

# Endocrine pathophysiology

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# Cell-cell communication

- Neurocrine (neurotransmitters)
- Endocrine (hormones)
- Paracrine (cytokines)
- Autocrine (various)

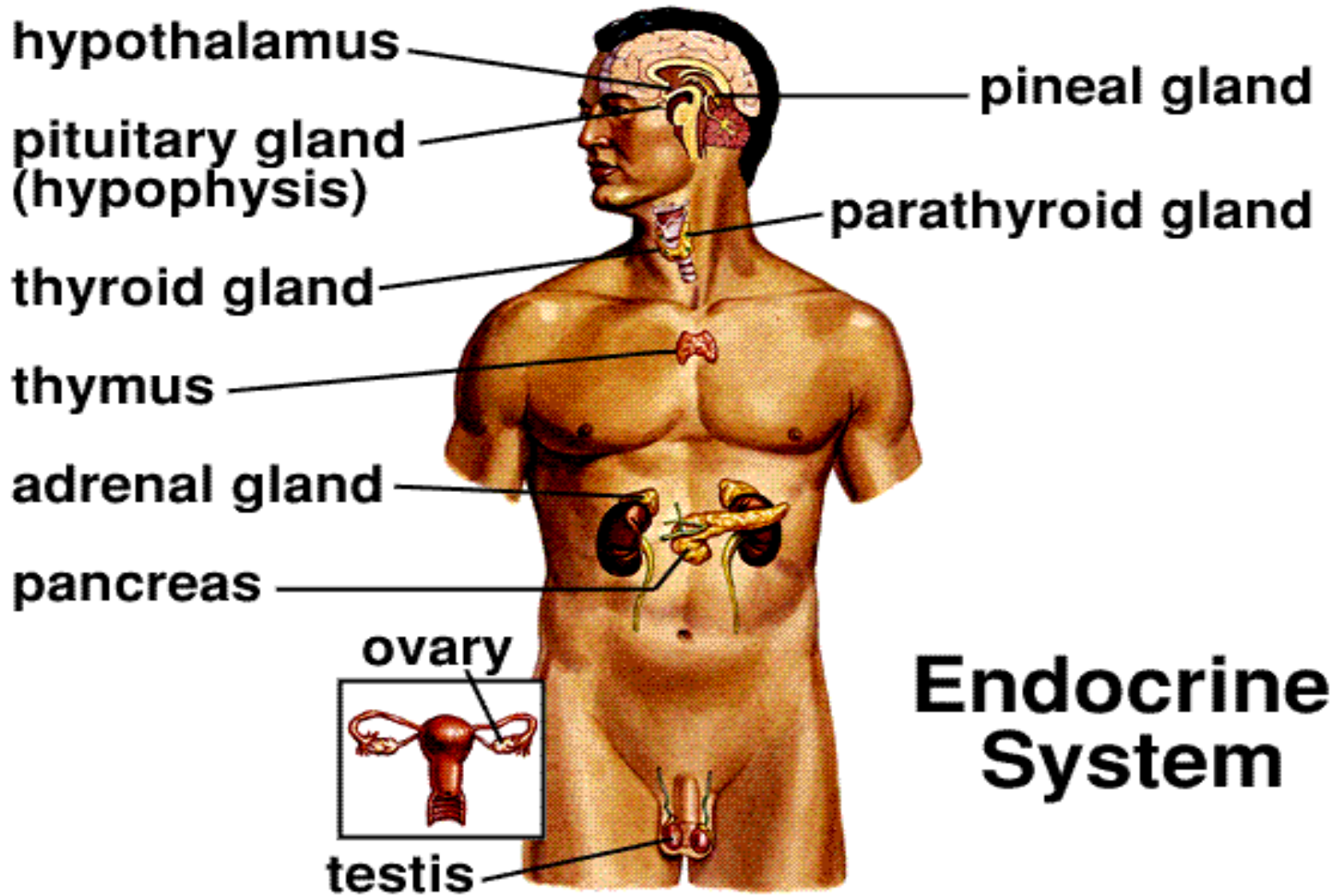
# Hormones

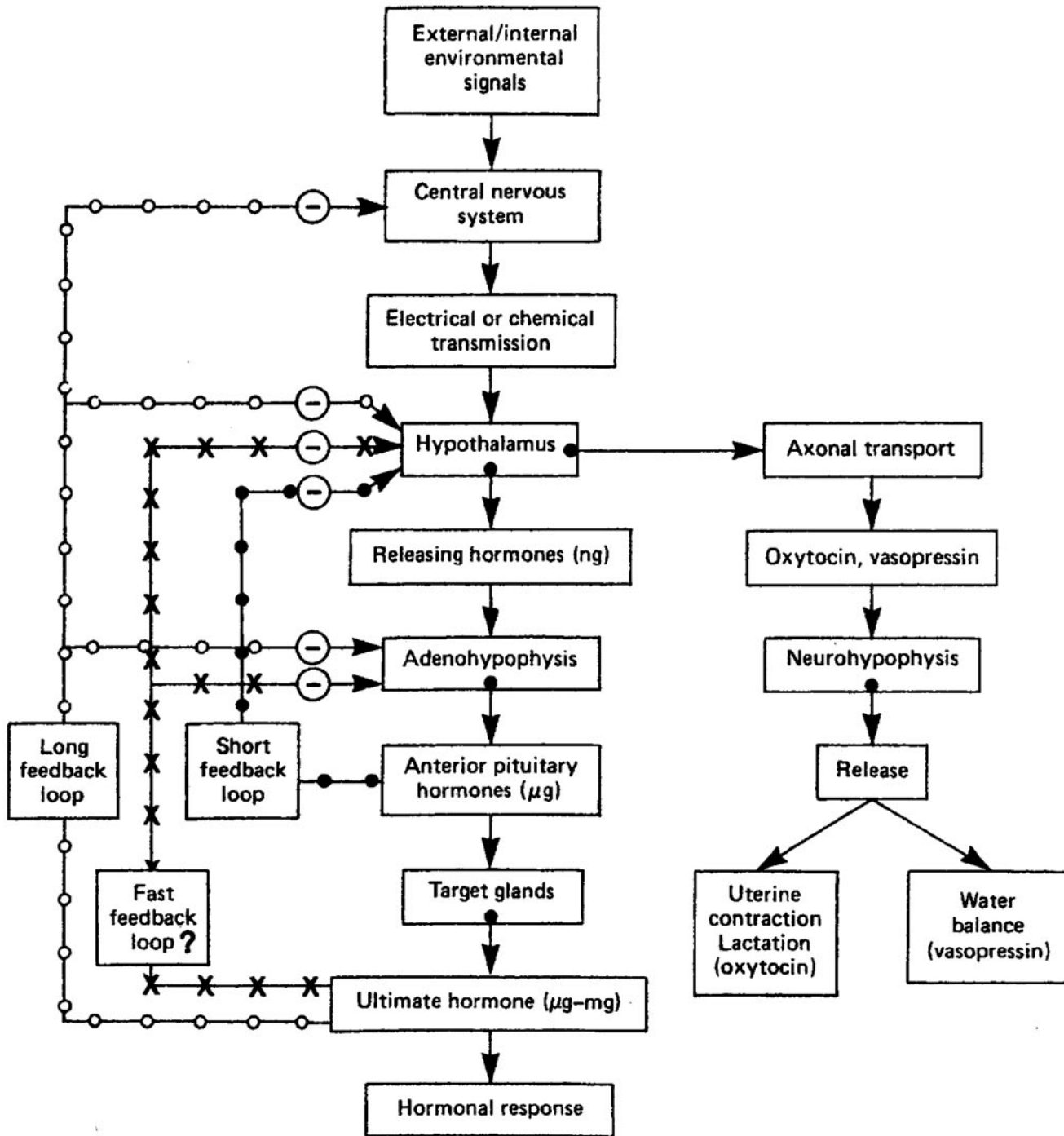
- Proteins / peptides
  - Preprohormone (ER, GA, secretion granules)
- Steroids
  - Cholesterol
- Amines
  - Tyrosine

# Endocrine regulation

- Negative feedback
- Positive feedback
  
- Production (endocrine gland)
- Transport (binding proteins in plasma)
- Target tissue (receptors on cells)

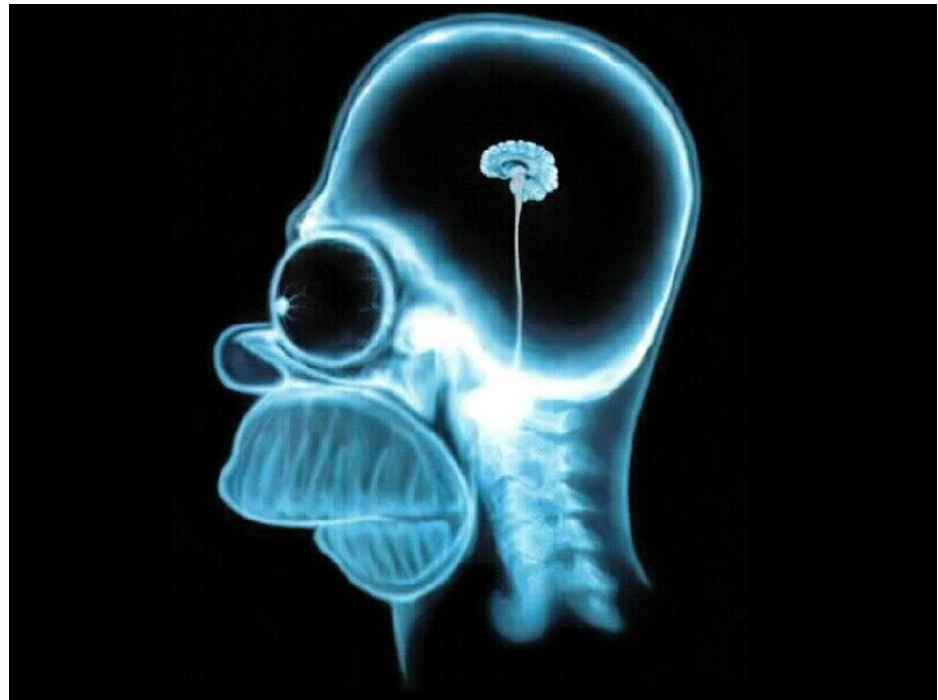
# Endocrine glands





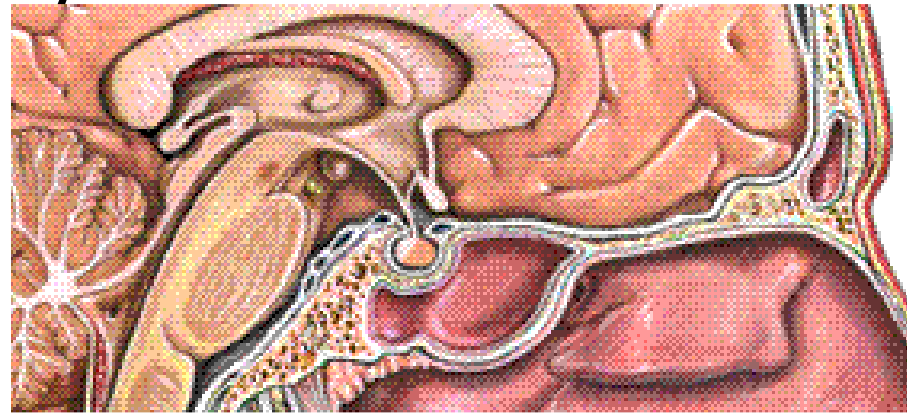
# Endocrine disorders

- Physiology &
- Overproduction
- Insufficiency
- Resistance



# Hypothalamus

- Neural regulation of the autonomic nervous system - adrenal medulla
- Production of ADH and oxytocin
- Regulation of the pituitary





# Hypothalamus

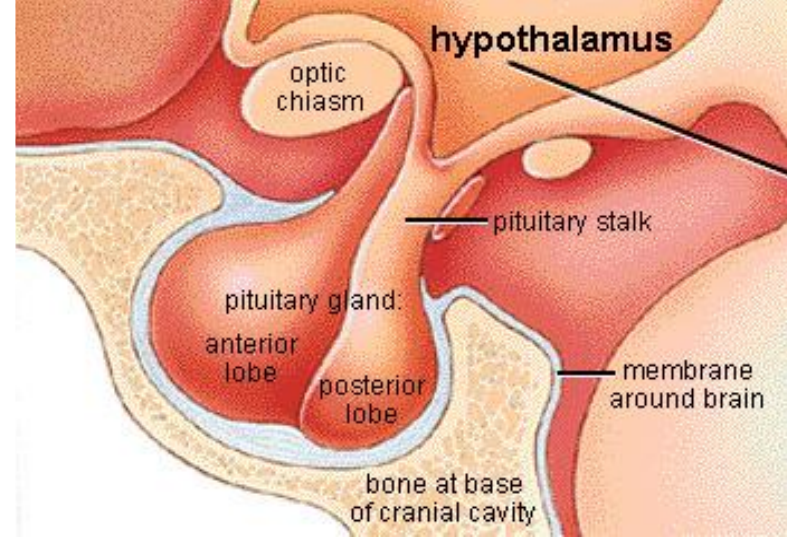
- Liberins
  - CRH (ACTH), TRH (TSH), GHRH (GH), GnRH (LH, FSH), Somatostatin (PRL)
- Statins
  - Somatostatin (GH), Dopamine (PRL)

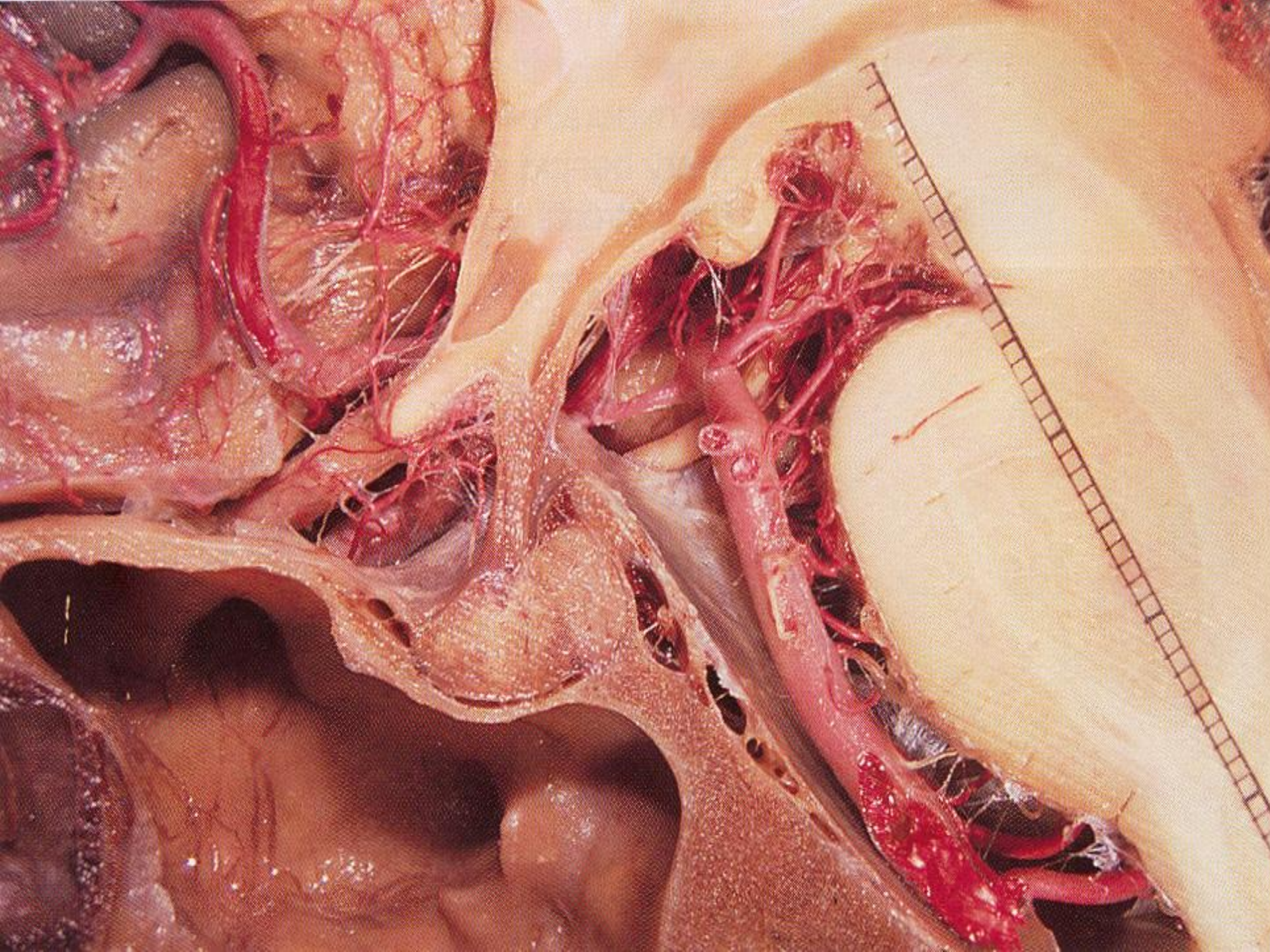
# Hypothalamus

- Hypothalamic - pituitary axis
- Control of the production and release of pituitary hormones
- Pulse secretion
- Specific membrane receptors
- Second messenger
- Autoregulation

