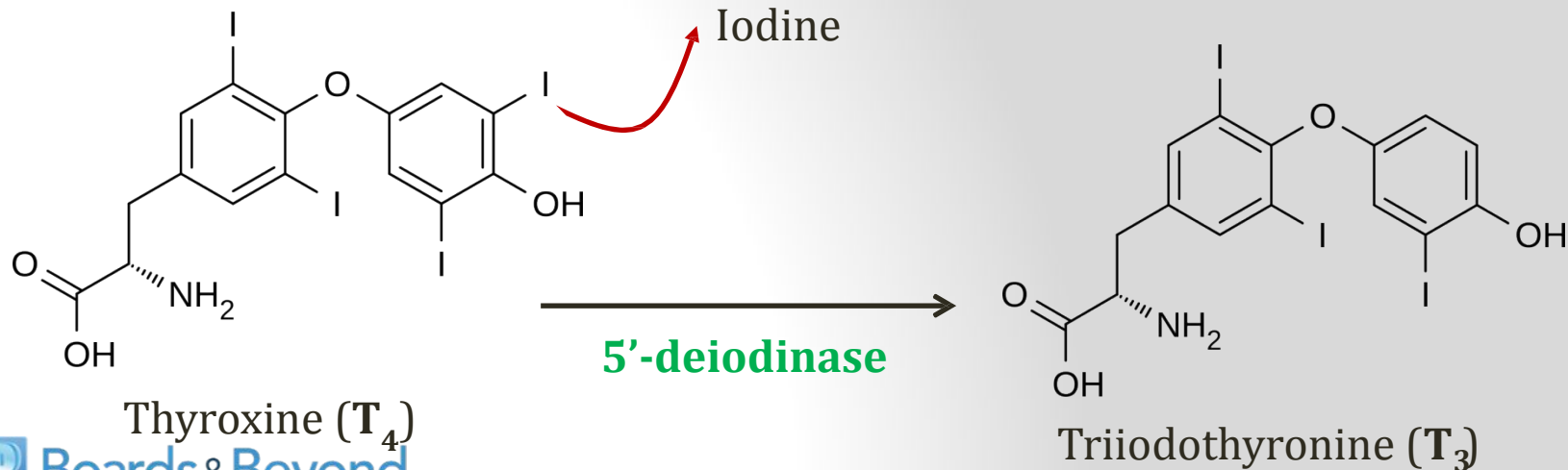
- Multifunctional enzyme
- Catalyzes:
 - Oxidation of iodide
 - Organification of iodine into MIT/DIT
 - Coupling of MIT/DIT into T3/T4
- TPO antibodies common in autoimmune thyroid disease

Hormone Synthesis



Thyroid Hormones

- T4 is major hormone produced by thyroid gland
 - >90% of thyroid hormone produced is T4
- T3 more potent hormone
- T4 is a “prohormone” for T3
- **5' deiodinase** converts T4 → T3
- Most conversion occurs in **peripheral tissues**



Hyperthyroid Medications

- **Propylthiouracil (PTU)**

- Inhibits TPO: ↓ T3/T4 from thyroid gland
- Inhibits 5'-deiodinase: ↓ T4 to T3 conversion peripherally

- **Methimazole**

- Inhibits TPO

- **Propranolol**

- Beta blocker
- Weak inhibitor of 5'-deiodinase
- Excellent drug in thyrotoxicosis
- Blocks catecholamines and T4-T3 conversion

PTU and Methimazole are both
“thioamides”

Wolff-Chaikoff

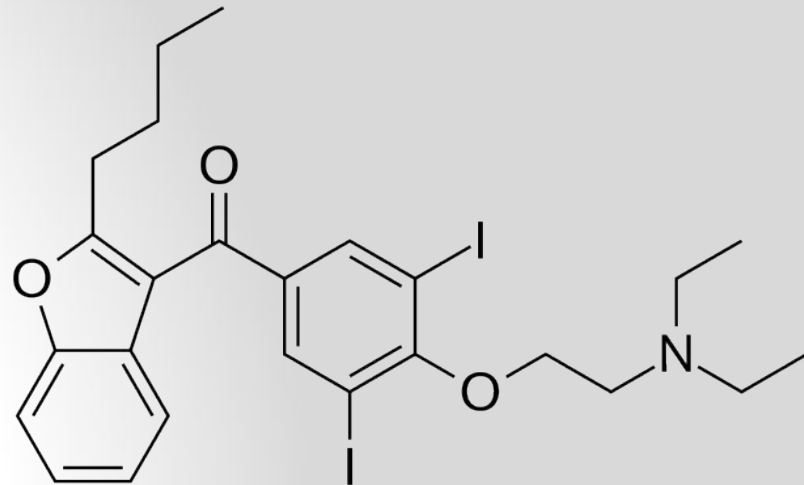
Effect

- Excessive iodide in diet could lead to hyperthyroidism
- Thyroid protects itself via **Wolff-Chaikoff Effect**
- **Organification** inhibited by $\uparrow$ iodide
 - Less synthesis of MIT/DIT

Amiodaron

e

- Class III antiarrhythmic drug
- Commonly used in atrial fibrillation
- Contains iodine
- Can cause **hypothyroidism** via excess iodine
 - Wolff-Chaikoff Effect

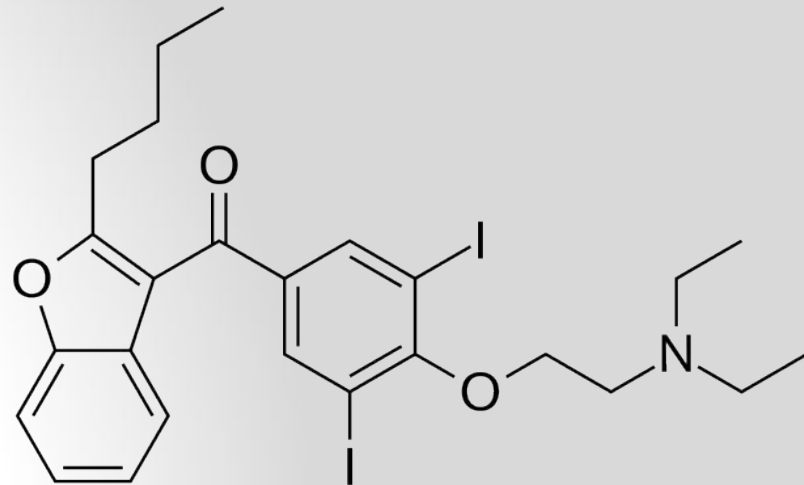


Amiodaron

e

- Mimics T4

- Inhibits **5'-deiodinase**
- ↓T3 □ ↑TSH from pituitary gland
- TSH rises after start of therapy then normalizes



Radioactive Iodine

- I^{131} is an isotope of iodine
 - Has 53 protons like elemental iodine
 - Extra neutrons
- Emits radiation (β -decay)
- Exposure $\square$ radioactive iodine in thyroid gland
 - Competes with elemental iodine for uptake
 - Will concentrate in thyroid gland
- Small dose: Used for imaging (I^{123})
- Large dose: Destroys thyroid tissue
 - Used as therapy for hyperthyroidism

TB

G Thyroxine-Binding Globulin

- Most plasma thyroid hormone is T4
- Thyroid hormones poorly soluble in water
- Most T4 is bound to TBG
 - Some with transthyretin and albumin
 - TBG present in small amount but has high affinity
 - TBG produced in liver
- Key point:
 - Less TBG $\square$ less available T4/T3 to tissues

TBG-T4 $\square$ T4

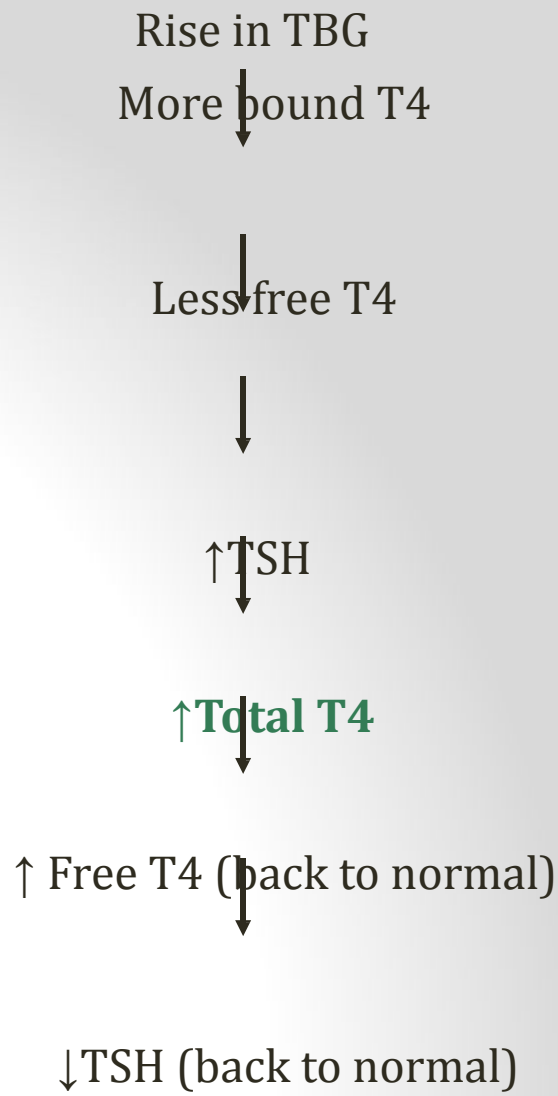
TB

G Thyroxine-Binding Globulin

- **Estrogen** raises TBG levels
 - Modifies TBG molecules
 - Slows clearance from plasma
 - **Pregnancy, OCP users**
 - Will raise total T4 levels
- **Liver failure** lowers TBG levels
 - Less production of protein
 - Can lower total T4 levels