# Pituitary

- Anterior pituitary
  - Adenohypophysis
  - ACTH, TSH, FSH, LH, PRL, GH, MSH
  - Endocrine regulation
- Posterior pituitary
  - Neurohypophysis
  - ADH, Oxytocin
  - Neural regulation of hormone release





# Hypopituitarism

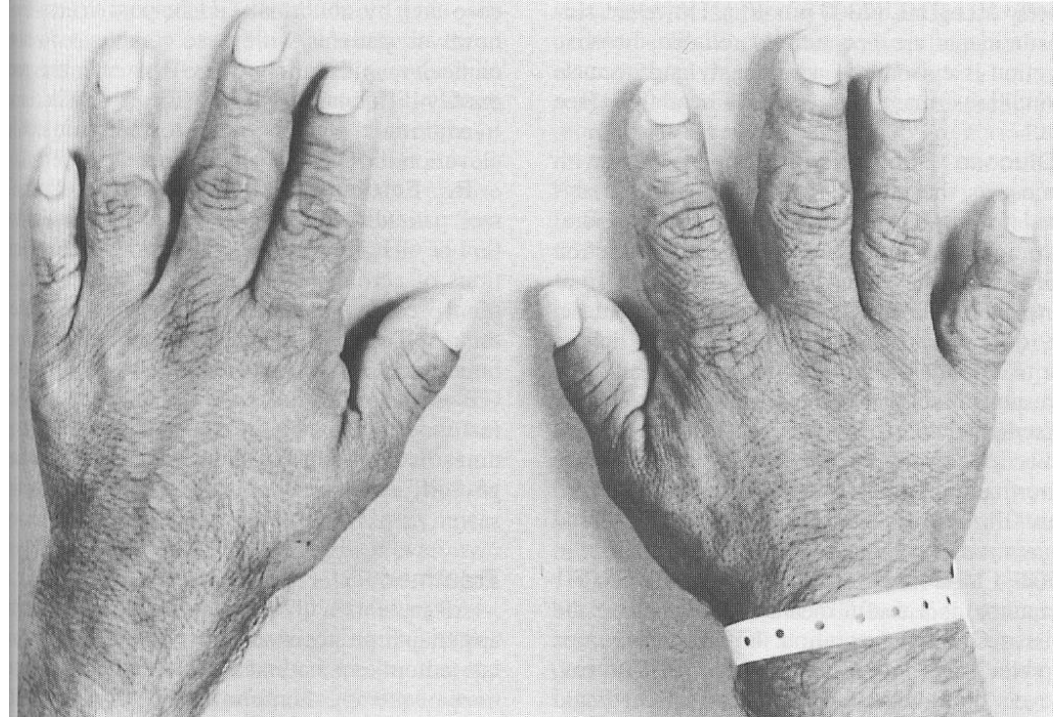
- General
- Selective
  
- Infections, infarctions, cysts, tumors, injuries, iatrogenic, Sheehan syndrome
- Fertility, Growth ...
- Therapy - supplementation

# GH disorders

- GH overproduction

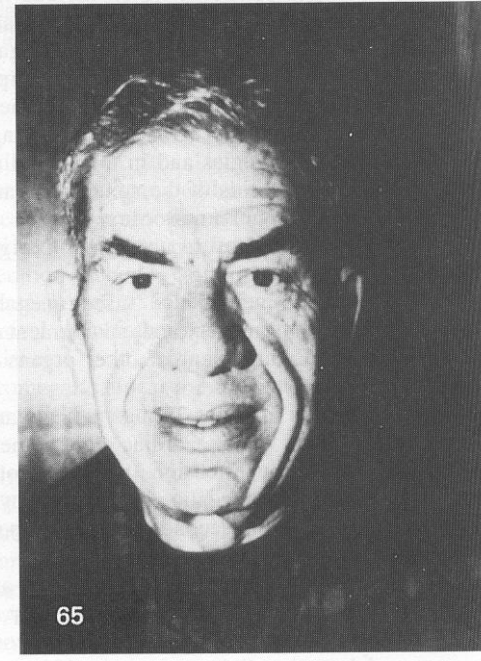
- Gigantism

- Before puberty

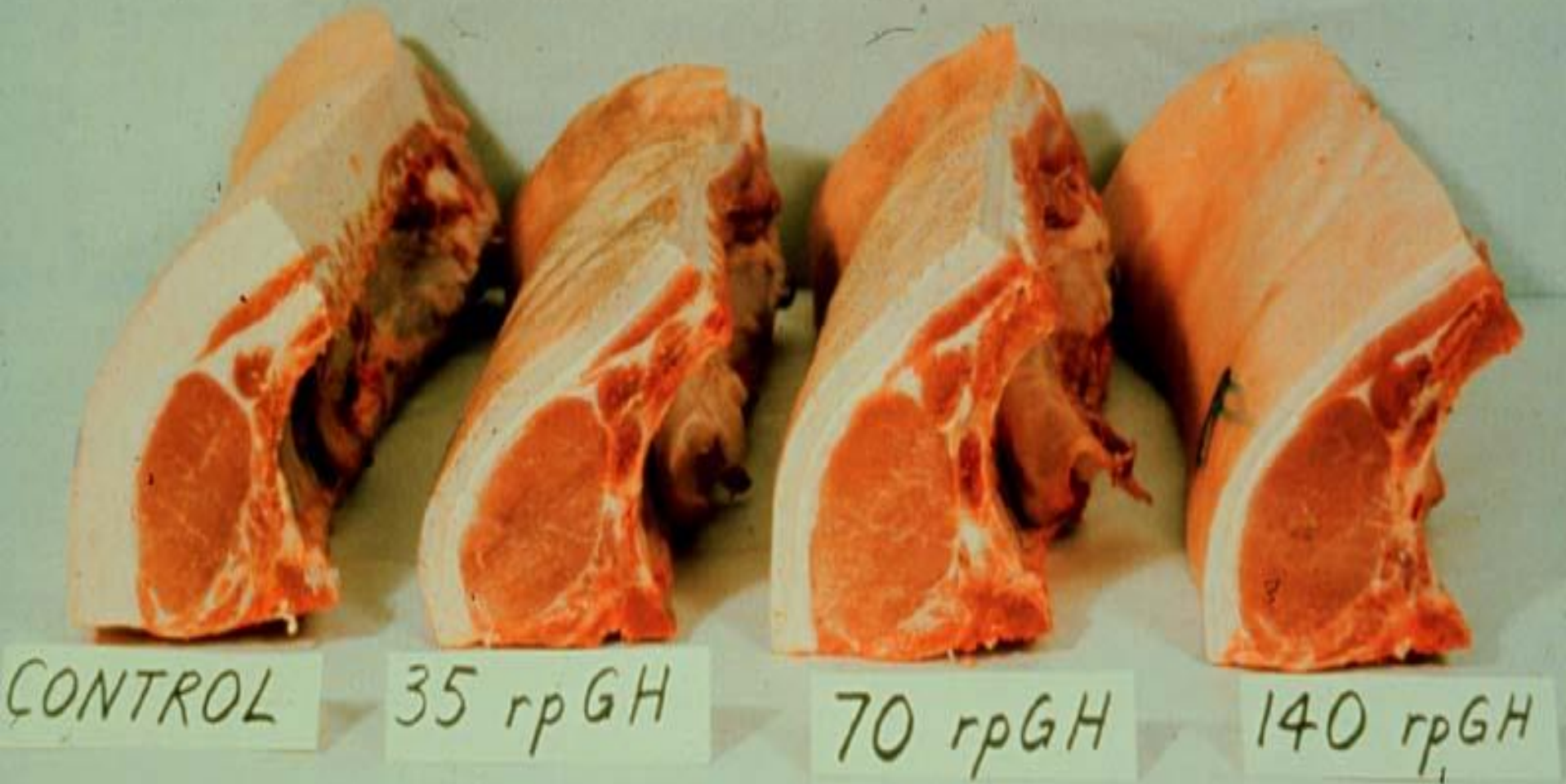


- Acromegaly

- After puberty







CONTROL

35 rpGH

70 rpGH

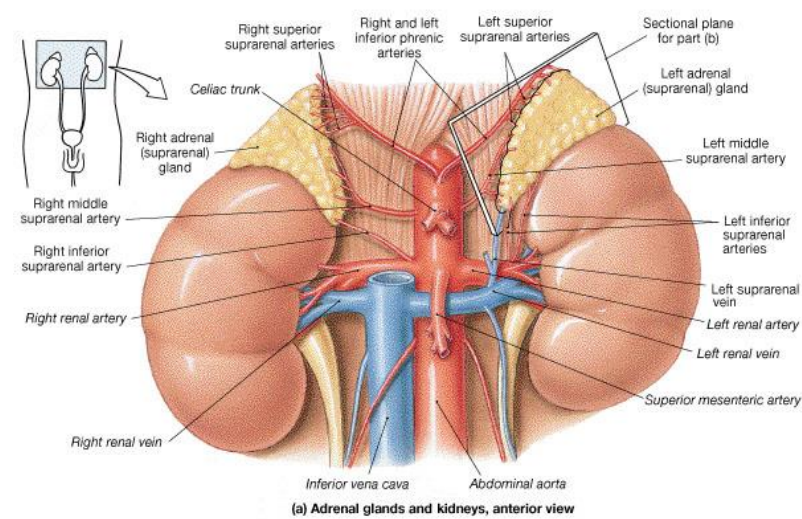
140 rpGH



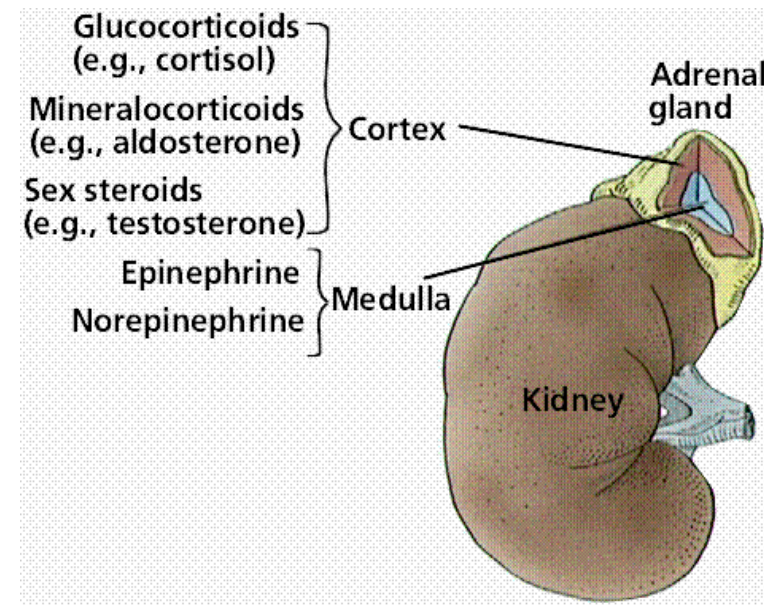
# ADH disorders

- ADH insufficiency
  - Diabetes insipidus
    - Polydipsia, polyuria
- Overproduction ADH
  - Syndrome of IADH
    - Hypoosmolarity of plasma, hyponatremia, oliguria

# Adrenal glands

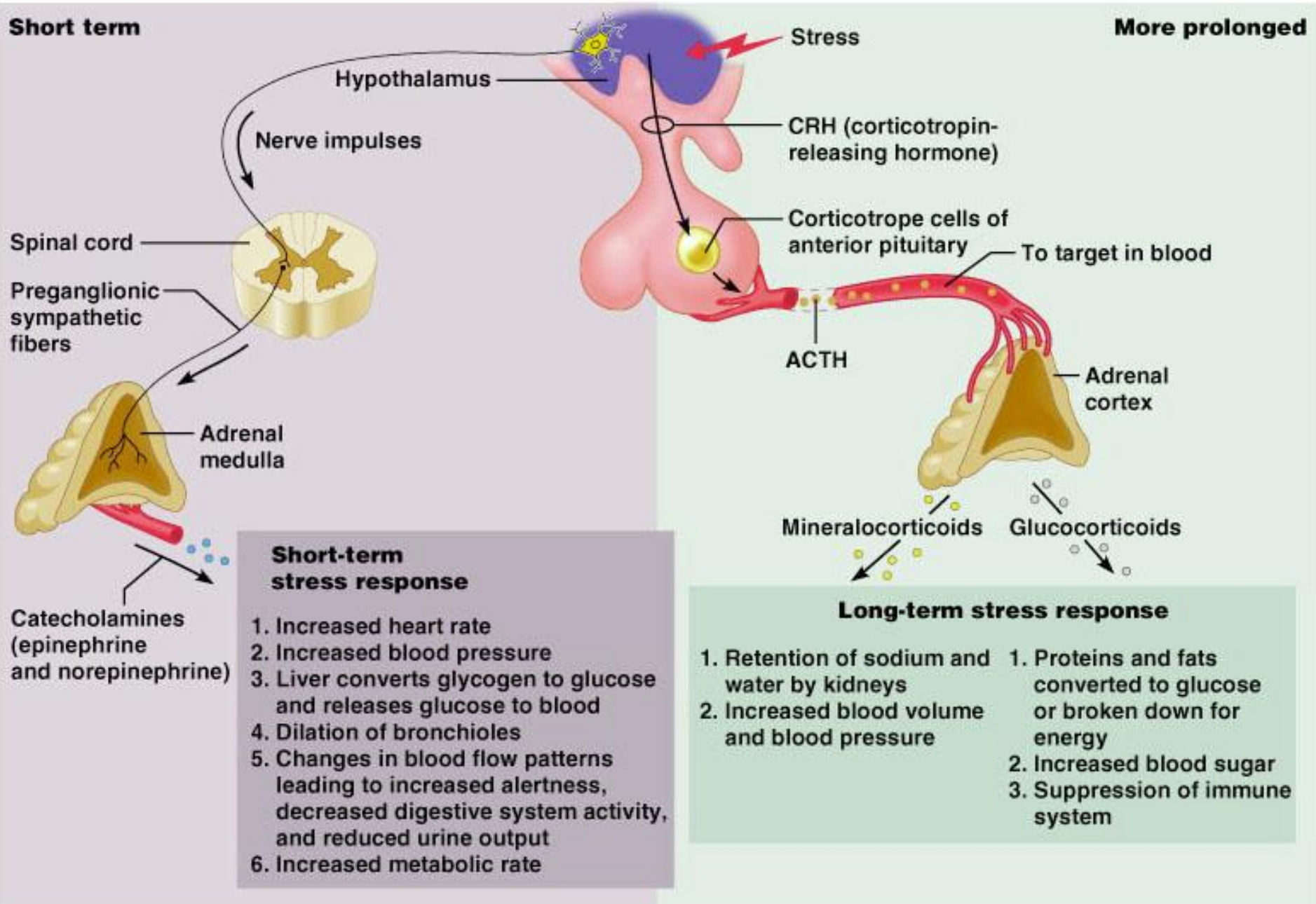


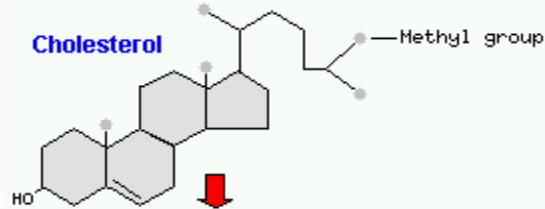
- Cortex
  - Zona glomerulosa (mineralocorticoids)
  - Zona fasciculata (glucocorticoids)
  - Zona reticularis (androgens)
- Medulla
  - catecholamines



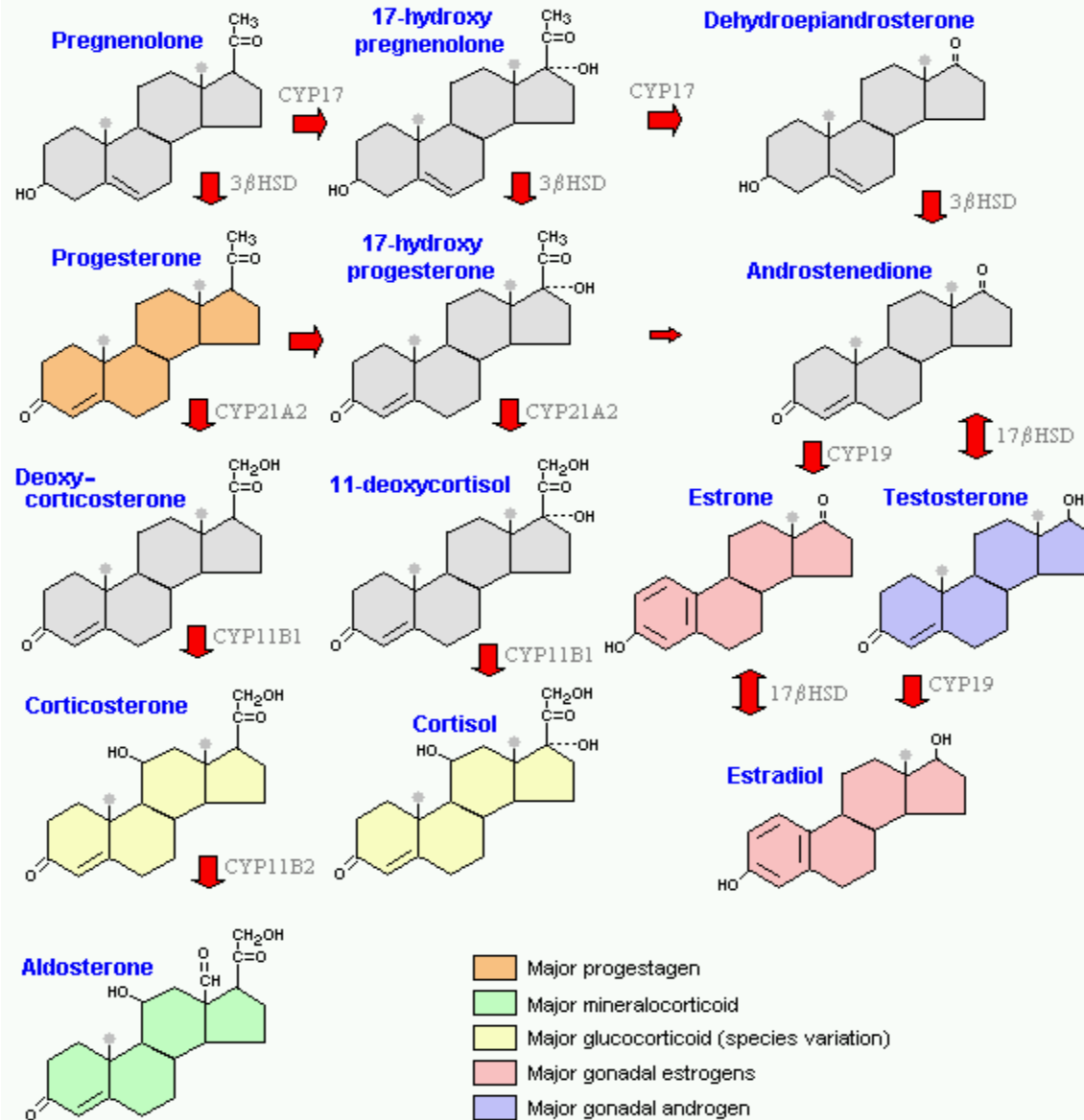
## Short term

## More prolonged





## Major Pathways in Steroid Biosynthesis



# Disorders of the adrenal glands

- Insufficiency
  - Primary – Addison's disease
    - Autoimmune, tuberculosis, hemorrhage (Waterhouse-Friderichsen syndrome in meningococcal infections)
  - Secondary – pituitary disorders, discontinuation of glucocorticoid therapy

# Addison's disease

- Aldosterone insufficiency
  - Hypotension, hyponatremia, hyperkalemia
- Skin pigmentation
  - Pro-Opioid-Melanocyte-Stimulating-Hormone
- ACTH increased (diff-dg secondary adrenal insufficiency)

# Conn's disease

- Primary hyperaldosteronism
  - Mostly unilateral endocrine active tumor
  - Hypertension
  - Hypernatremia
  - Hypokalemia

# Cushing's syndrome

- Hypercortisolism
  - Primary
    - Adrenal adenoma
  - Secondary
    - Cushing's disease - overproduction of ACTH
    - Ectopic production - lung ca
    - Iatrogenic



# Cushing's syndrome

- Central obesity
- Hypertension
- Osteoporosis
- Reduced growth
- Mental changes
  
- Hirsutism, acne, oligomenorrhea

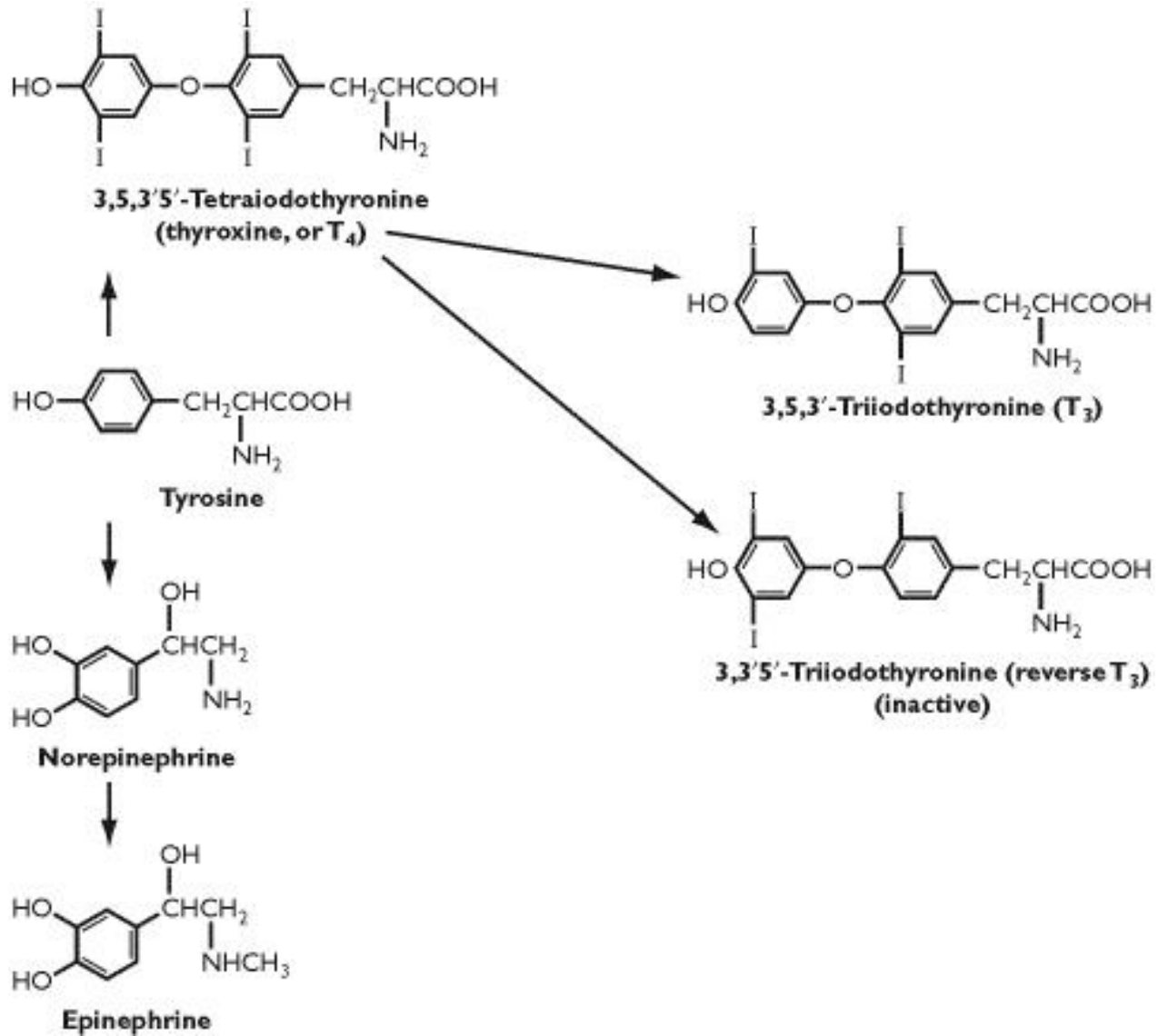
# Thyroid gland – physiology

- Actions of the thyroid
  - Controls body temperature
  - How body burns calories
  - Controls how fast food moves through digestive tract
  - Muscle strength
- Thyroid hormones
  - T4-thyroxine
  - T3-triiodothyronine
  - Calcitonin

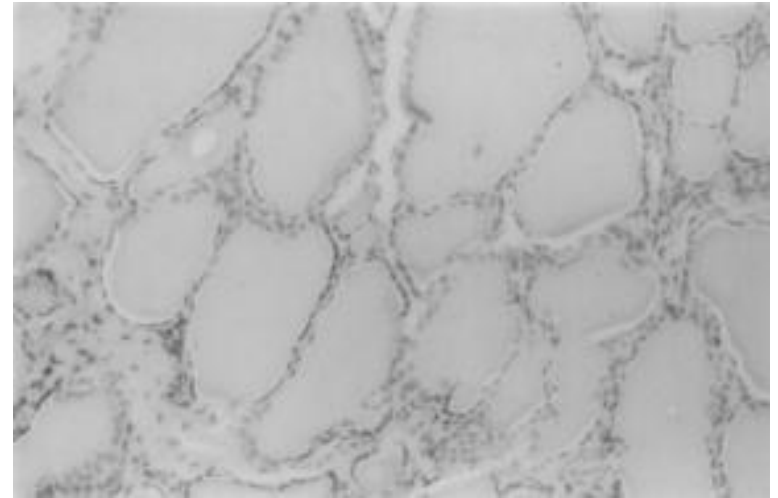
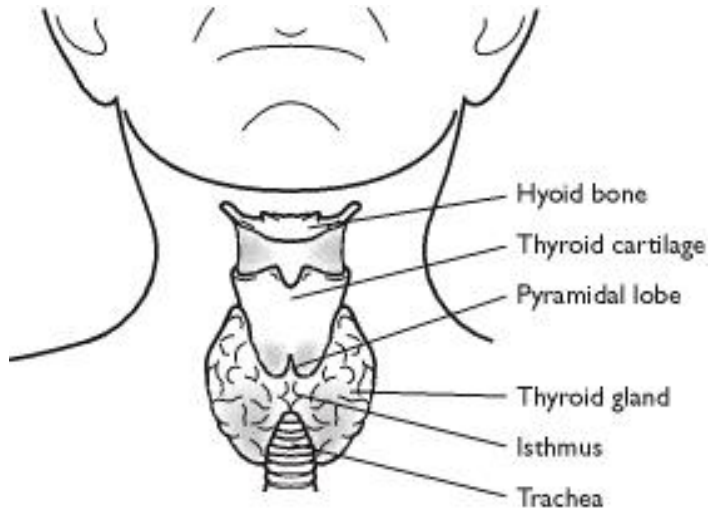
# Specifics

- Iodine is rare
- Ubiquitary receptors
- Highly potent action
- Very common disorders
  - 5% women
  - 0,5% men