TB

G Thyroxine-Binding Globulin



Thyroid Hormone Receptor

- Family of nuclear receptors
- Hormone-activated transcription factors
- Modulate gene expression

Effects of Thyroid Hormone

- Major regulator of **metabolic activity** and **growth**
- Glucose, lipid metabolism
- Cardiac function
- Bone growth
- CNS development

Thyroid

Metabolic Effects

Hormone

- ↑ Carbohydrate Metabolism
 - ↑ glycogenolysis, gluconeogenesis
- ↑ Fat Metabolism
 - ↑ lipolysis
 - ↓ concentrations of cholesterol, triglycerides
 - ↑ low-density lipoprotein receptors in liver (↓ LDL)
 - ↑ cholesterol secretion in bile
- Hypothyroid patients: ↑ **cholesterol**
- Hyperthyroid patients: **hyperglycemia**

Thyroid

Metabolic Effects Hormone

- ↑ basal metabolic rate
 - Basal rate of energy use per time
 - Amount of energy burned if you slept all day
- ↑ Na/K ATPase pumps
 - More pumps = more ATP consumed
 - ↑ oxygen demand to replenish ATP
 - ↑ respiratory rate
 - ↑ body temperature
- Hyperthyroid patients: **weight loss**

McDonough AA, et al. **Thyroid hormone coordinately regulates Na⁺-K⁺-ATPase alpha- and beta-subunit mRNA levels in kidney.** [Am J Physiol.](#) 1988 Feb;254(2 Pt 1):C323-9.

Thyroid

Cardiac Effects

Hormone

- $\uparrow$ CO/HR/SV/contractility
- $\uparrow$ β 1 receptors in heart
- Hyperthyroid patients:
Tachycardia

Thyroid

CNS and Bone effects Hormone

- TH required for normal bone growth/CNS maturation
- Childhood hypothyroidism □ **cretinism**
 - Stunted growth
 - Intellectual disability
- Causes
 - Iodine deficiency
 - Thyroid dysgenesis
 - Inborn errors of hormone synthesis (dyshormonogenesis)
 - TPO most common

Thyroid

CNS and Bone effects

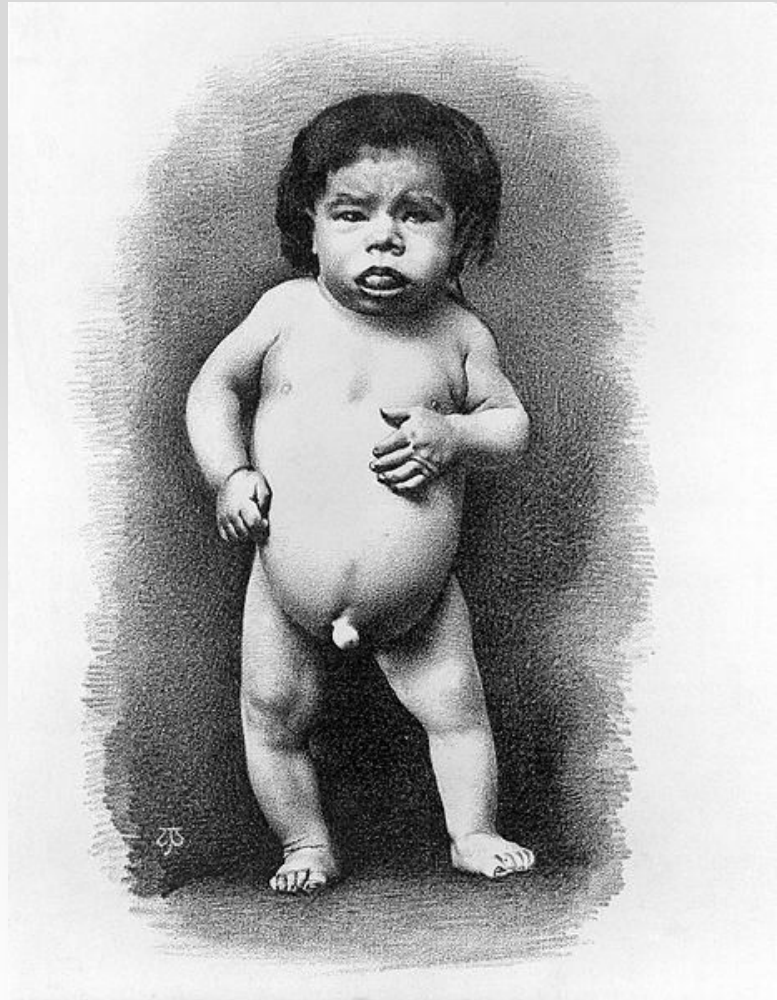
Hormone

- Most common **treatable** cause intellectual disability
- Most babies appear normal
 - Maternal T3/T4 crosses placenta
 - Newborn screening programs
 - Measure T4 or TSH from heel-stick blood specimens

Thyroid

CNS and Bone effects Hormone

- Intellectual disability
- Coarse facial features
- Short stature
- Umbilical hernia
- Enlarged tongue



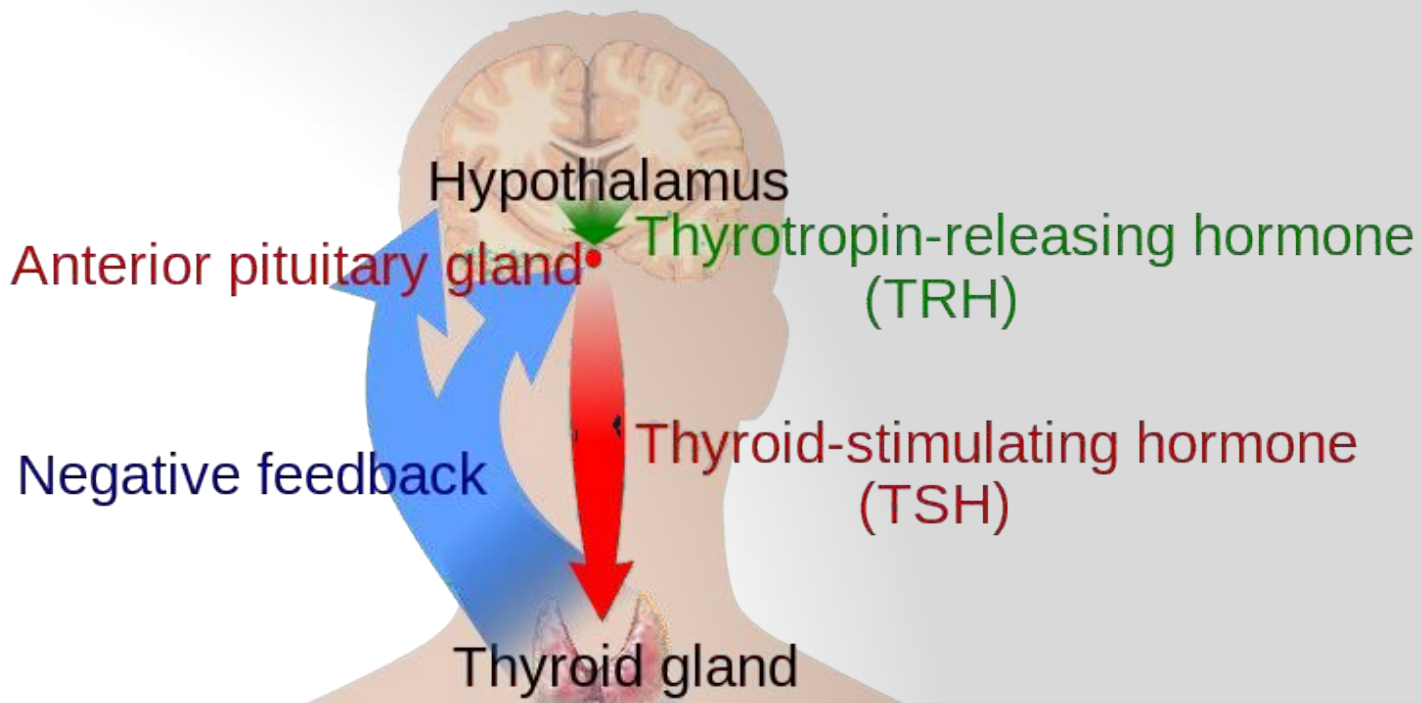
Wellcome Images/Wikipedia

Thyroid Hormone Regulation

- **TSH (thyrotropin)** released by anterior pituitary
- Binds to receptors on follicular cells
- Activates cAMP/PKA 2nd messenger system
- ↑ T3/T4 release
 - ↑ rate of proteolysis of thyroglobulin
 - Leads to rapid release of more T3/T4
 - Also stimulates thyroid cell growth, TG synthesis