# Structure

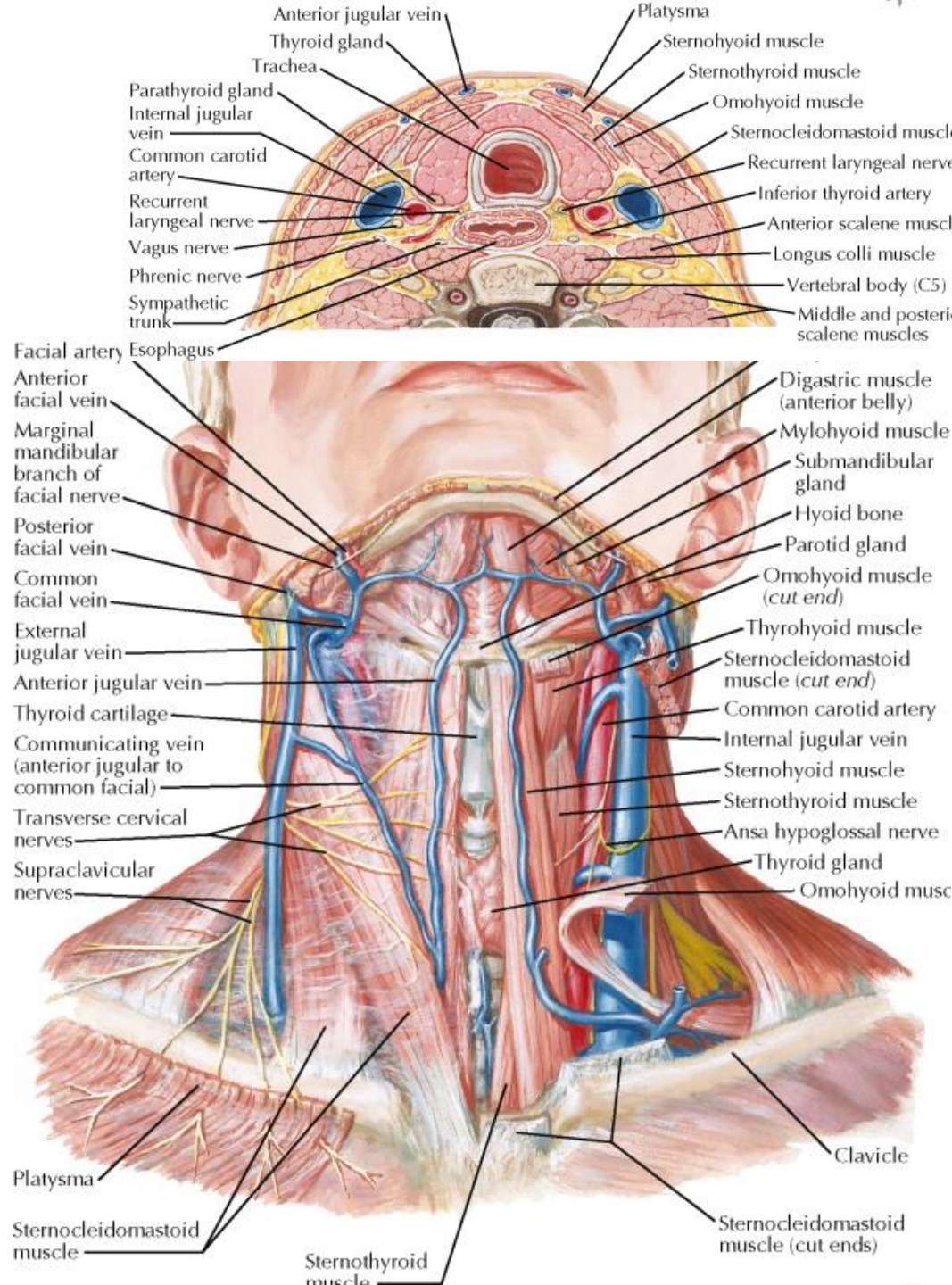


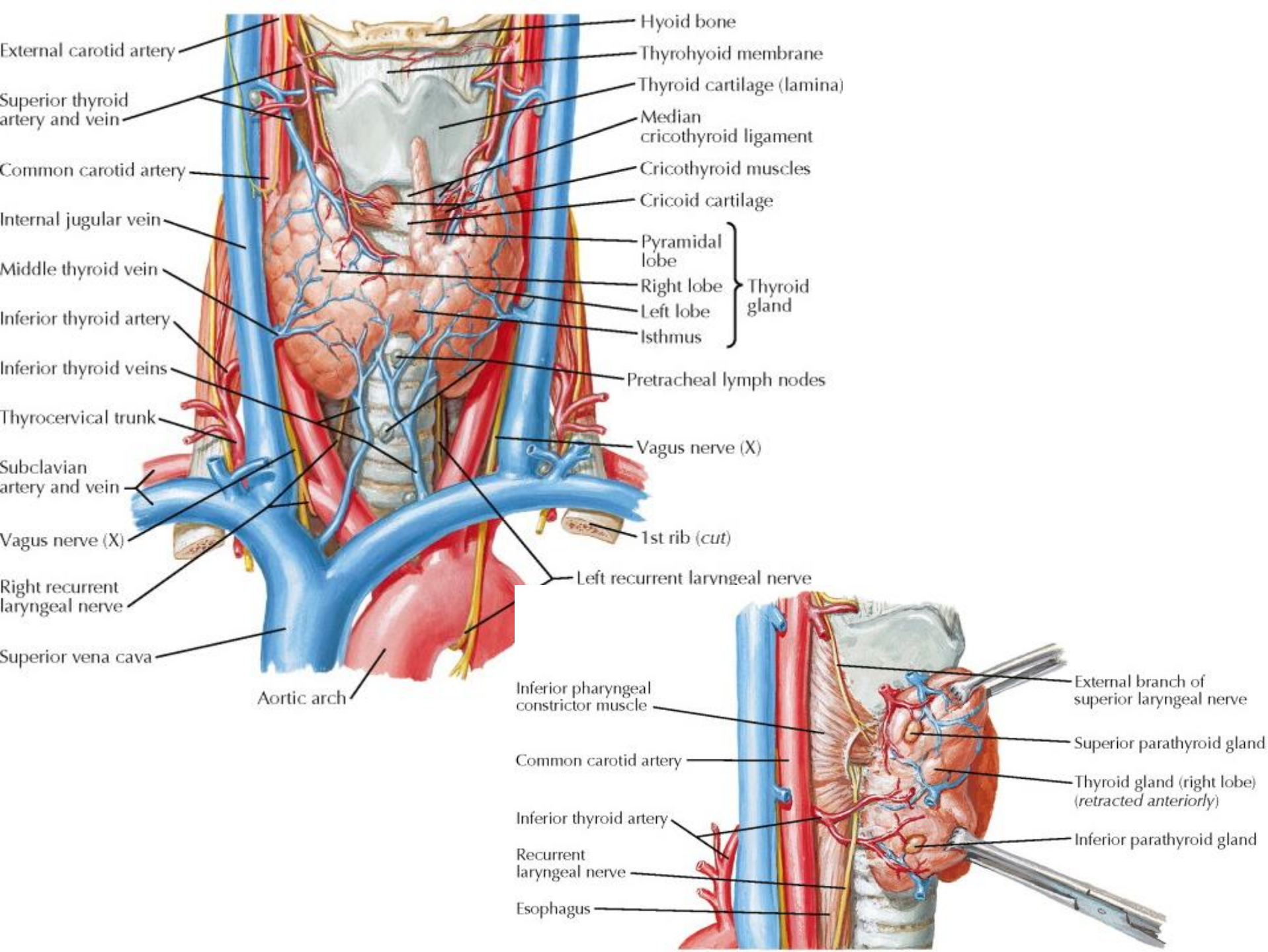
# Thyroid gland



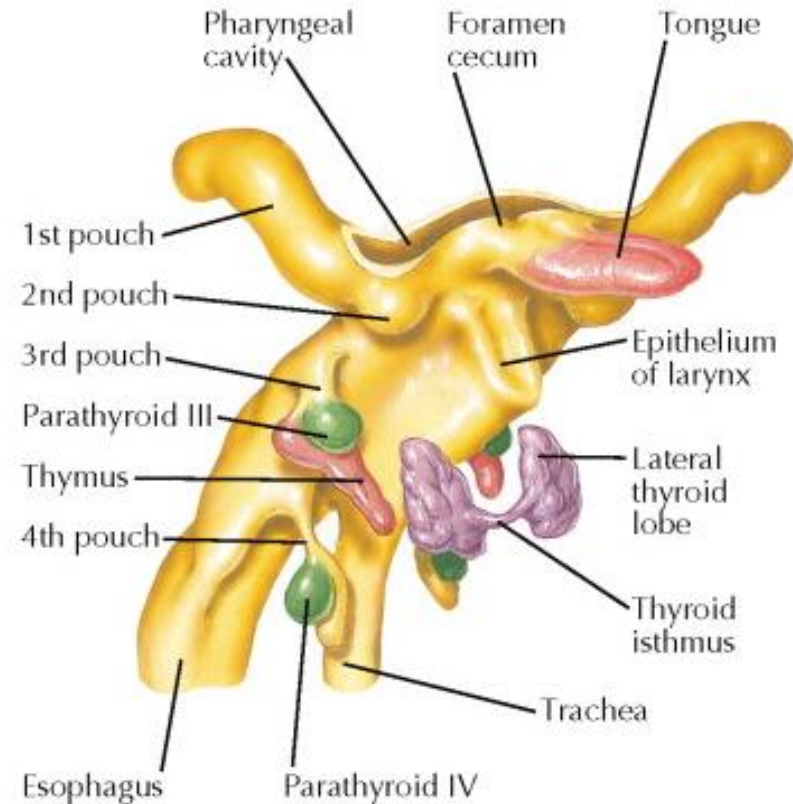
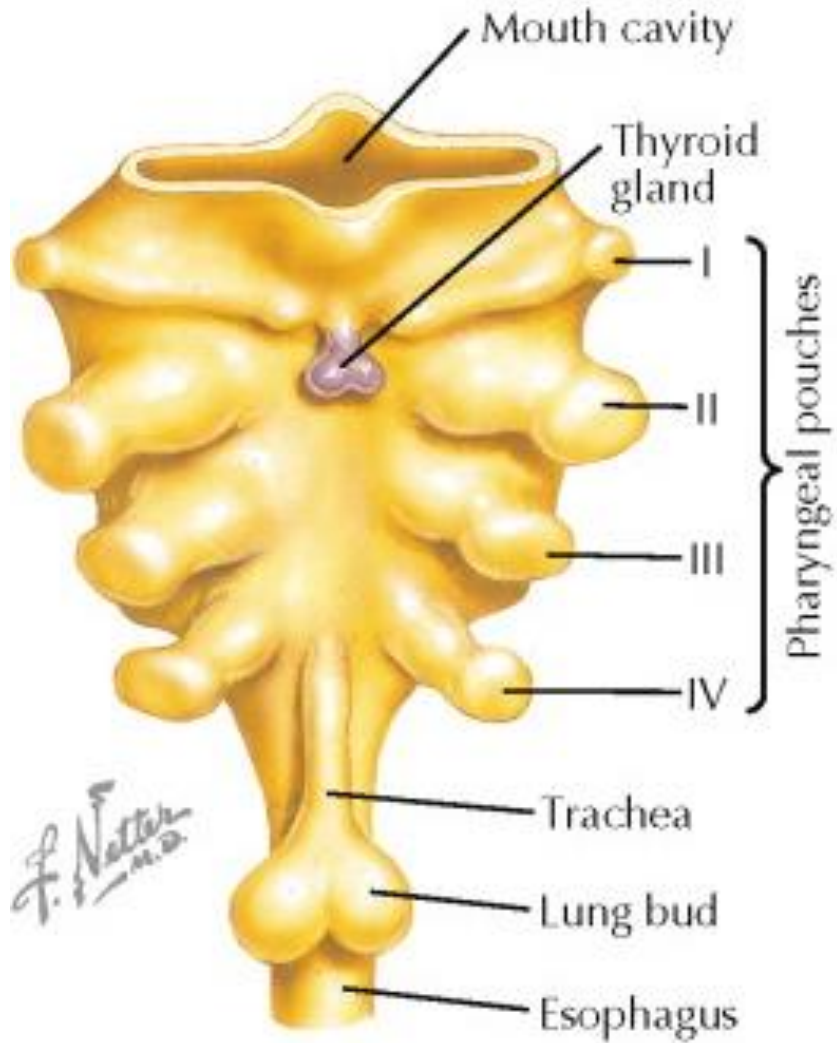
# Anatomy

- 20g
- CAVE!
  - Pyramidal lobe
  - Anomalies
  - Right lobe is bigger
  - PTH glands
  - Hypoglossal nerve
  - Nervus vagus





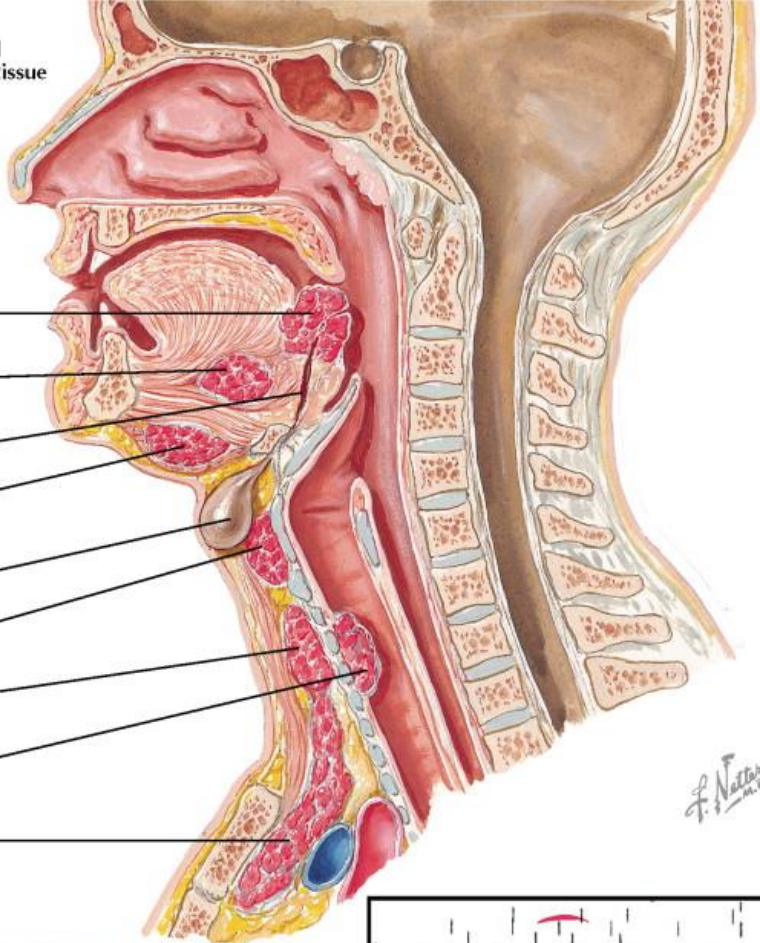
# Development



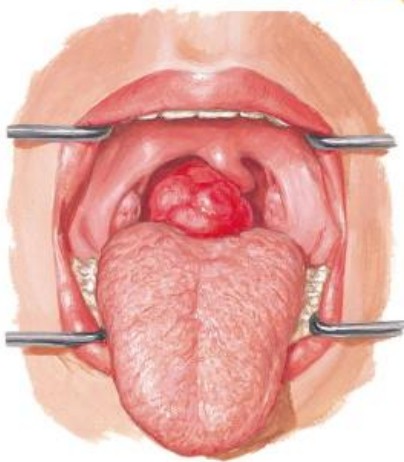


Aberrant and normal locations of thyroid tissue

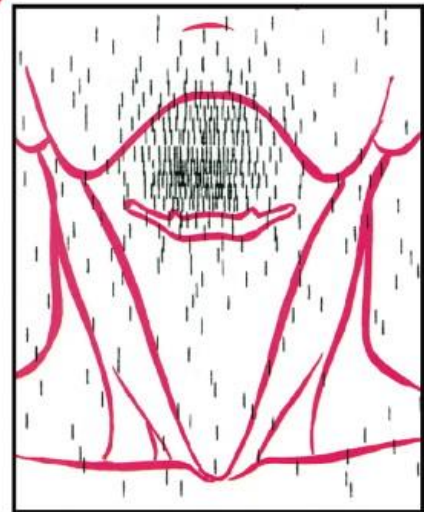
- Lingual
- Intralingual
- Thyroglossal tract
- Sublingual
- Thyroglossal cyst
- Prelaryngeal
- Normal
- Intratracheal
- Substernal



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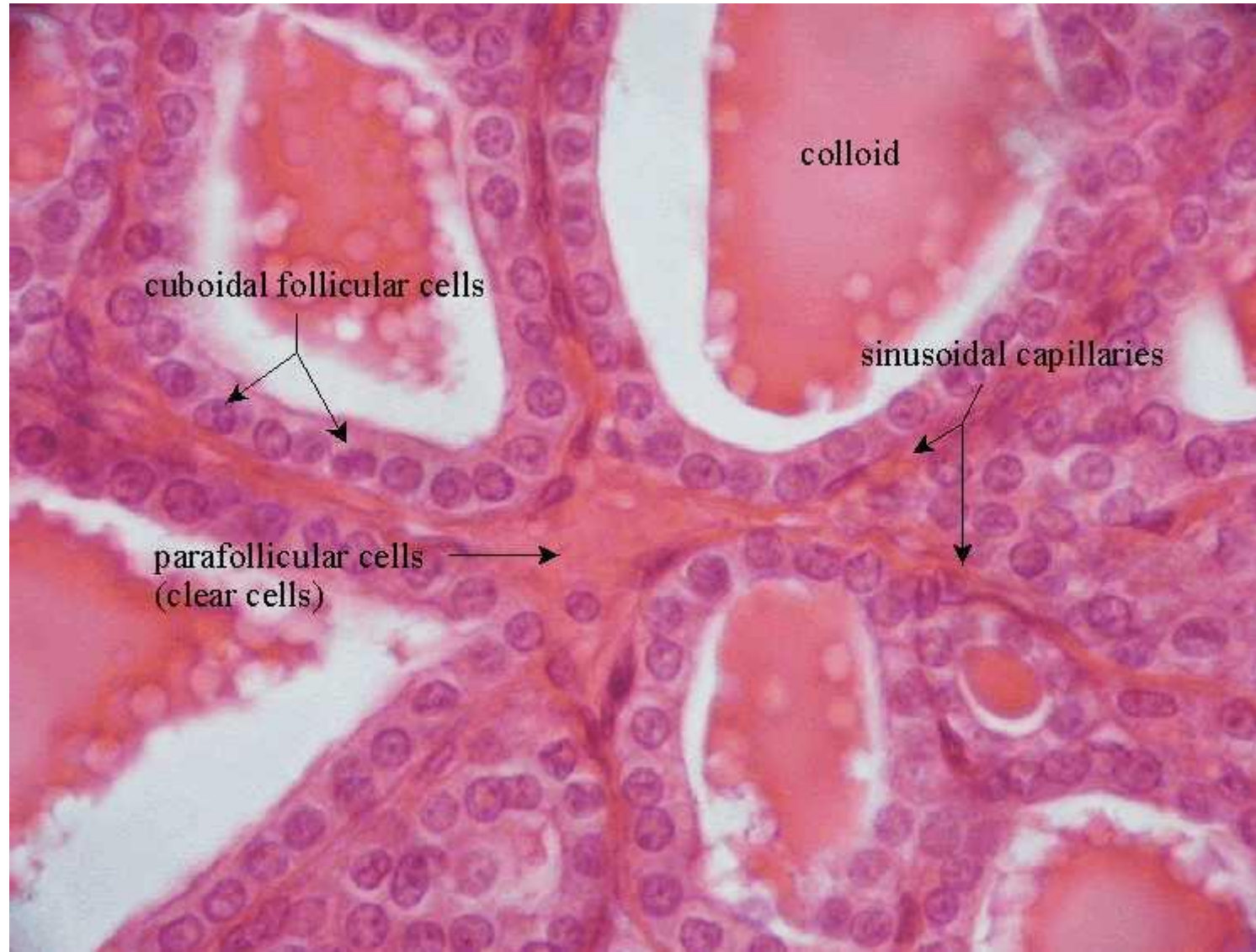