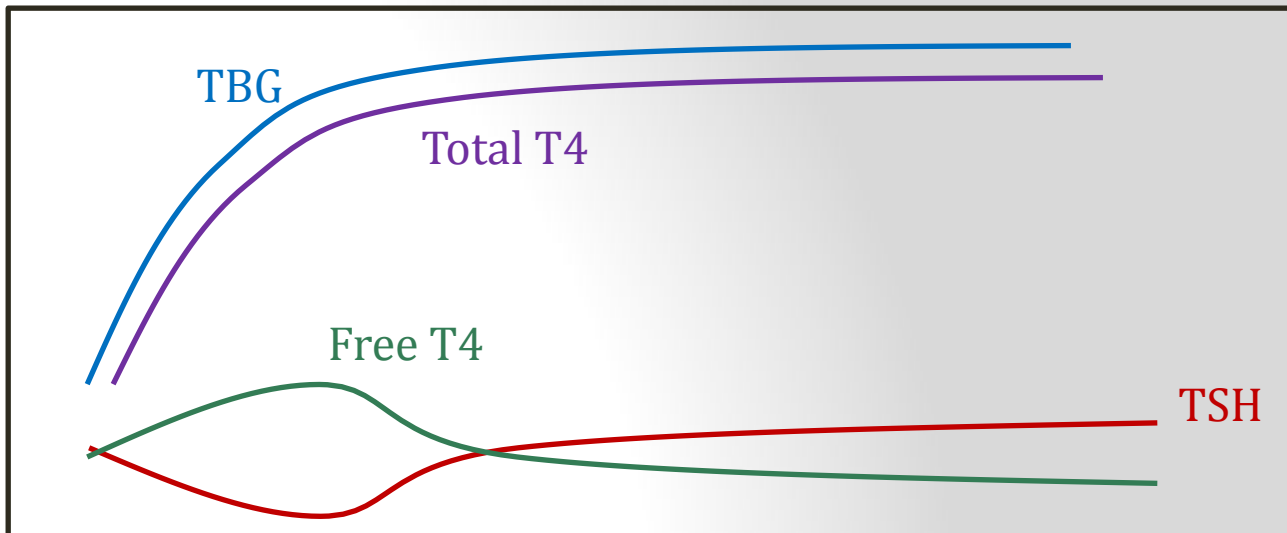
Thyroid Hormone Regulation

- Serum T4/T3 level sensed by hypothalamus
- Releases thyroid releasing hormone (TRH)



Pregnanc

- y
- Multiple effects on thyroid hormone production
 - Rise in total plasma T4/T3 levels
 - Rise in TBG levels (estrogen)
 - hCG stimulates thyroid (same alpha unit as TSH)
 - Raises free T4 $\square$ lower TSH



Thyroid Panel

- Four standard measurements to assess thyroid

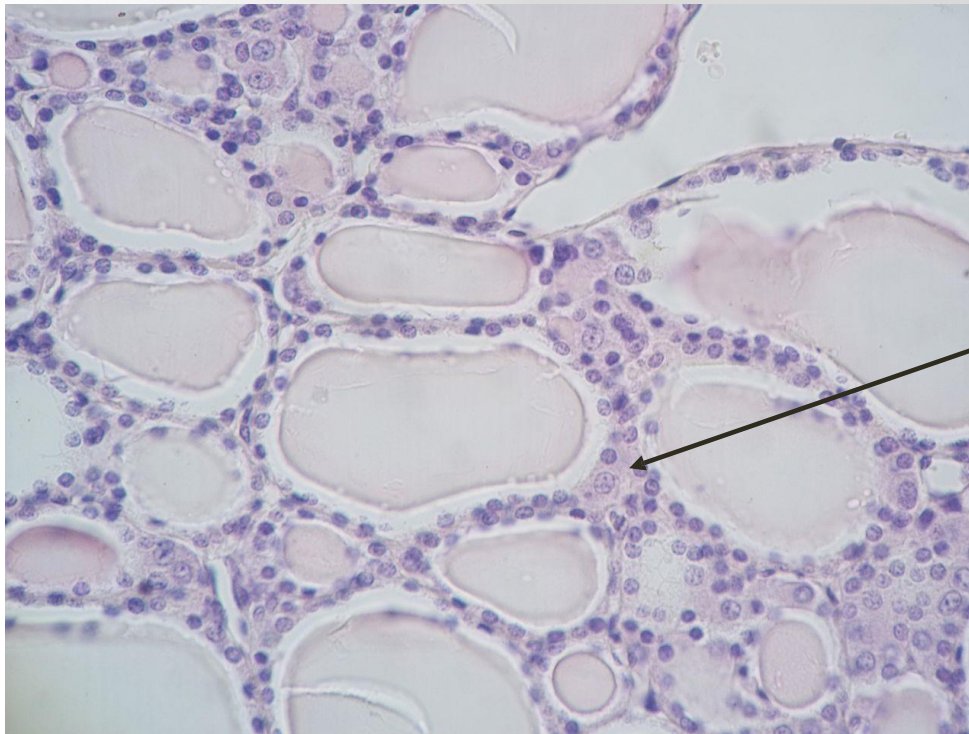
Test	Normal Value
TSH	0.4 to 5.0 mU/L
Total T4	60 to 145 nmol/L
Total T3	1.1 to 3 nmol/L
Free T4	0.01-0.03nmol/L

Note:
T4 > T3
Total T4 >> Free T4
(most bound to TBG)

Calcitonin

n

- Hormone produced by thyroid
- Synthesized by **parafollicular cells** (C-cells)



C cell

Calcitoni

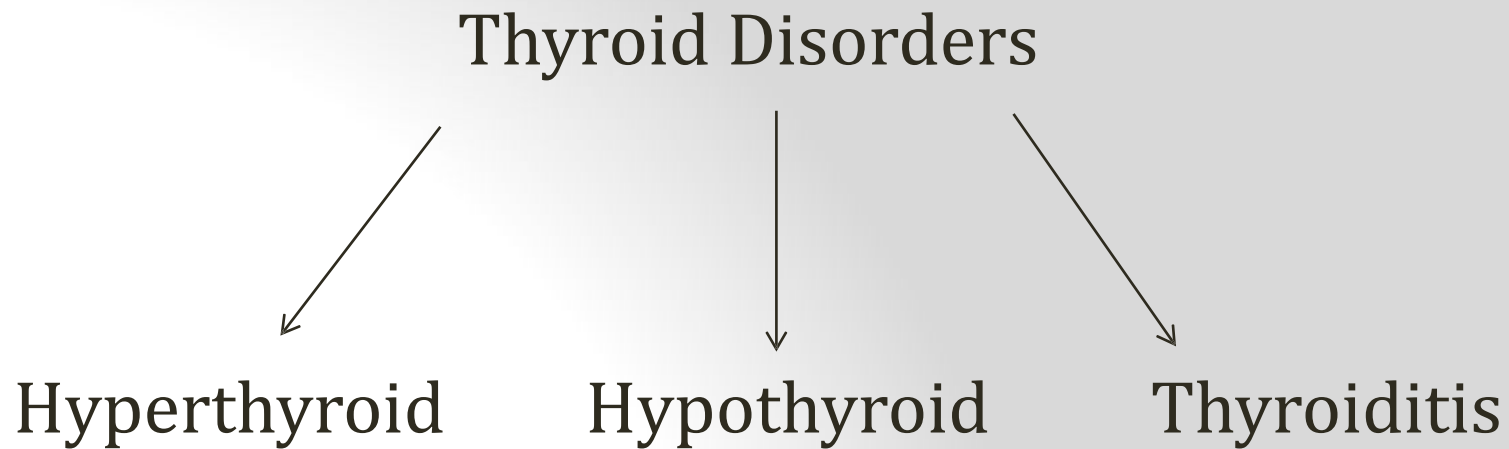
n

- Lowers serum **calcium**
 - Suppresses resorption of bone; inhibits osteoclasts
 - Inhibits renal reabsorption of calcium, phosphorus
 - Increased calcium in urine
- Probably minor role in calcium handling in humans
- Used as pharmacologic therapy for **hypercalcemia**

Thyroid Disorders

Jason Ryan, MD, MPH

Thyroid Disorders



Hypothyroidis

m

- Metabolism **SLOWS DOWN**
- Lethargy, fatigue
- Weakness; dyspnea on exertion
- Cold intolerance
- Weight gain with loss of appetite
- Constipation
- Hyporeflexia
- Dry, cool skin
- Coarse, brittle hair
- Bradycardia

Hyperlipidemi

a

- Classic feature of hypothyroidism
- ↑ total cholesterol
- ↑ LDL cholesterol
- Primary mechanism: ↓ **LDL receptor density**
 - T_3 upregulates LDL receptor gene activation

Myxedem

Thyroid dermopathy
a

- **Non-pitting** edema of the skin from hypothyroidism
- Hyaluronic acid deposits in dermis
- Draws water out → swelling
- Usually facial/periorbital swelling
- Pretibial myxedema
 - Special form of myxedema over shin
 - Seen in Graves' disease (hyperthyroidism)
- Myxedema coma = coma from hypothyroidism

Myxedem

a

Thyroid
dermopathy

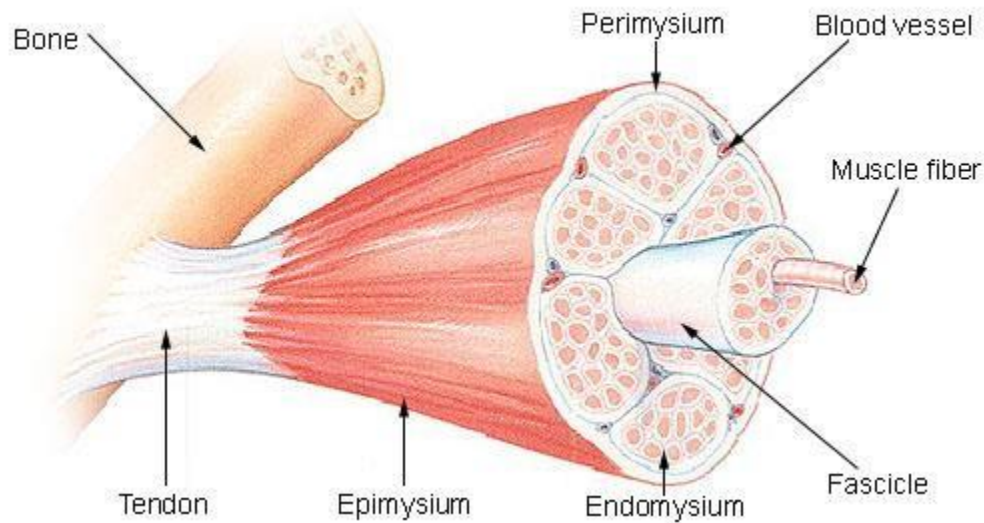


Herbert L. Fred, MD and Hendrik A. van Dijk

Hypothyroid Myopathy

- Muscle symptoms common in hypothyroid
- Weakness, cramps, myalgias
- ↑ serum **creatine kinase (CK)** common (up to 90%)

Structure of a Skeletal Muscle



Wikipedia/Public Domain

Hyponatremi

a

- Hypothyroidism is a well-described cause $\downarrow$ Na
- High levels of ADH (SIADH)
- May lead to confusion

Thyroid Replacement

- Levothyroxine (Synthroid): synthetic T4
- Liothyronine (Cytomel): synthetic T3
- Levothyroxine preferred
 - T3 absorbed from intestines rapidly
 - Can cause mild **hyperthyroidism symptoms**
 - Tachycardia, tremor
 - Also, T4 converted to T3
- Titrate dose until **TSH is normal**

Hyperthyroidis

m

- Metabolism **SPEEDS UP**
- Hyperactivity
- Heat intolerance
- Weight loss with increased appetite
- Diarrhea
- Hyperreflexia
- Warm, moist skin
- Fine hair
- Tachycardia (atrial fibrillation)

Thyroid Storm

- Life-threatening hyperthyroidism (thyrotoxicosis)
- Usually precipitated by **acute event**
 - Patient with pre-existing hyperthyroid disease
 - Graves' or toxic multinodular goiter
 - Surgery, trauma, infection
- Massive **catecholamine** surge
- Fever, delirium
- Tachycardia with **death from arrhythmia**
- Hyperglycemia (catecholamines/thyroid hormone)
- Hypercalcemia (bone turnover)

Goite

r

- Enlarged thyroid
- High TSH, inability to produce T3/T4
- Thyroid stimulating antibodies (Graves')



Wikipedia/Public Domain

Lab

Findings

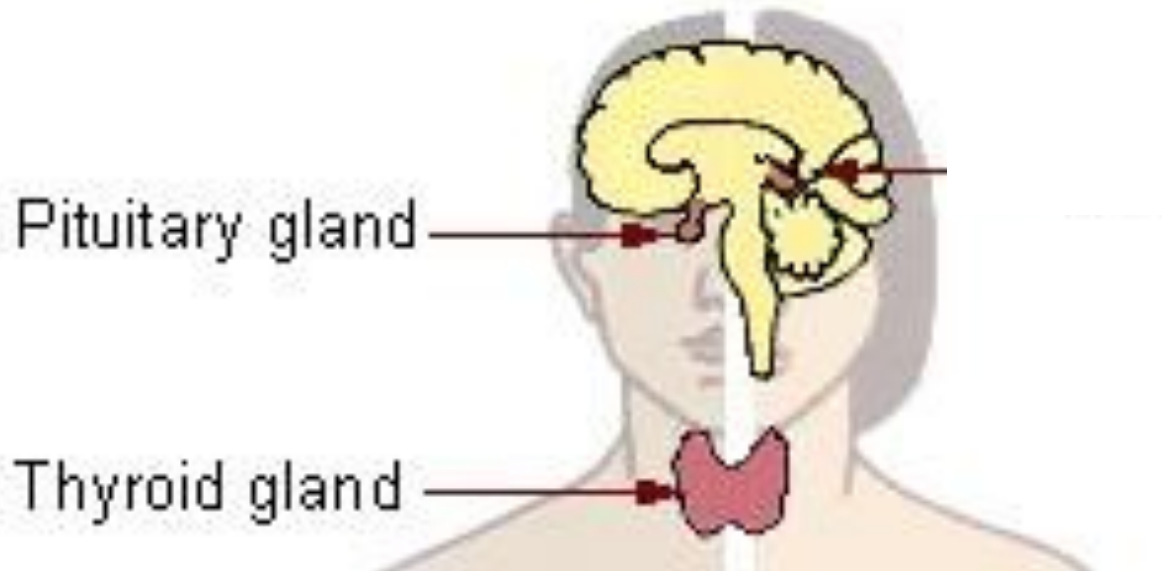
- Best initial test is **TSH**

TSH

Lab

Findings

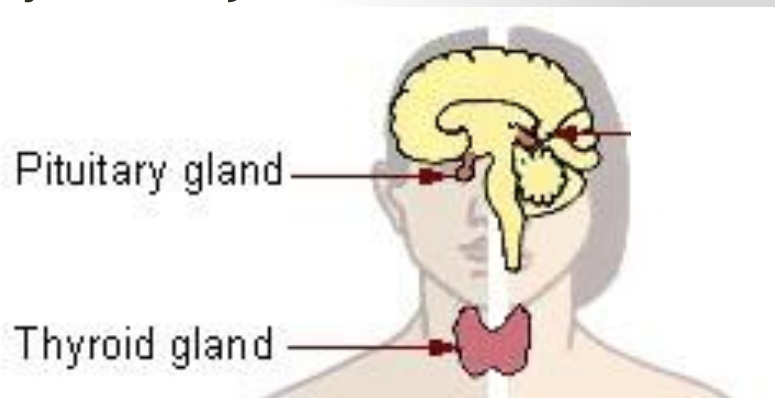
- Most disorders are primary disease
 - Disorder of the thyroid gland
 - TSH is opposite thyroid hormone
 - Hypothyroidism = $\uparrow$ TSH with low T3/T4
 - Hyperthyroidism = $\downarrow$ TSH with high T3/T4



Lab

Findings

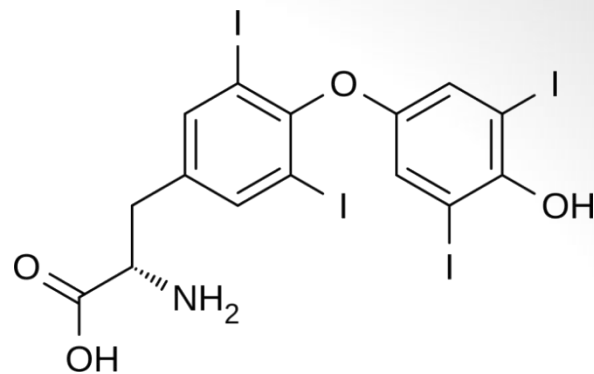
- Central hyper/hypo thyroid disease
 - Low TSH and low T3/T4; High TSH and high T3/T4
 - Rare disorders of the pituitary, hypothalamus
 - Usually hypothalamic-pituitary tumors
 - Tumors block secretion TRH/TSH (hypothyroidism)
 - Rarely a TSHoma can secrete TSH (hyperthyroidism)
 - Pituitary resistance to thyroid hormone (hyperthyroidism)



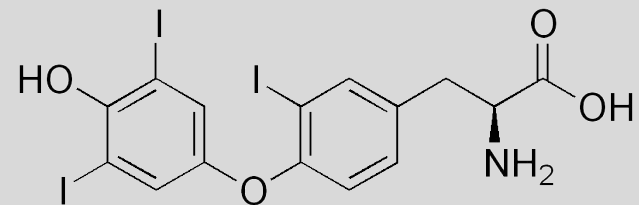
Reverse

T₃

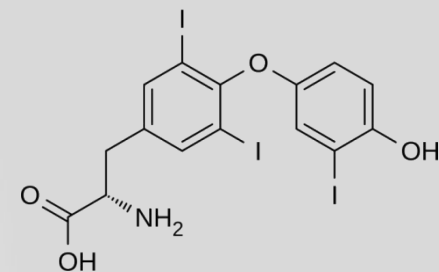
- Isomer of T₃ also derived from T₄



Thyroxine (T₄)



Reverse T₃



Triiodothyronine (T₃)

Reverse

T3

- Level usually parallels T4
 - Low T4 $\square$ Low rT3
- One special use: **Euthyroid sick syndrome**
 - Critically ill patients $\square$ low TSH $\square$ Low T3/T4
 - Can look like central hypothyroidism
 - rT3 rises in critical illness (impaired clearance)
- Critically ill patient with low TSH/T4/T3
 - Check rT3
 - Low $\square$ central hypothyroidism
 - High $\square$ sick euthyroid syndrome