Lingual thyroid

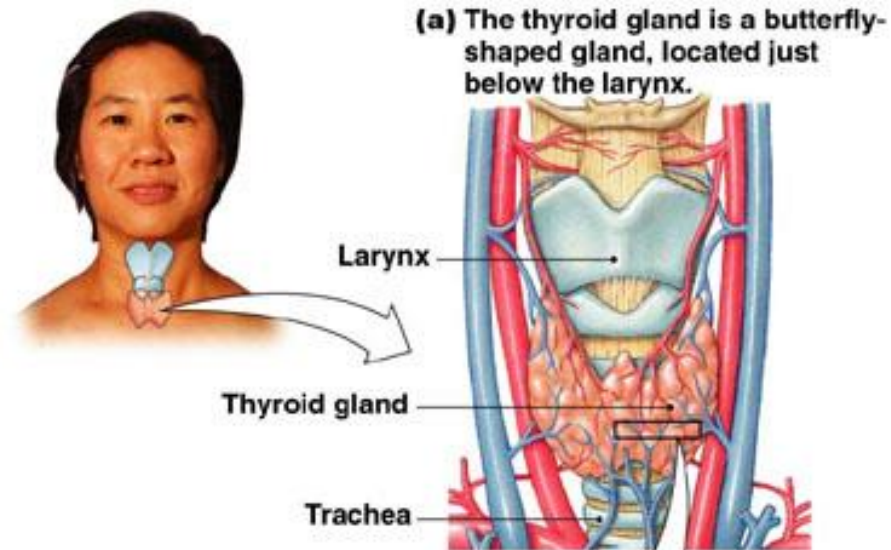


Scintigram; lingual thyroid

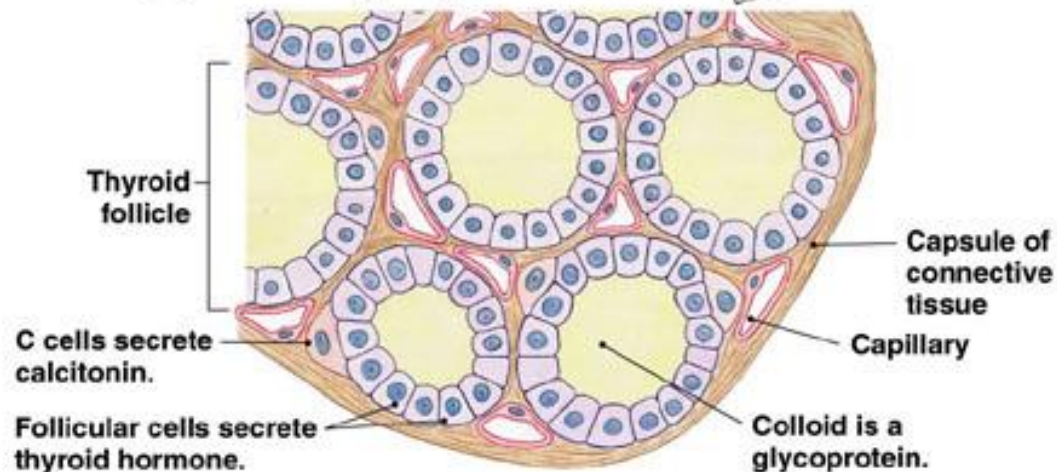
# Thyroid gland

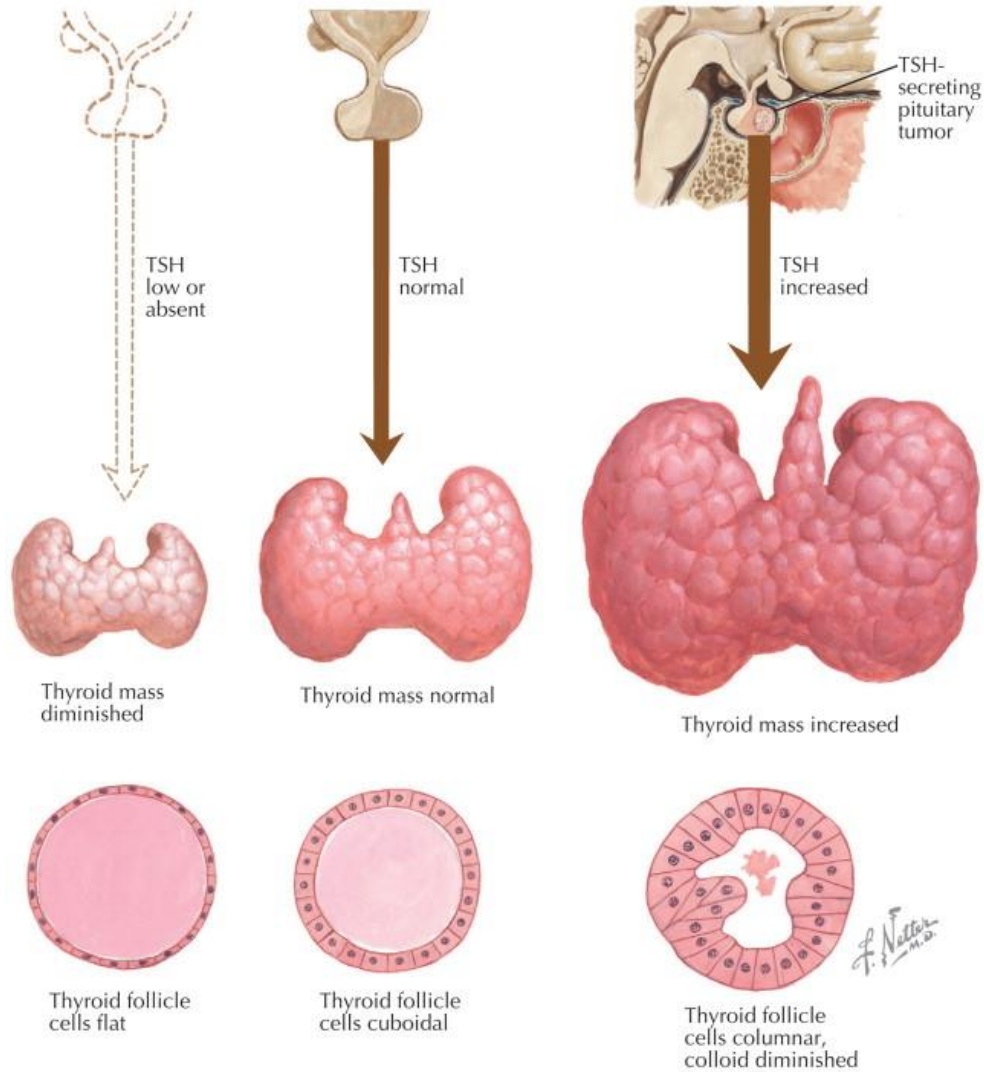


# Thyroid gland

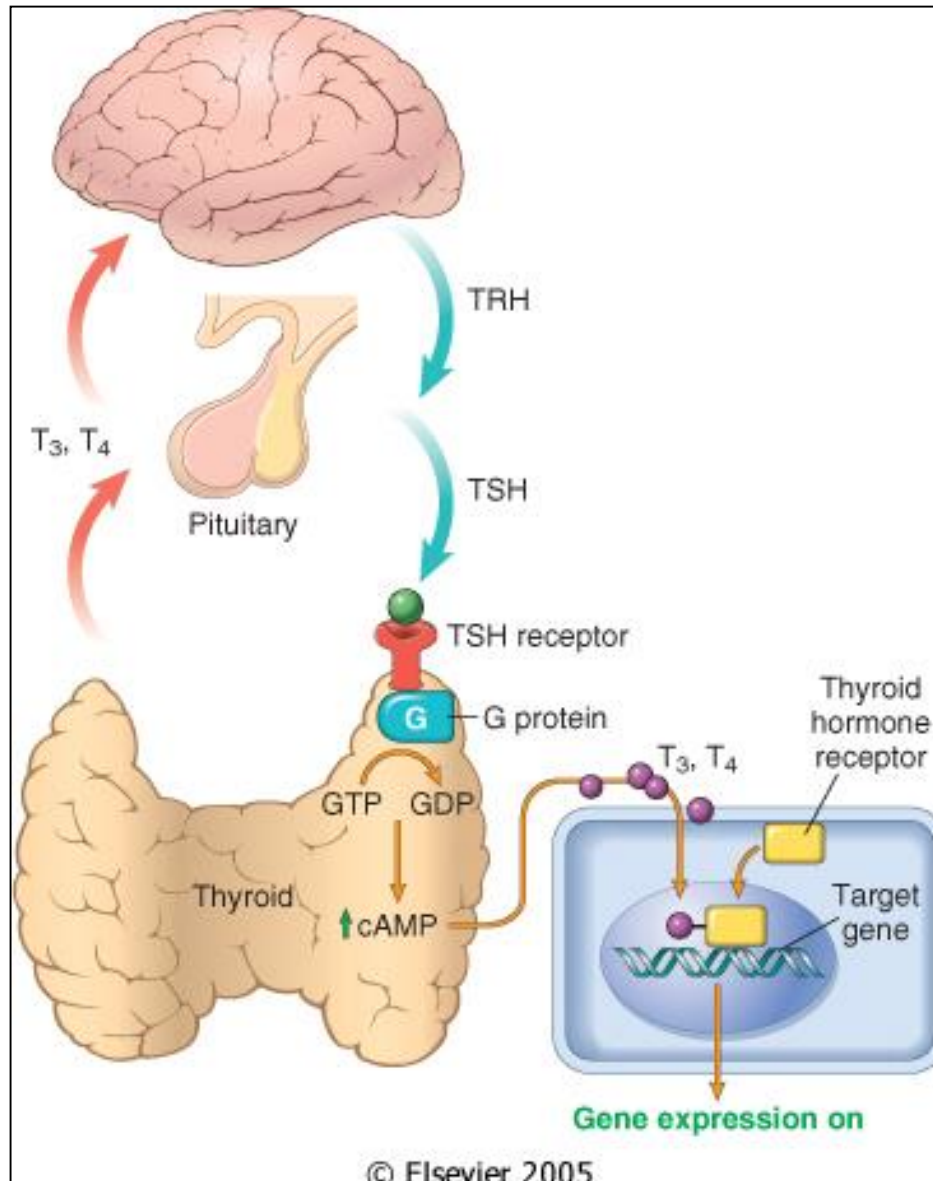


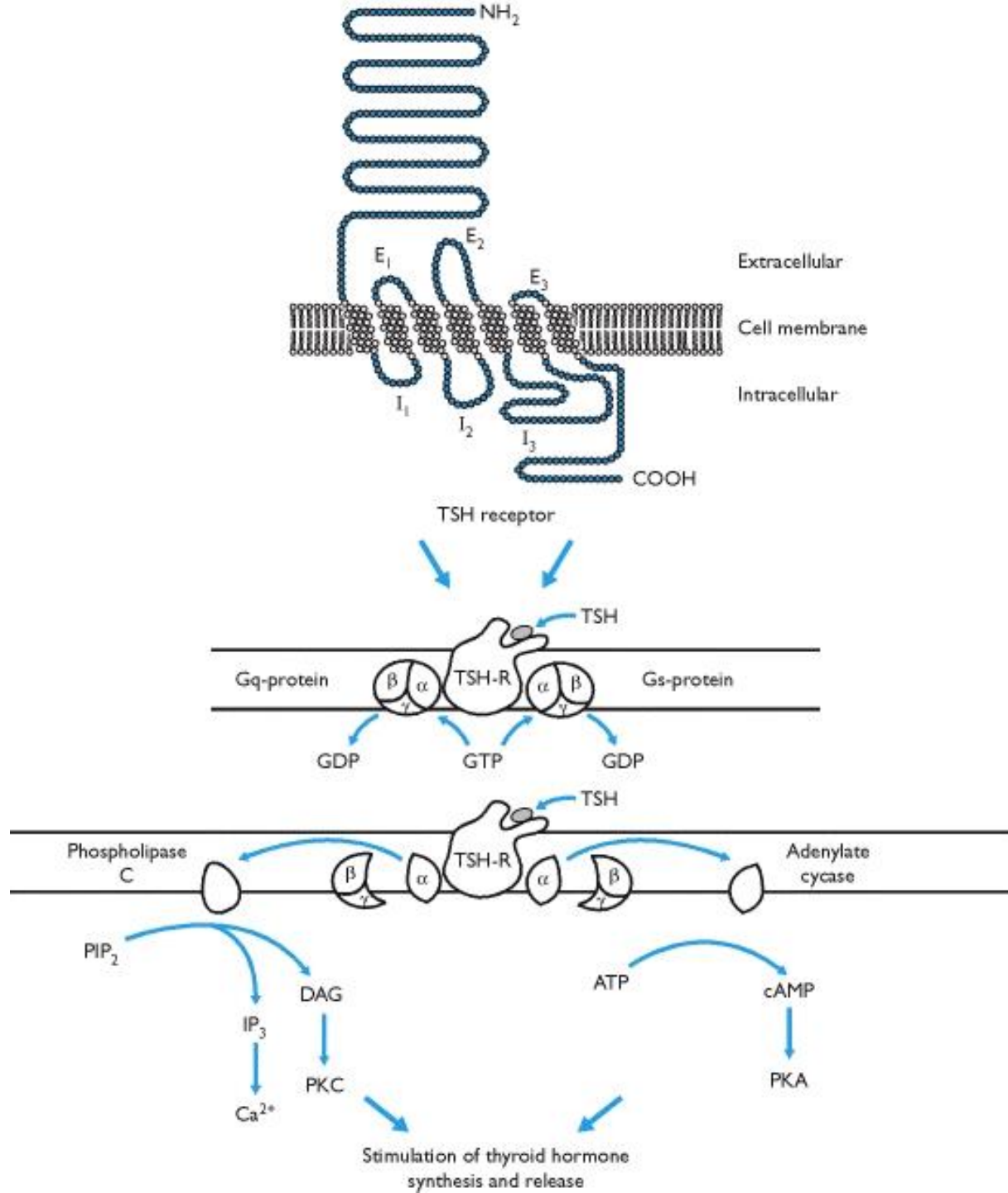
**(b) Section of thyroid gland**

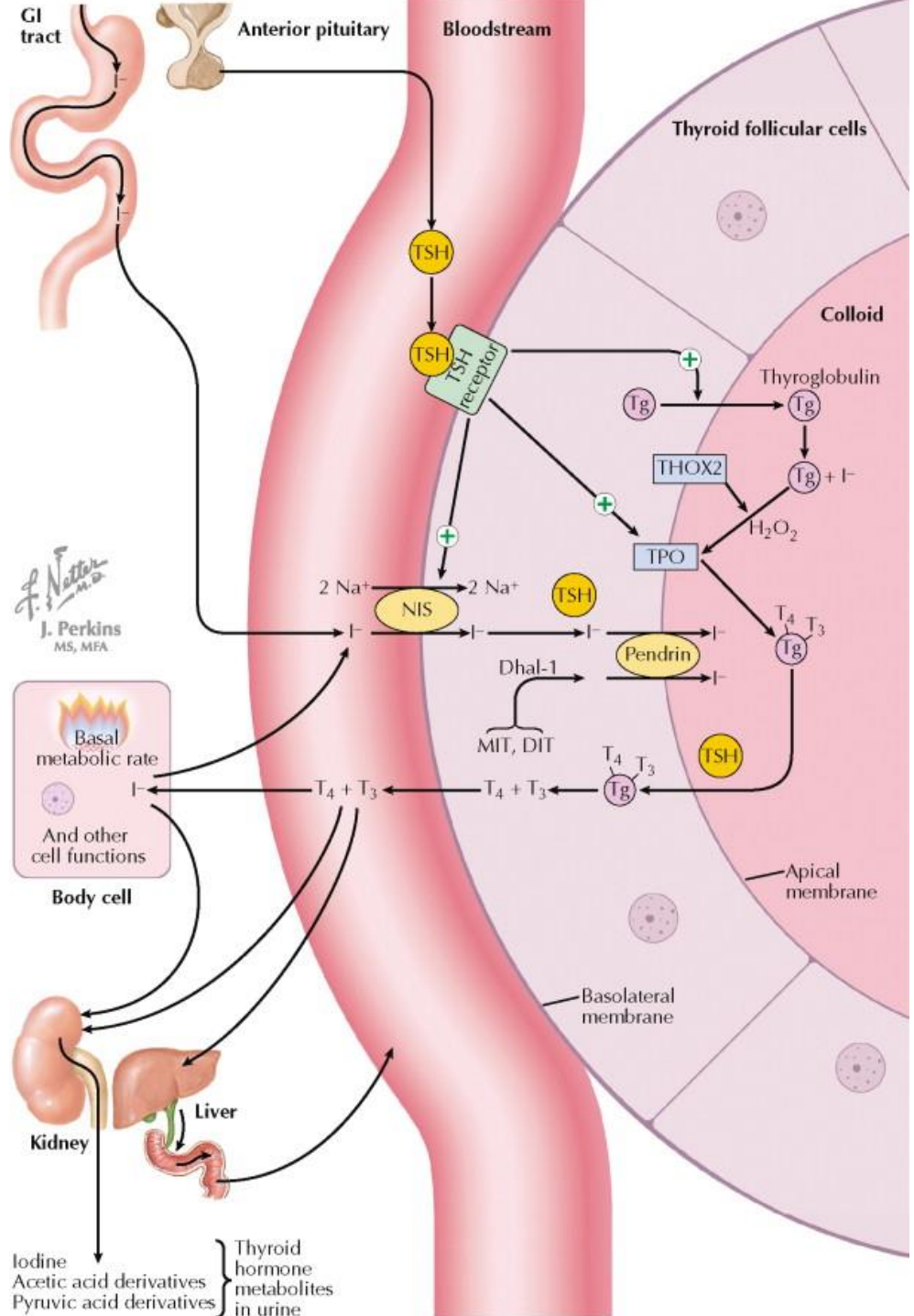




TSH: low	TSH: normal	TSH: high
Free T <sub>4</sub> : low	Free T <sub>4</sub> : normal	Free T <sub>4</sub> : high
Total T <sub>3</sub> : low	Total T <sub>3</sub> : normal	Total T <sub>3</sub> : high
<sup>131</sup> I-uptake: low	<sup>131</sup> I-uptake: normal	<sup>131</sup> I-uptake: high







*J. Perkins  
MS, MFA*

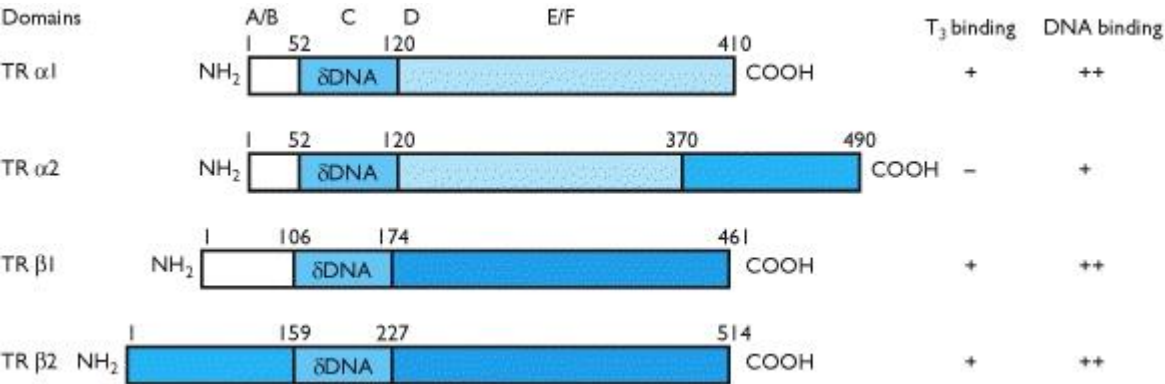
# Iodine intake

- 150 ug – daily intake of iodine
- 125 ug – taken up by the thyroid gland
- Iodine in the soil – region dependent
- Iodide supplementation of salt

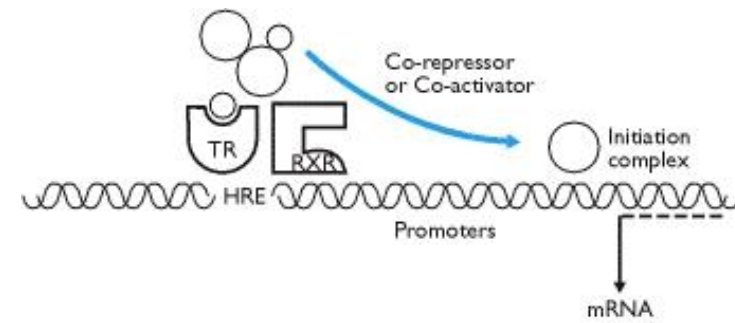


- T4:T3 15:1
- TBG
- Peripheral conversion
- T4 receptor... T3:T4 15:1
- 5mg T4 per gland
- Inflammation and trauma lead to thyreotoxicosis

# Receptors



- Membrane bound receptors



# Action

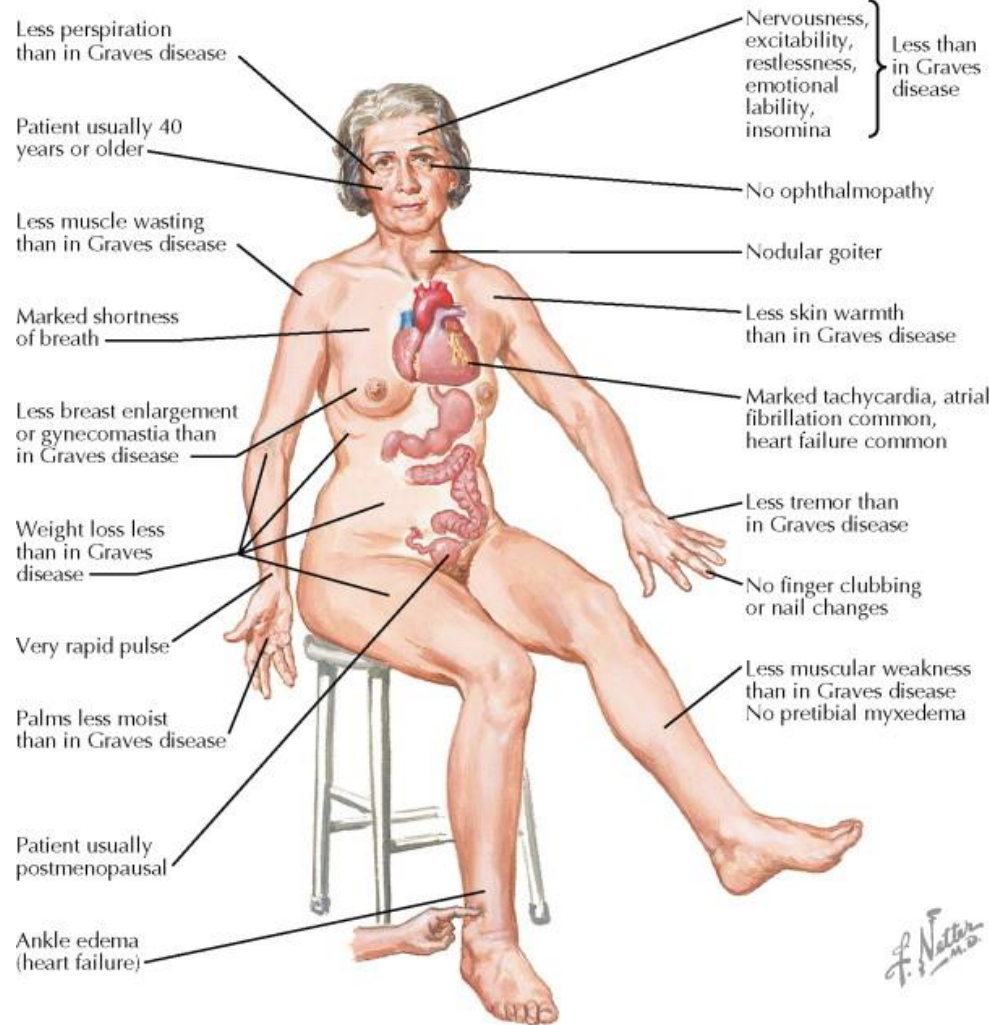
- Increase of number and size of mitochondria
- Synthesis of respiratory chain enzymes
- Na<sup>+</sup> K<sup>+</sup> ATPase
- Uncoupling proteins
- Increase in resting metabolic activity

# Hyperthyroidism

Symptoms	
<b>Common</b>	
Anxiety and irritability (~ >90%)	Tachycardia (~ 100%)
Palpitations (~ 90%)	Tremor (~ 95%)
Increased perspiration and heat intolerance (~ 90%)	Goiter (~ 100%)
Fatigability (~ 80%)	Warm moist skin (~ 95%)
Weakness (~ 70%)	
Increased appetite and weight loss (~ 85%)	
<b>Less common</b>	
Dyspnoea (~ 65%)	Atrial fibrillation (~ 10%)
Increased bowel frequency (~ 30%)	Onycholysis (~ <5%)
Anorexia (~ 10%)	'Liver palms' (~ 5%)
Weight gain (~ <5%)	Heart failure (~ 5%)
Oligomenorrhea (~ 25%)	
<b>Rare</b>	
Pruritus (~ <1%)	
Periodic paralysis (~ <1%)	

# Hyperthyroidism

- Emotional symptoms
  - Nervousness
  - Restlessness
  - Anxiety
  - Irritability
  - Sleeplessness or insomnia
  - Exhaustion



Laboratory findings



**Basal metabolic rate**  
Moderately elevated (25%–30%)



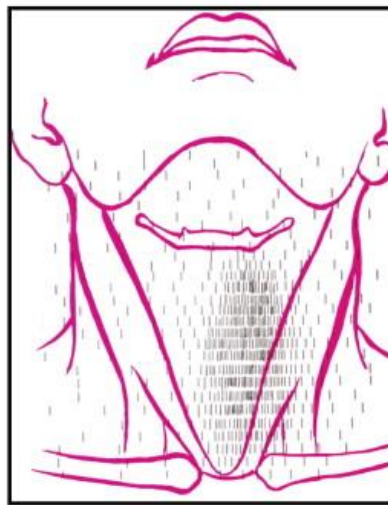
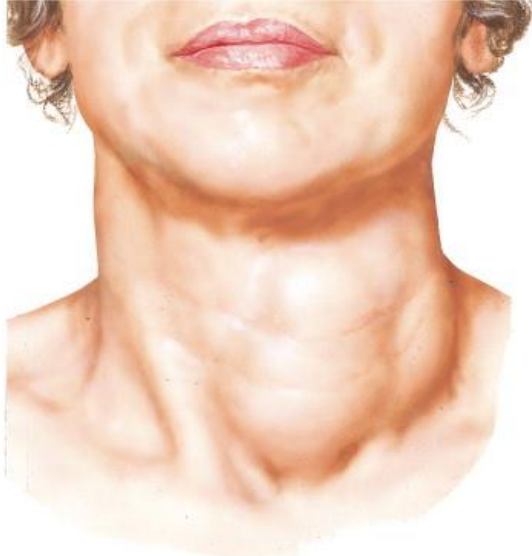
**<sup>131</sup>I uptake**  
Elevated less than in Graves disease (40%–55%) localized in functioning adenoma

**Blood tests:**

Decreased TSH  
Increased free T<sub>4</sub>  
Increased total T<sub>3</sub>  
Undetectable TSH-receptor antibodies  
Decreased total and HDL cholesterol  
Increased sex hormone-binding globulin  
Increased estradiol (in men and women)  
Increased osteocalcin and bone-specific alkaline phosphatase

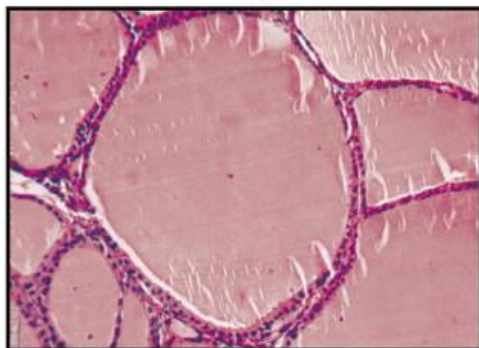
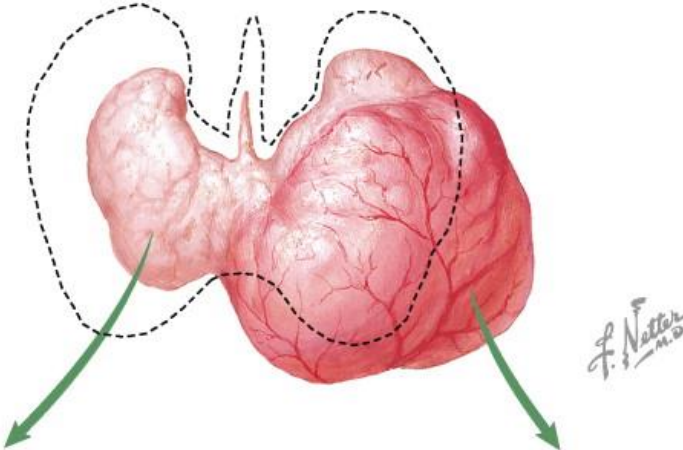
# Causes of hyperthyroidism

- Grave's disease
- A benign nodule on the thyroid
- Thyroiditis
- Taking too much of the synthetic thyroid hormone

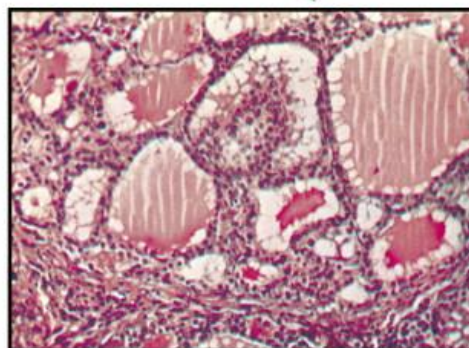


Scintigram

Hyperfunctioning adenoma



Remainder of gland—involution



Adenoma—hyperplasia



# Hyperthyroidism DiffDg

- Graves' Disease
- Toxic Multinodular Goiter
- Toxic Adenoma
- Thyroiditis
  - silent (Hashimoto's) – painless, often post partum
  - subacute (de Quervain's) – painful, post viral
  - drug-induced – amiodarone, lithium, interferon
- Thyrotoxicosis factitia
  - ingestion

# Thyroid storm (crisis)

- Sudden onset
- Fever
- Profuse diaphoresis
- Flushed warm skin
- Tachycardia
- Weakness, lethargy and confusion
- Coma
- Nausea, vomiting, diarrhea

# Treatment of hyperthyroidism

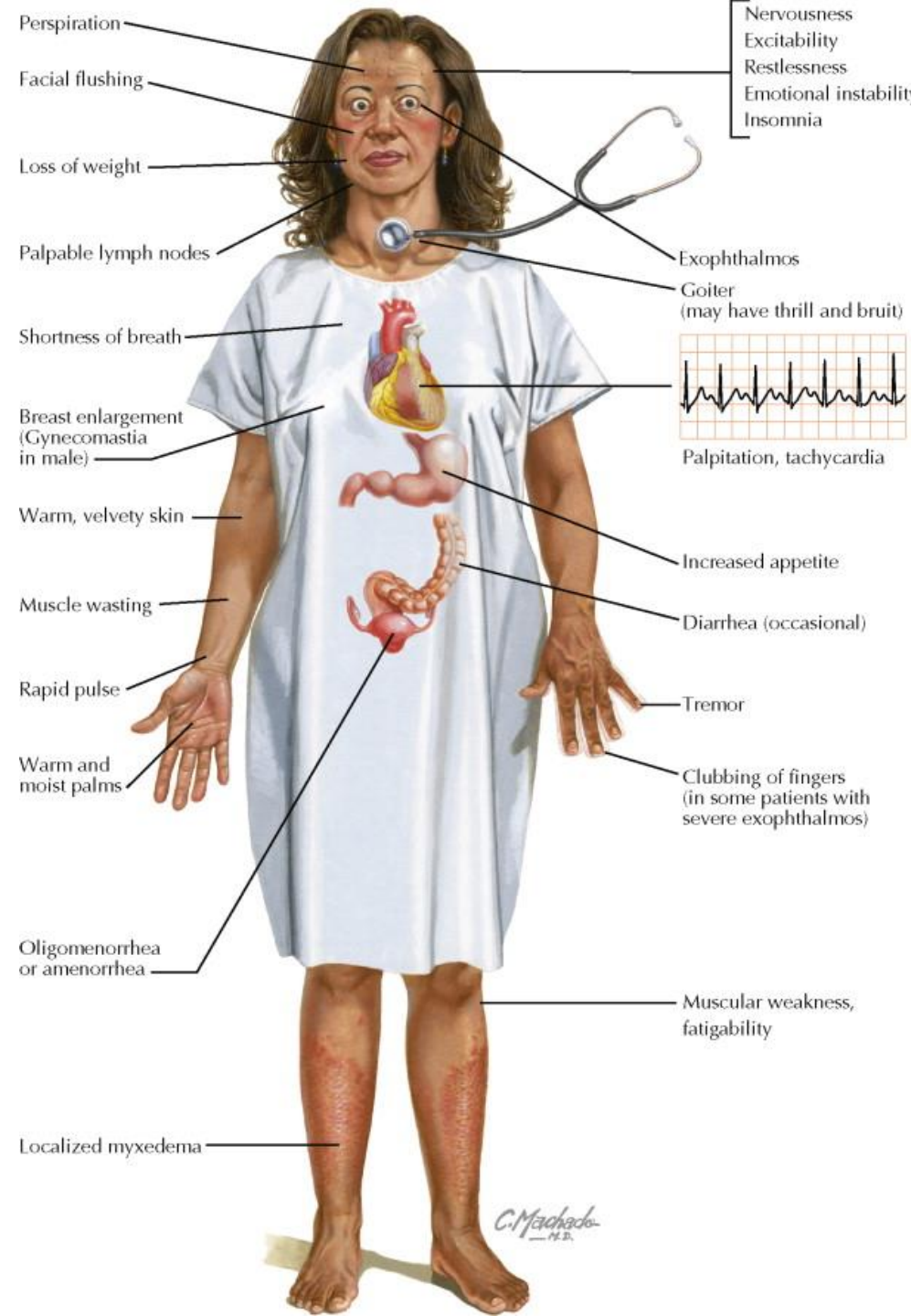
- Causative
- Radioactive iodine
  - Supplementation
- High-dose iodine – Wolff-Chaikoff effect
- Beta-blockers
- Antithyroid treatment
  - Propylthiouracil (PTU)
- Thyroidectomy

# Grave's disease

- Grave's Basedow trias
  - Goiter
  - Exophthalmus
  - Hyperthyroidism
- Autoimmune disease
  - Anti-TSH receptor

# Graves

- SHBG – amenorrhea
- Osteoporosis





Moderately severe ophthalmopathy

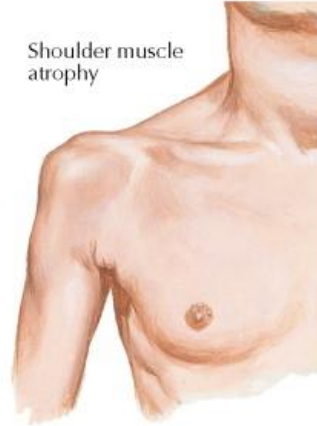
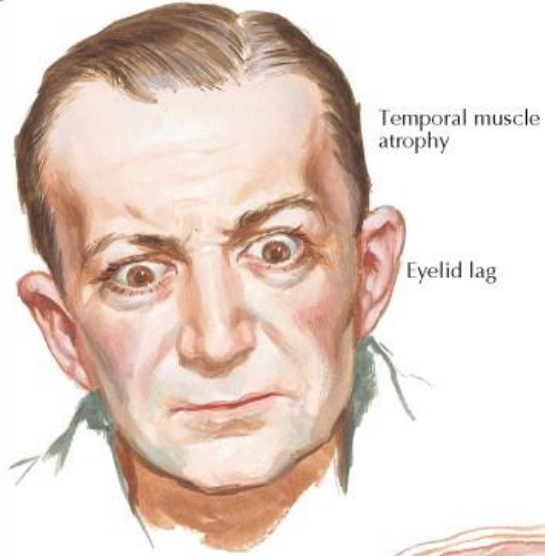


Testing for resiliency

Severe progressive ophthalmopathy

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M.D.*

Muscles



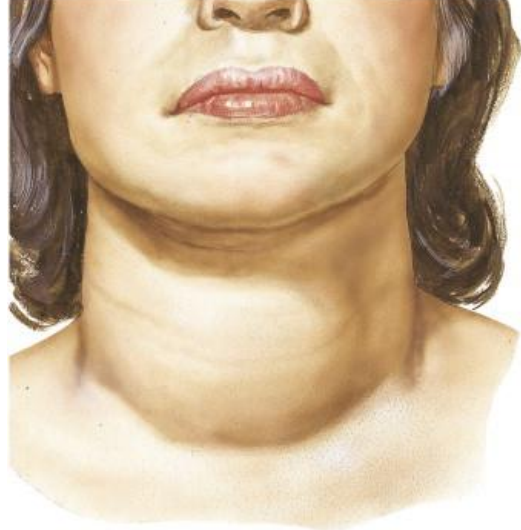
*F. Netter M.D.*

Skin

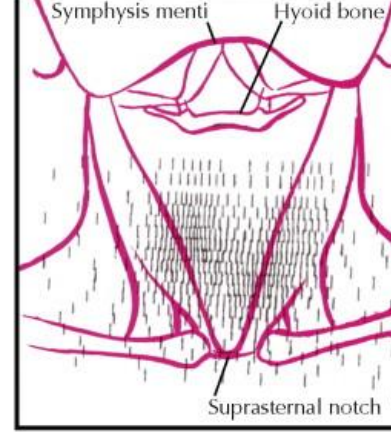


Heart





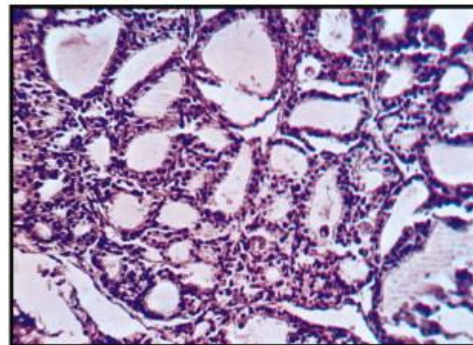
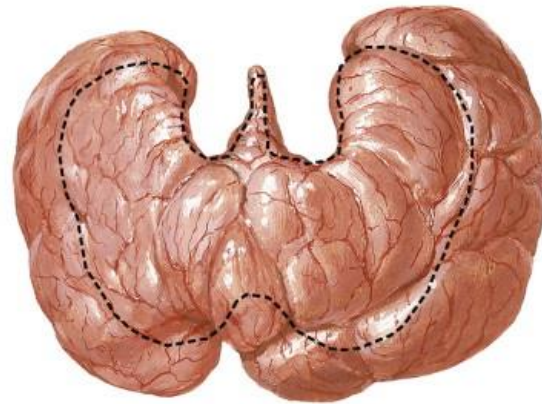
Diffuse goiter of moderate size



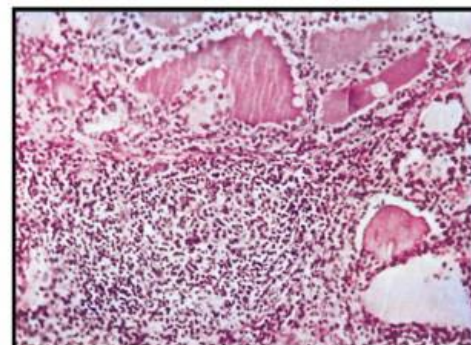
Scintigram

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M.D.