Hyperthyroidis

m

- **Graves' disease** (#1 cause)
- Toxic multinodular goiter
- Amiodarone
- Iodine load
- Early thyroiditis

Graves'

Disease

- Autoimmune disease
- Thyroid stimulating antibodies produced
- Symptoms of hyperthyroidism occur

Graves' Disease

- Exophthalmos (bulging eyes)
 - Proptosis (protrusion of eye) and periorbital edema
 - Usually no ocular symptoms
- Pretibial myxedema (shins)
- T-cell lymphocyte activation of fibroblasts
- Fibroblasts contain TSH receptor
- Stimulation $\rightarrow$ secretion of glycosaminoglycans
 - Hydrophilic substances, mostly hyaluronic acid
 - Draws in water $\rightarrow$ swelling

Graves' Disease



Jonathan Trobe, M.D./Wikipedia



Herbert L. Fred, MD and Hendrik A. van Dijk

Graves' Disease

- Diagnosis:

- Usually hyperthyroid labs plus exophthalmos
- Can measure TSH receptor antibodies
- “Thyroid stimulating immunoglobulins”

- Treatment

- Symptoms: beta blockers, thionamides
- Drugs often started in preparation for definitive therapy
- Radioactive iodine ablation or surgery

Thionamide

S

- Methimazole
 - Inhibits thyroid peroxidase (TPO)
 - Organification of iodine
 - Coupling of MIT/DIT
- Propylthiouracil (PTU)
 - Inhibits TPO
 - Also inhibits 5'-deiodinase
 - Blunts peripheral conversion $T4 \rightarrow T3$

Thionamide

S

- Skin rash (common)
- Agranulocytosis
 - Rare **drop in WBC**
 - May present as fever, infection after starting drug
 - WBC improves with stopping drug
 - **Aplastic anemia** cases reported
- Hepatotoxicity

Thionamide

S • Methimazole: teratogen

- Associated with congenital malformations
- Especially 1st trimester
- PTU often used during early pregnancy

Thyroid

Treatment Storm

- Propranolol
 - Beta blocker
 - Blocks T4 $\rightarrow$ T3 conversion
- Thionamides (PTU, Methimazole)
- SSKI (saturated solution of potassium iodide)
 - Iodide load $\rightarrow$ shuts down T4 production
 - Wolff-Chaikoff effect
- Steroids
 - Reduce T4 $\rightarrow$ T3 conversion
 - Suppress auto-immune damage
 - Treat possible concomitant adrenal insufficiency

Graves' Ophthalmopathy

- Sometimes worsens despite treating hyperthyroidism
- Can cause irritation, excessive tearing , pain
- Symptoms often worse by cold air, wind, bright lights
- Severe inflammation treatments:
 - **Steroids**
 - Radiation
 - Surgery



Jonathan Trobe, M.D./Wikipedia

Toxic Adenomas

- Nodules in thyroid that function independently
 - Usually contain mutated TSH receptor
 - Do not respond to TSH
 - One nodule: Toxic adenoma
 - Multiple: Toxic multinodular goiter
- Findings:
 - Palpable nodule
 - Hyperthyroidism symptoms/labs
- Treatment: Radioactive iodine or surgery

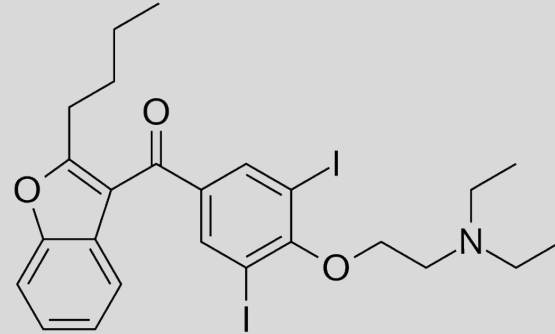
Radioactive Iodine Uptake

- Important test for thyroid nodules
- Administration of I^{131} (lower dose than ablation)
- Contraindicated in pregnancy/breast feeding
- “Hot” nodule
 - Takes up I^{131}
 - Not-cancerous
- “Cold” nodule
 - Chance of cancer (~5%)
 - Often biopsied (Fine-needle aspiration)

Jod-Basedow Phenomenon

- **Iodine-induced hyperthyroidism**
- Often occurs in regions of **iodine deficiency**
 - Introduction of iodine $\rightarrow$ hyperthyroidism
- Often occurs in patients with **toxic adenomas**
 - Drugs administered with high iodine content
 - Expectorants (potassium iodide)
 - CT contrast dye
 - Amiodarone

Amiodaron



e

- Two types of hyperthyroidism
 - Type I
 - Occurs in patients with **pre-existing thyroid disease**
 - Graves' or Multi-nodular goiter
 - Amiodarone provides iodine $\square$ excess hormone production
 - Type II
 - Destructive thyroiditis
 - Excess release T4/ T3 (no $\uparrow$ hormone synthesis)
 - Direct toxic effect of drug
 - Can occur in patients **without pre-existing thyroid illness**

Hypothyroidis

m

- Iodine deficiency
- Iodine excess
- Congenital hypothyroidism
- Amiodarone
- Thyroiditis
 - Hashimoto's (#1 cause when dietary iodine is sufficient)
 - Subacute
 - Riedel's

Iodine Deficiency

- “Endemic goiter”
 - Goiter in region with widespread iodine deficiency
 - Common in mountainous areas (iodine depleted by run-off)
- Constant elevation of TSH $\rightarrow$ enlarged thyroid



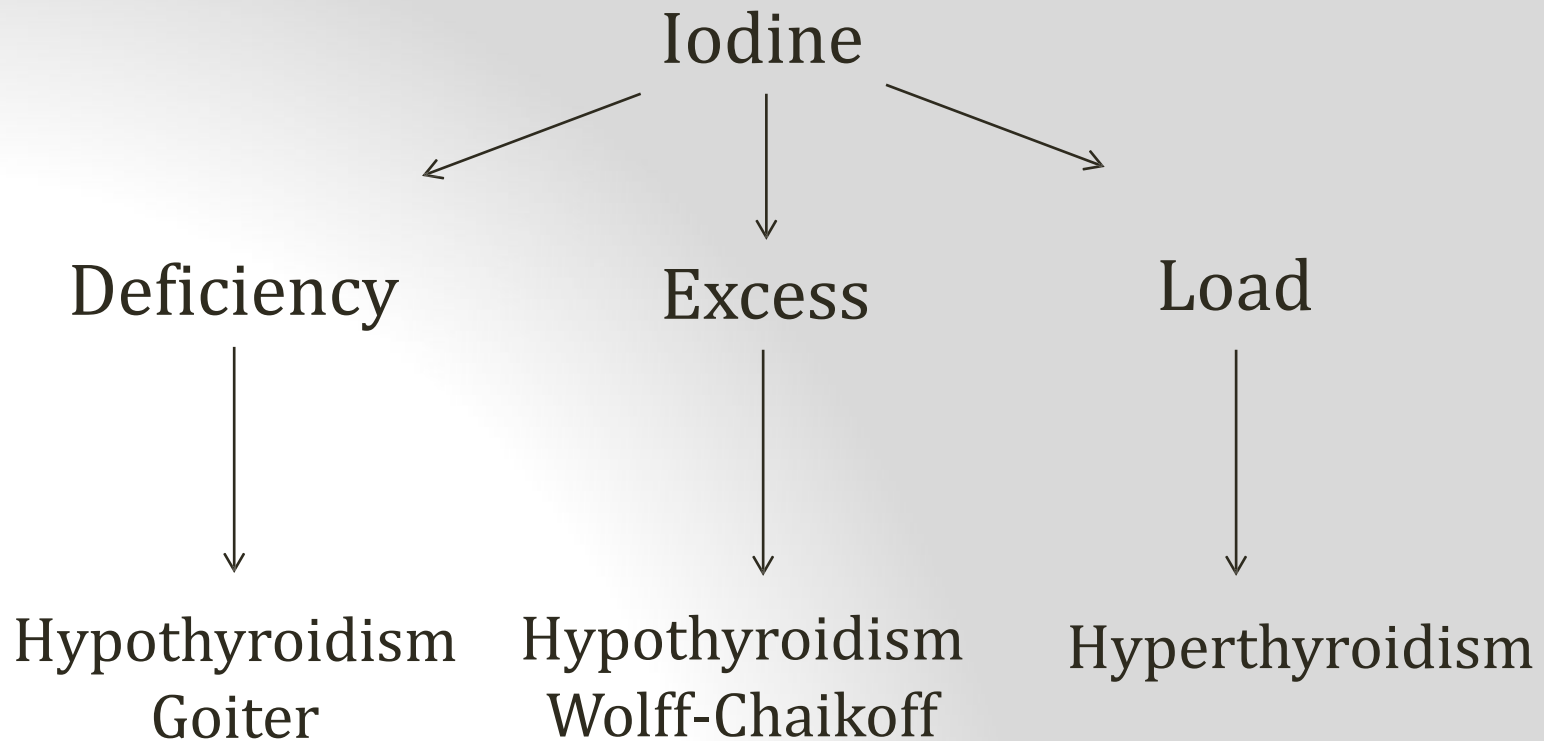
Wellcome Images

Iodine

Excess

- Excessive iodide in diet could lead to hyperthyroidism
- Thyroid protects itself via **Wolff-Chaikoff Effect**
- **Organification** inhibited by $\uparrow$ iodide
 - Less synthesis of MIT/DIT
- Chronic, high iodine intake $\square$ goiter/hypothyroidism