Diffuse enlargement and engorgement of thyroid gland (*broken line indicates normal size of gland*)



Diffuse hyperplasia



Hyperplasia with lymphocytic infiltration



# Goiter



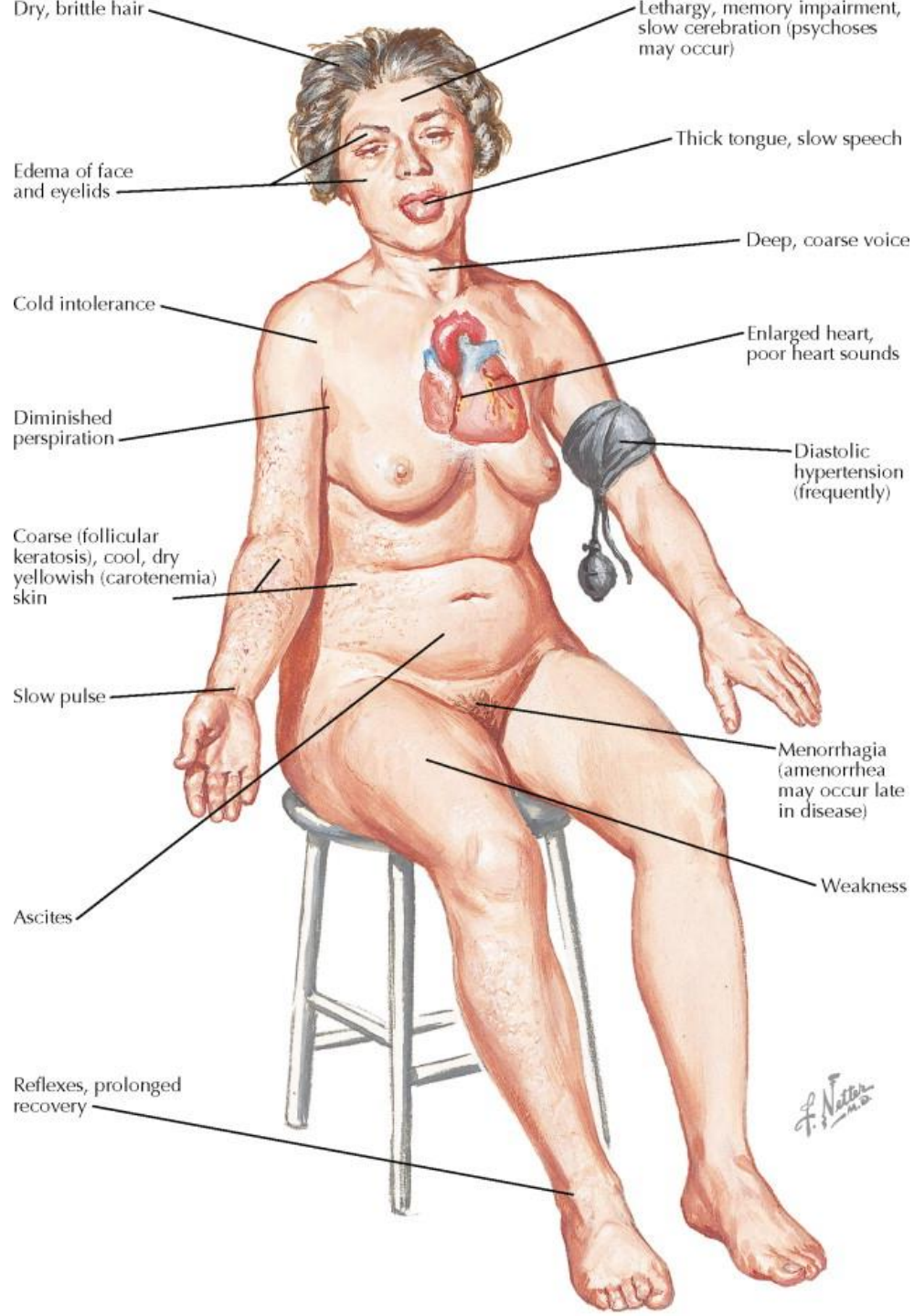
Grade	Definition
0	No palpable or visible goiter
1	Palpable goiter <ul style="list-style-type: none"><li>A Only palpable</li><li>B Palpable and visible with the neck extended</li></ul>
2	Goiter visible with neck in normal position
3	Very large goiter visible from distance

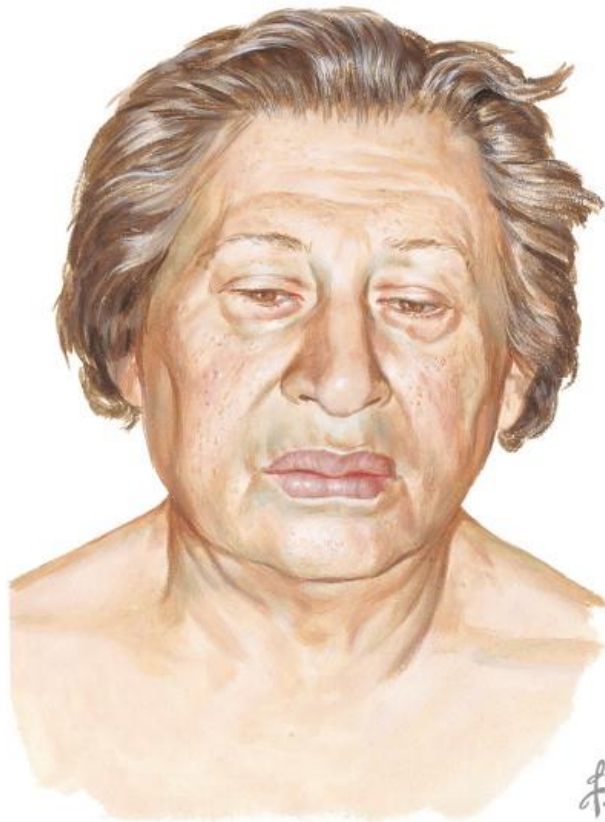
# Hypothyroidism



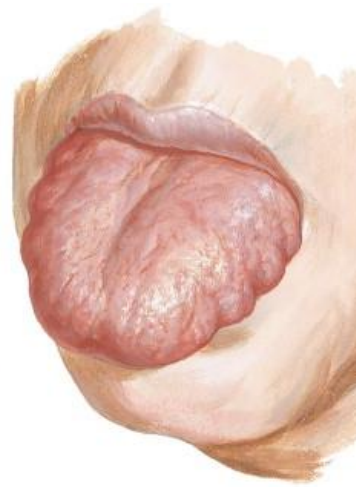
# Hypothyroidism

Symptoms	Signs
<b>Common</b>	
Fatigue (~ 90%)	Dry, scaly skin (~ 90%)
Cold intolerance (~ 80%)	Coarse, brittle thinning hair (~ 60%)
Depression (~ 70%)	Bradycardia (~ 40%)
Poor concentration (~ 65%)	Hair loss or dryness (~ 70%)
Musculoskeletal aches and pains (~ 25%)	Anemia
Carpal tunnel syndrome (~ 15%)	Puffy eyes (~ 90%)
<b>Less common</b>	
Constipation (~ 50%)	Edema (~ 30%)
Hoarse voice (~ 40%)	Cerebellar signs*
Menorrhagia (~ 30%)	Deafness*
	Psychiatric*





Characteristic facies in hypothyroidism:  
coarse features; thick lips; dry skin;  
puffy eyelids; dull, lethargic expression;  
coarse hair

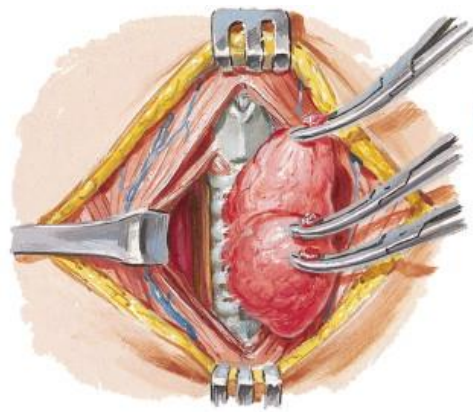


Macroglossia, showing  
dental impressions



Pudgy hands; chipped nails;  
dry, wrinkled skin;  
hyperkeratosis of elbow

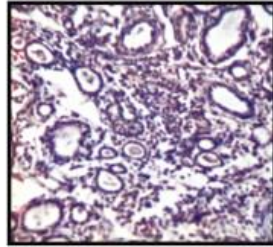
Primary hypothyroidism



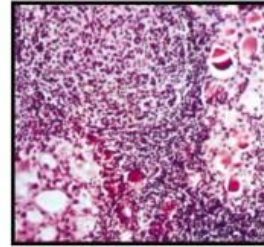
After thyroidectomy



After radioactive iodine to treat Graves disease

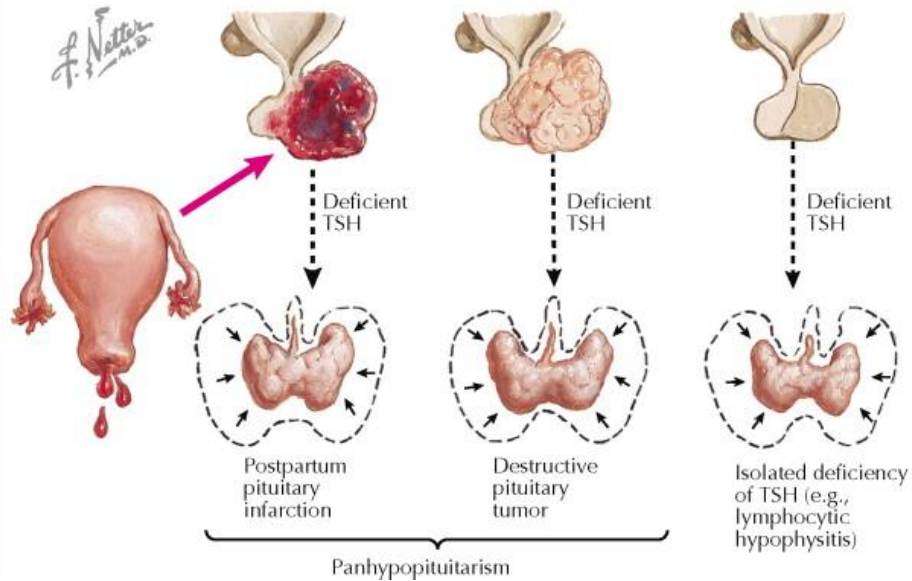


After acute thyroiditis



After Hashimoto thyroiditis

Central hypothyroidism (hypothalamic or pituitary origin)



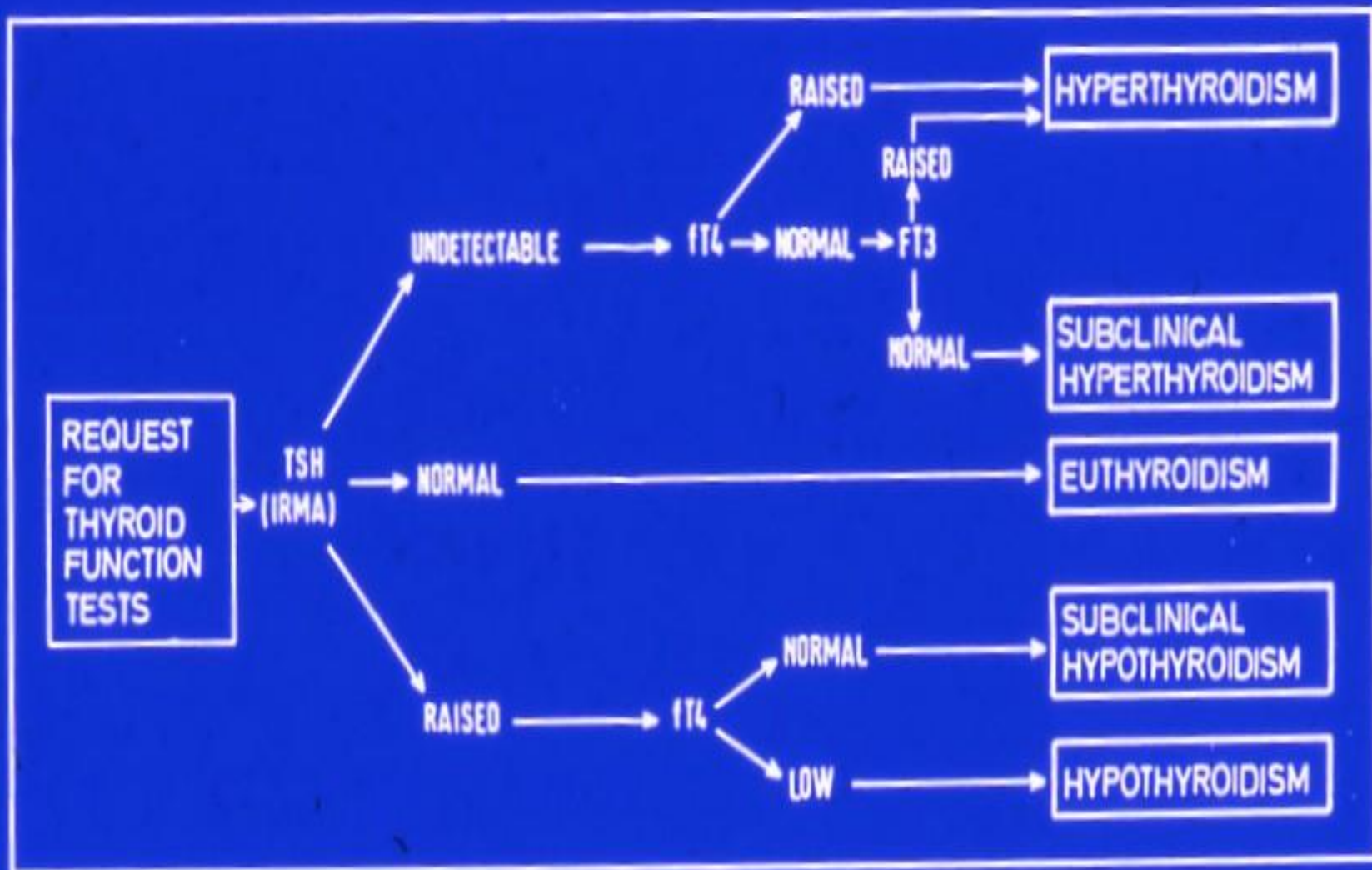
# Hypothyroidism

- Primary
  - Thyroid gland
  - Hashimoto's disease
    - Autoimmune thyroid destruction
  - Creteinism
    - Neonatal screening
- Secondary
  - Pituitary gland