Iodine



Goitrogen

- S
- Substances that inhibit thyroid hormone production
 - Most common is iodine
 - **Lithium** (inhibits release of thyroid hormone)
 - Certain foods (cassava and millet)

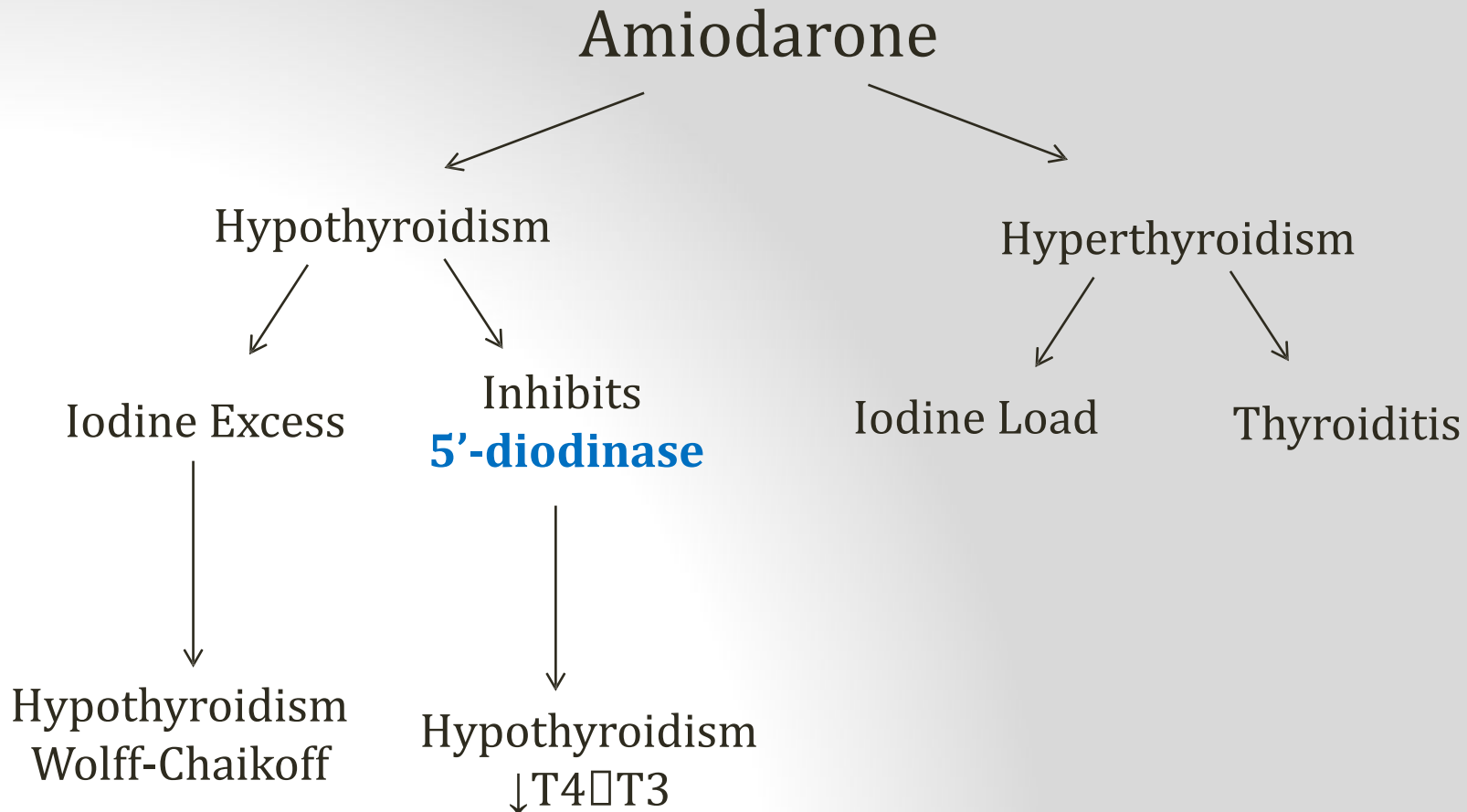
Amiodaron

e

- Can cause **hypothyroidism**
- Excess iodine □ Wolff-Chaikoff Effect
 - Suppression of thyroid hormone synthesis
 - Normal patients “escape” in few weeks
 - Pre-existing subclinical thyroid disease □ “failure to escape”
- Also mimics T4
 - Inhibits **5'-diodinase**

Amiodarone

Always check TSH
before starting
amiodarone



Congenital Hypothyroidism

- TH required for normal bone growth/CNS maturation
- Childhood hypothyroidism □ **cretinism**
 - Stunted growth
 - Intellectual impairment
- Causes
 - Iodine deficiency
 - Thyroid dysgenesis
 - Inborn errors of hormone synthesis (dyshormonogenesis)
 - TPO most common

Thyroid

CNS and Bone effects

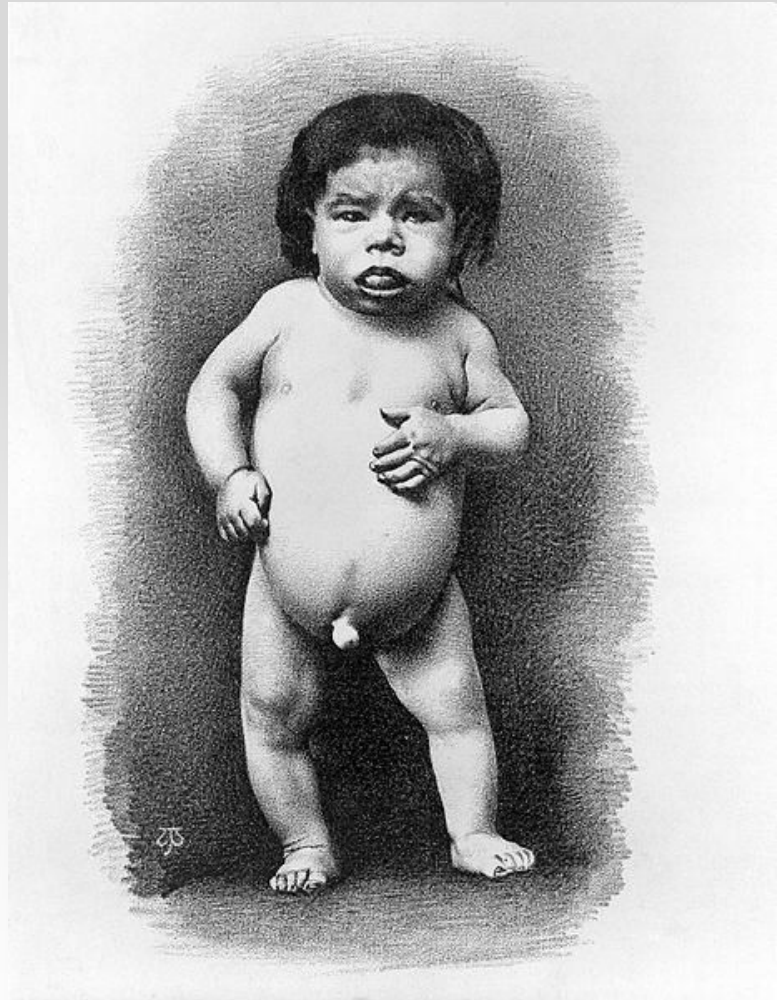
Hormone

- Most common **treatable** cause intellectual disability
- Newborn screening programs
 - Measure T4 or TSH from heel-stick blood specimens

Thyroid

CNS and Bone effects Hormone

- Intellectual impairment
- Coarse facial features
- Short stature
- Umbilical hernia
- Enlarged tongue



Wellcome Images/Wikipedia

Iatrogenic Hypothyroidism

- Thyroid surgery
 - Often done for Graves' or malignancy
- Radioiodine therapy
 - I^{131} administered orally as solution or capsule
 - Beta-emissions $\square$ tissue damage
 - Ablation of thyroid function over weeks
 - Done for Graves' or malignancy
- Neck radiation
 - Hodgkin's lymphoma
 - Head and neck cancer

Hashimoto's

Chronic Autoimmune Thyroiditis Thyroiditis

- Most common cause of hypothyroidism (non-diet)
- **Lymphocytes** infiltrate thyroid gland
 - Autoimmune disorder (T-cell attack thyroid; B cell activation)
 - HLA-DR3, HLA-DR5 and others

Hashimoto's

Chronic Autoimmune Thyroiditis

Thyroiditis

- Antibodies produced
 - Anti-TPO
 - Anti-thyroglobulin
- Histology:
 - Massive lymphocytic infiltrate (germinal centers)
 - Hurthle cells (enlarged eosinophilic follicular cells)

Hashimoto's

Chronic Autoimmune Thyroiditis Thyroiditis

- Primarily occurs in women
- Enlarged non-tender thyroid gland
- Gradual loss of thyroid function → symptoms
- Symptoms/labs of hypothyroidism
- Treatment: thyroid hormone replacement
- Increased risk of Non Hodgkin B cell lymphoma

Subacute

de Quervain's / granulomatous thyroiditis

- **Granulomatous** inflammation of thyroid
- Occurs in young females
- **Tender**, enlarged thyroid gland
- Hyperthyroid $\square$ euthyroid $\square$ hypothyroid
- Treatment:
 - Anti-inflammatories (aspirin, NSAIDs, steroids)
 - Thyroid symptoms usually mild (no treatment)
 - Usually resolves in few weeks

Riedel's Thyroiditis

- Fibroblast activation/proliferation
- **Fibrous tissue** (collagen) deposition in thyroid
- “Rock hard” thyroid
- Often extends **beyond the thyroid**
 - Parathyroid glands □ hypoparathyroidism
 - Recurrent laryngeal nerves □ hoarseness
 - Trachea compression □ difficulty breathing
- Associated with **IgG4 plasma cells**
 - May be an “IgG4-related disease” (autoimmune pancreatitis)
 - IgG4 plasma cells identified in biopsy specimens

Lymphocytic

Painless Thyroiditis

Thyroiditis

- Variant of Hashimoto's
- Lymphocytic infiltration of thyroid gland
- Transient hyperthyroidism
 - Can look like Graves' without eye/skin findings
 - Serum thyroid stimulating immunoglobulins not elevated
- Followed sometimes by hypothyroidism
 - Can look like Hashimoto's
- Usually self-limited (weeks)

Thyroid Cancer

Jason Ryan, MD, MPH

General Principles

- Thyroid cancer usually no hyper/hypo symptoms
- Often presents as nodule
- Differential is benign adenoma versus cancer
- Biopsy done by **fine needle aspiration**

Thyroid Imaging

- **Ultrasound**

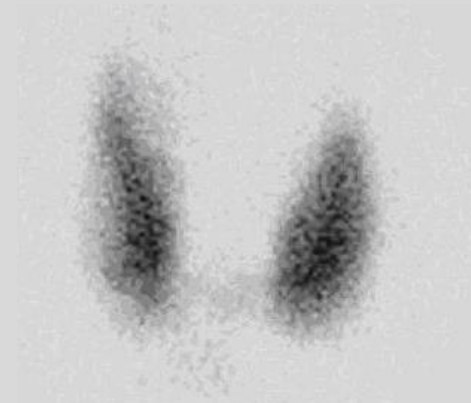
- Some characteristics suggest cancer
- Borders, vascularity, calcifications



Nevit Dilmen/Wikipedia

Radioactive Iodine Uptake

- Small oral dose I^{131} given to patient
- Scintillation camera → image of thyroid
- Normal: diffuse, even uptake
- Diffuse high uptake: Graves'
- Diffuse low uptake: Hashimoto's
- Multiple areas of high uptake: nodular goiter
- Single "hot" nodule: adenoma
- Single "cold" nodule: Possible cancer
 - Most cancers do not make hormone
 - About 10% cold nodules are malignant



Myohan /Wikipedia

Follicular Adenoma

- Common cause of thyroid nodules
- Benign proliferation of follicles
- Normal follicular tissue seen on biopsy
- **Completely surrounded by fibrous capsule**
- **FNA cannot distinguish between adenomas/cancer**
 - Cannot see entire capsule
 - Follicular carcinoma has similar histology by FNA
- FNA follicular pathology followed over time
 - Growth, suspicious new findings → surgery

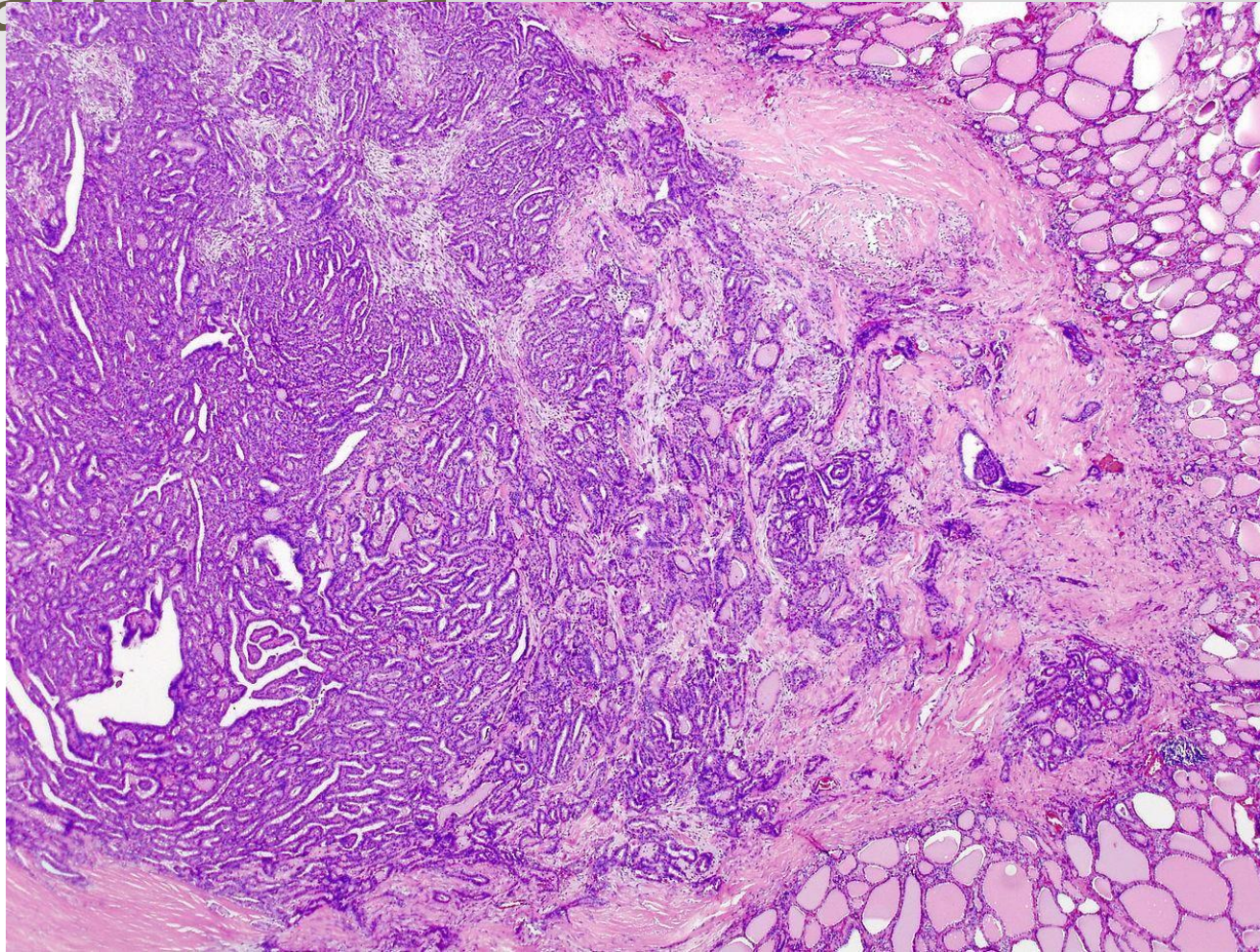
Thyroid Cancer

- Papillary
- Follicular
- Medullary
- Anaplastic

Papillary Carcinoma

- Most common form thyroid cancer (~80%)
- Increased risk with **prior radiation exposure**
 - Childhood chest radiation for mediastinal malignancy or acne
 - Survivors of atomic bomb detonation (Japan)
 - Nuclear power plant accidents (Chernobyl)
- Presents as thyroid nodule
 - Sometimes seen on chest/neck imaging (CT/MRI)
 - Diagnosis made after fine needle aspiration (FNA)
- Excellent prognosis
 - Treated with surgery plus radioactive iodine ablation

Papillary Carcinoma



KGH/Wikipedia

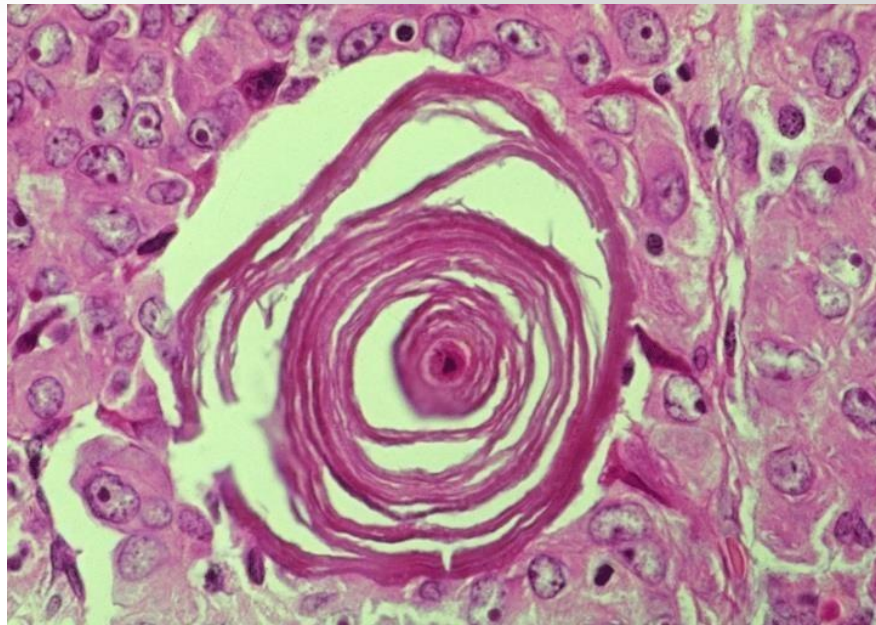
Papillary Carcinoma

- Three key pathology findings:
 - Psammoma bodies
 - Nuclear grooves
 - Orphan Annie's Eye Nuclei
- Diagnosis made by **nuclear findings**

Psammoma

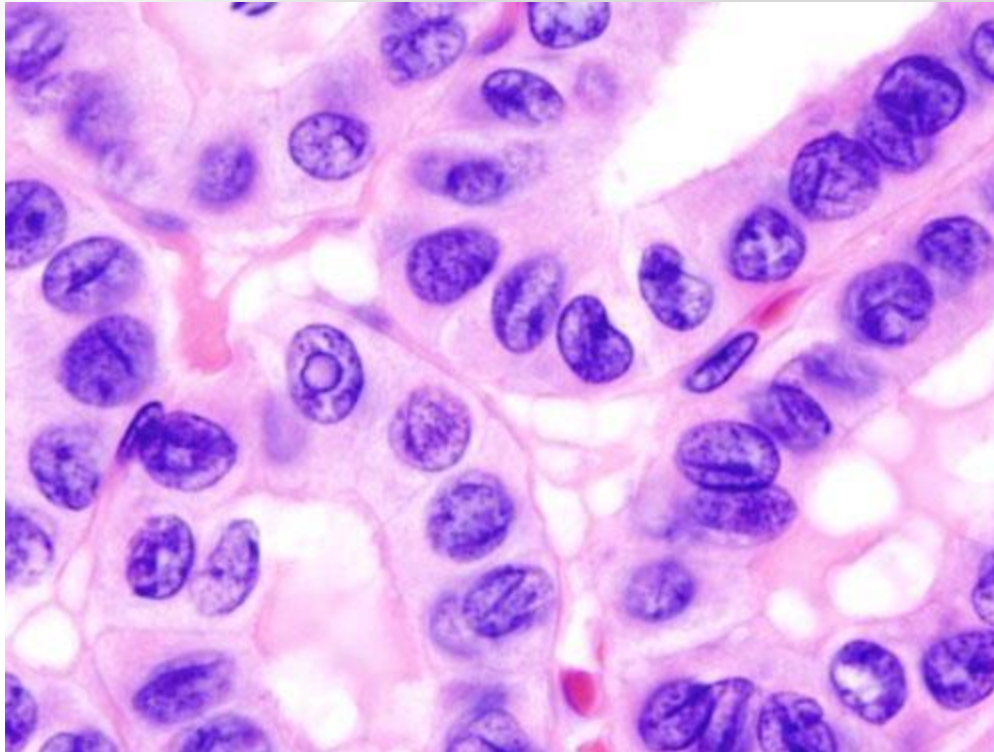
Bodies

- Calcifications with an layered pattern
- Seen in other neoplasms but only papillary for thyroid



Wikipedia/Public Domain

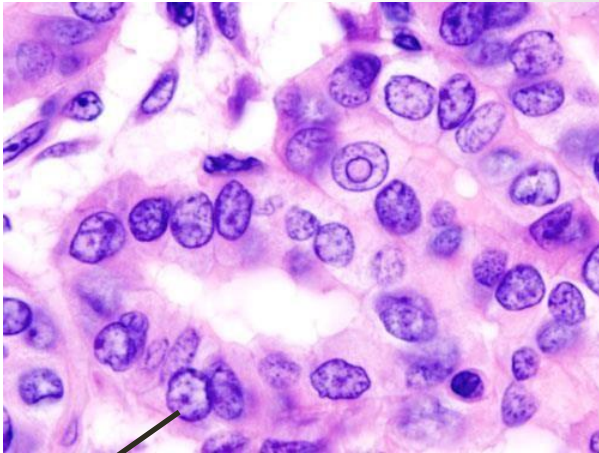
Nuclear Grooves



KGH/Wikipedia

Orphan Annie's Eyes

- Empty-appearing nuclei



KGH/Wikipedia

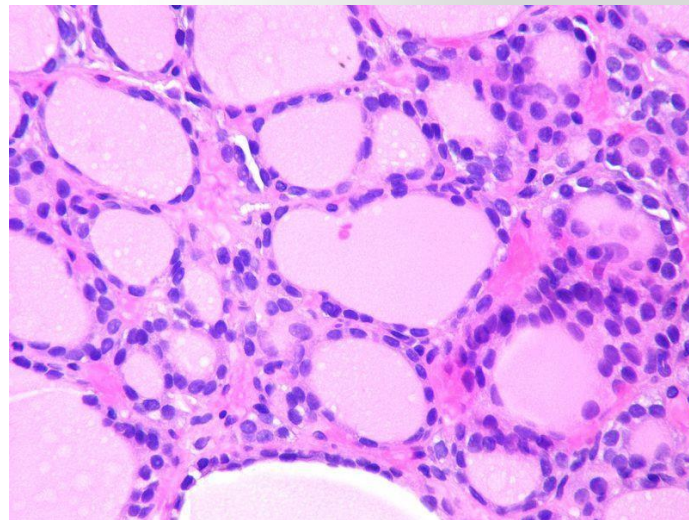
White clearing



William Creswell/Flickr

Follicular Carcinoma

- Similar to follicular adenoma
- Breaks through (“**invades**”) fibrous capsule
- **FNA cannot distinguish between adenomas/cancer**
- Follicular pathology followed over time
 - Growth, suspicious new findings → surgery



Yale Rosen/Wikipedia

Follicular Carcinoma

- Possible **hematogenous** metastasis
- Treatment:
 - Thyroidectomy
 - I¹³¹ to ablate any remaining tissue or metastasis

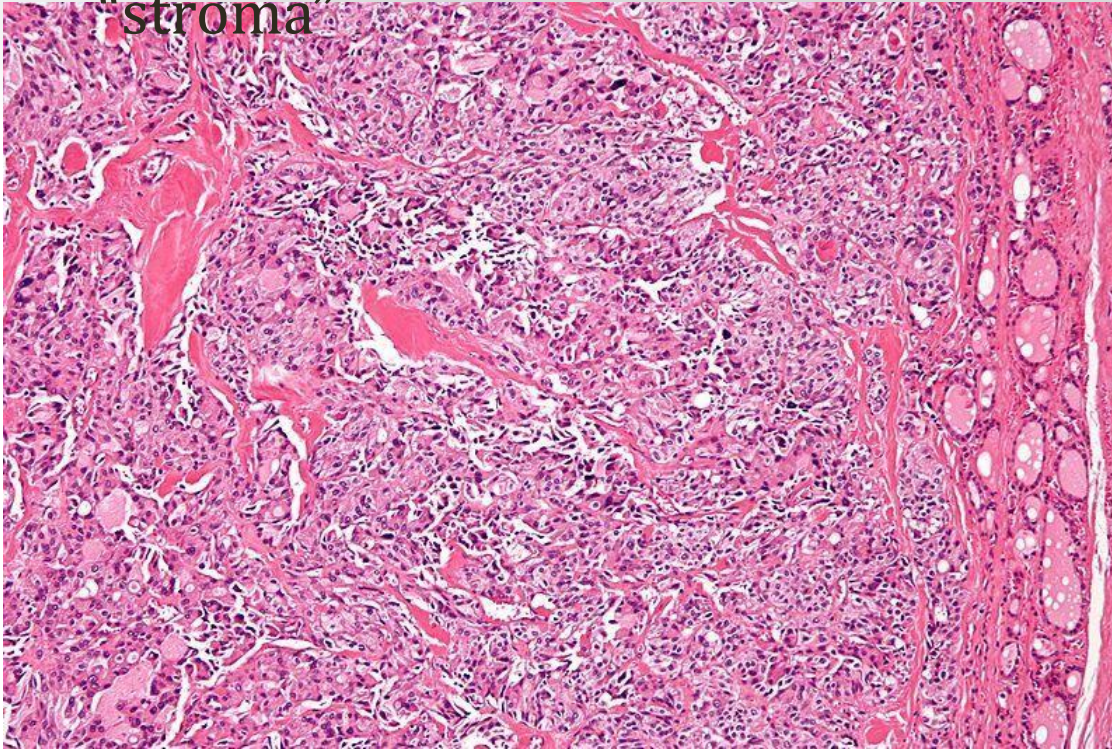
Medullary Carcinoma

- Cancer of parafollicular cells (C cells)
- Produces **calcitonin**
 - Lowers serum calcium
 - Normally minimal effect on calcium levels
 - Used for monitoring
- **Amyloid** deposits in thyroid
 - Amyloid = protein deposits
 - Calcitonin = peptide
 - Appearance of amyloid on biopsy

Medullary Carcinoma

Malignant cells/Amyloid

“stroma”



Nephron/Wikipedia

MEN

Multiple Endocrine Neoplasia Syndromes

- Gene mutations that run in families
- Cause multiple endocrine tumors
- MEN 2A and 2B associated with medullary carcinoma
 - Caused by RET oncogene mutation
 - Some patients have **elective thyroidectomy**

Anaplastic

Undifferentiated Carcinoma

Carcinoma

- Occurs in **elderly**
- Highly malignant - invades local tissues
 - Dysphagia (esophagus)
 - Hoarseness (recurrent laryngeal nerve)
 - Dyspnea (trachea)
 - Don't confuse with Riedel's ("rock hard" thyroid/young pt)
- Poor prognosis
- Pathology: Undifferentiated cells
 - No papilla, follicles, or amyloid