# Hypothyroidism

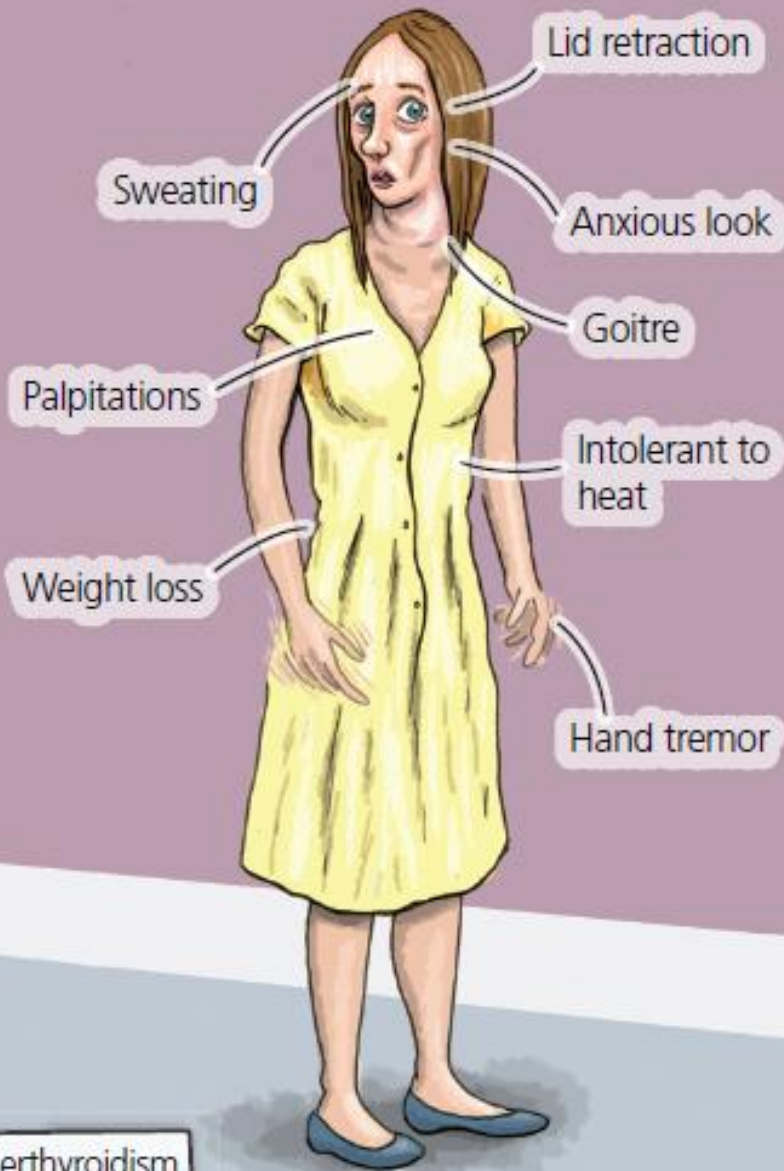
- Treatment of hypothyroidism
  - Causative
  - Thyroid hormone replacement
  - Iodine
    - Jod-Basedow effect

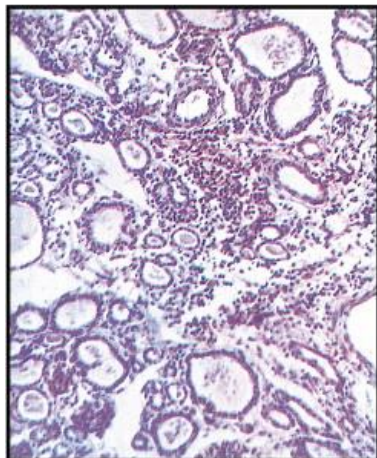
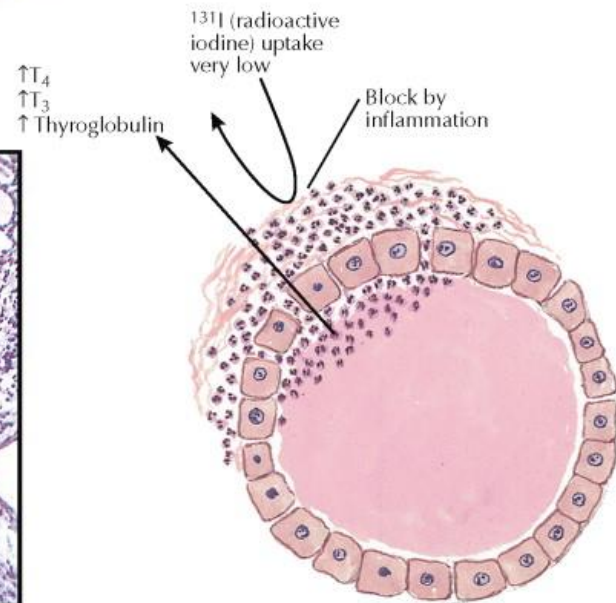
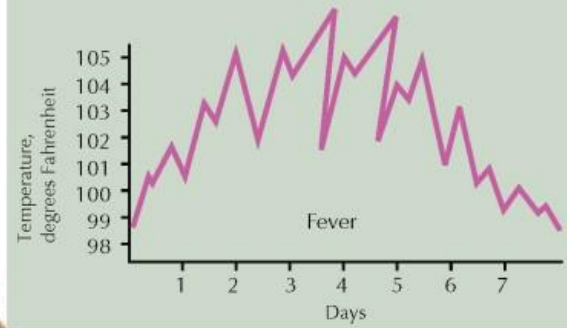
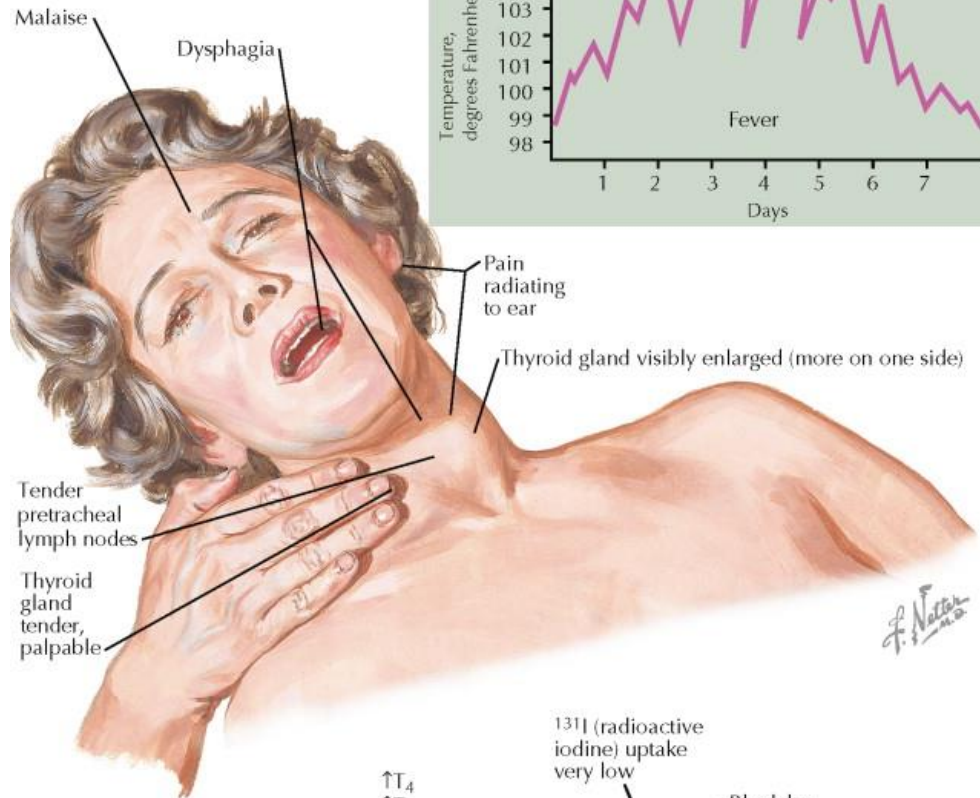




Proposed strategy for investigation of thyroid function in patients with suspected thyroid disease. *FT3* = free triiodothyronine; *FT4* = free thyroxine; *IRMA* = immunoradiometric assay; *TSH* = thyrotropin. (From Caldwell G, Kellett HA, Gow SM, Beckett GJ, Sweeting VM, Seth J, Toft AD: A new strategy for thyroid function testing. *Lancet* 1:1117-1119, 1985. By permission.)

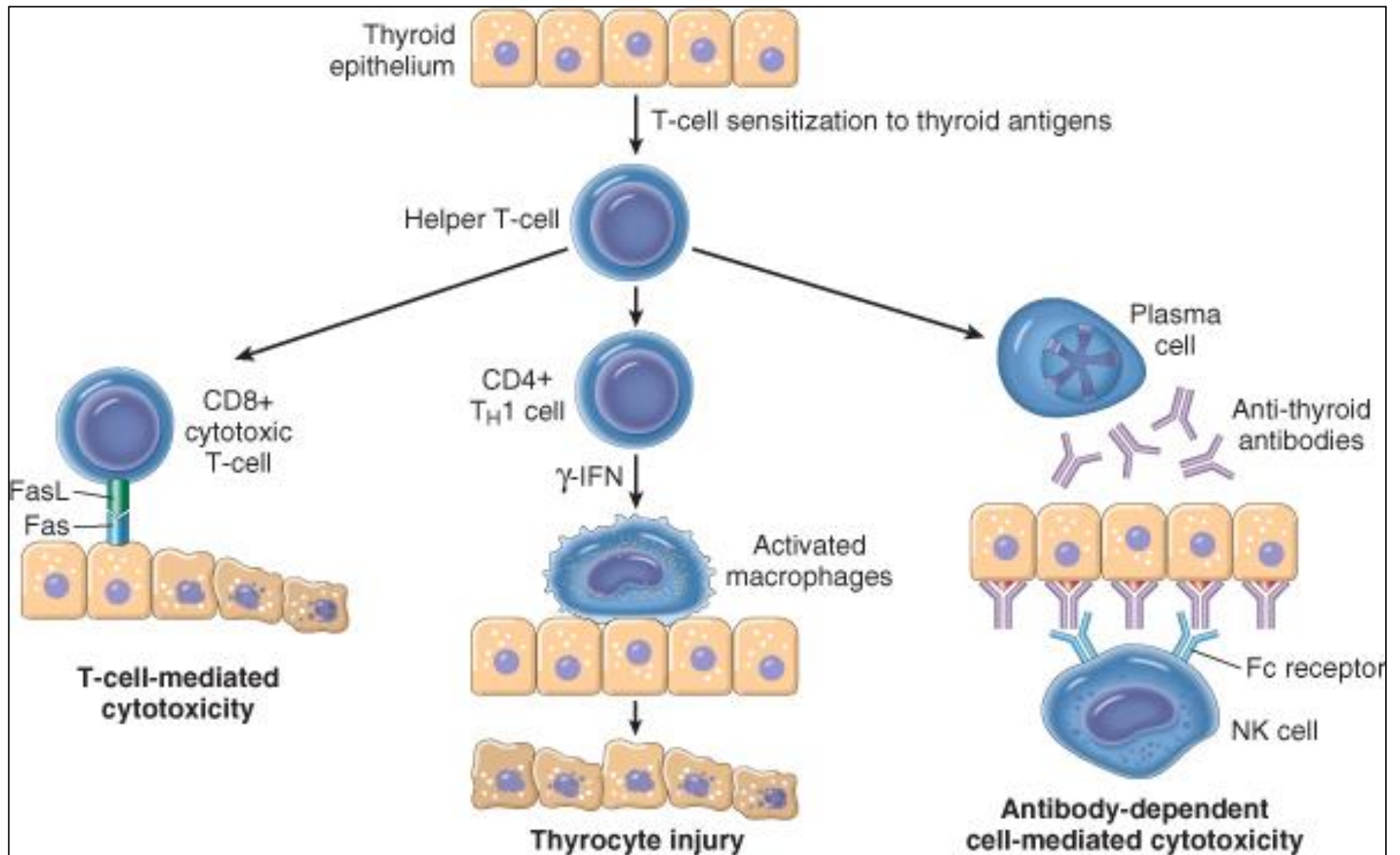
# Features of hypothyroidism and hyperthyroidism





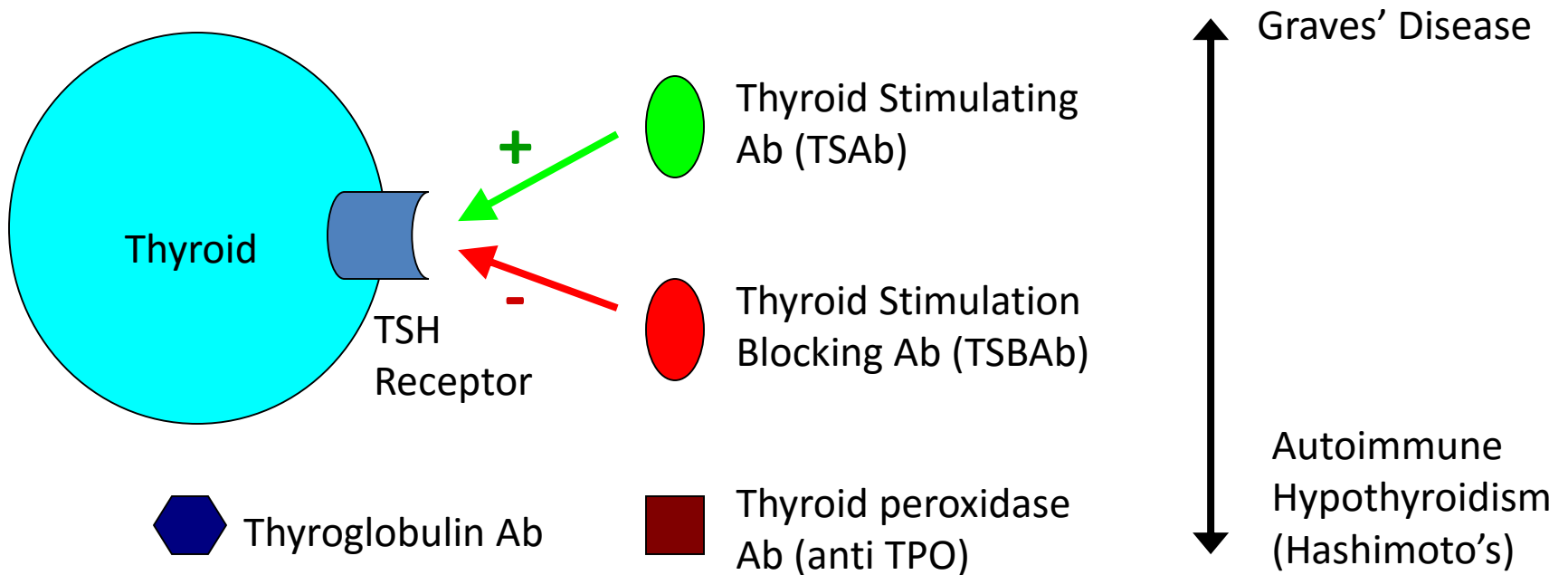
Diffuse infiltration of thyroid stroma

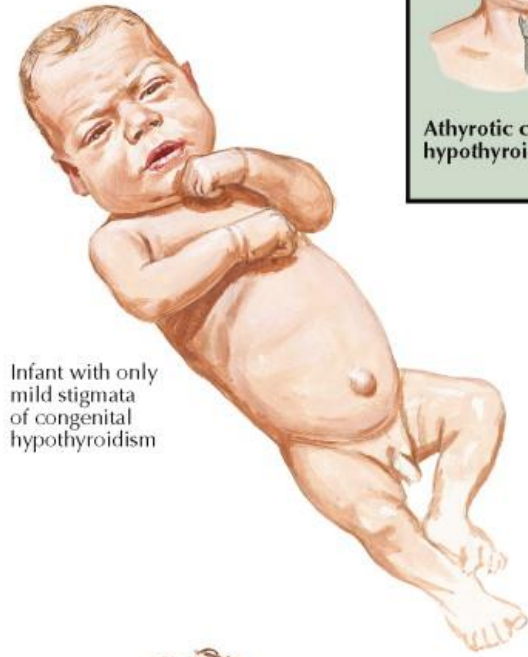
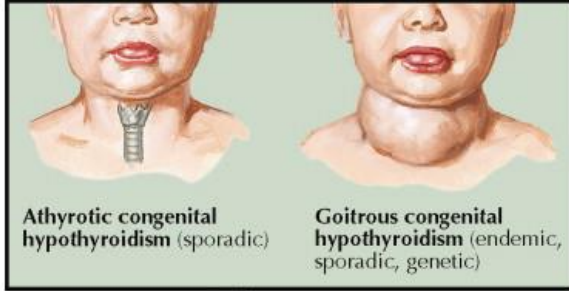
# Hashimoto's disease



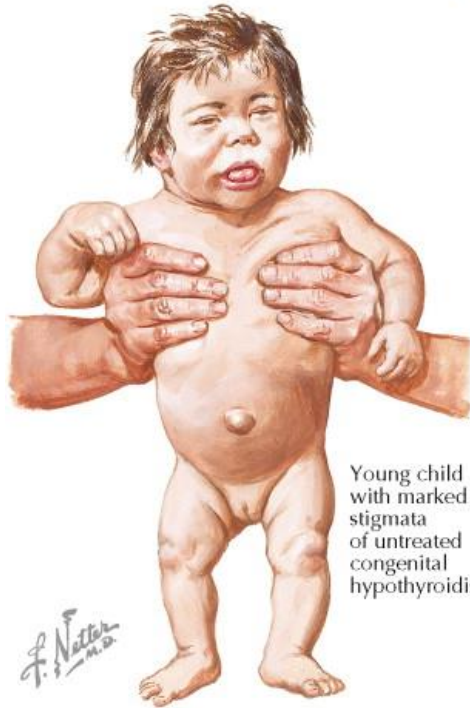
# Pathogenesis

- An autoimmune phenomenon – presentation determined by ratio of antibodies



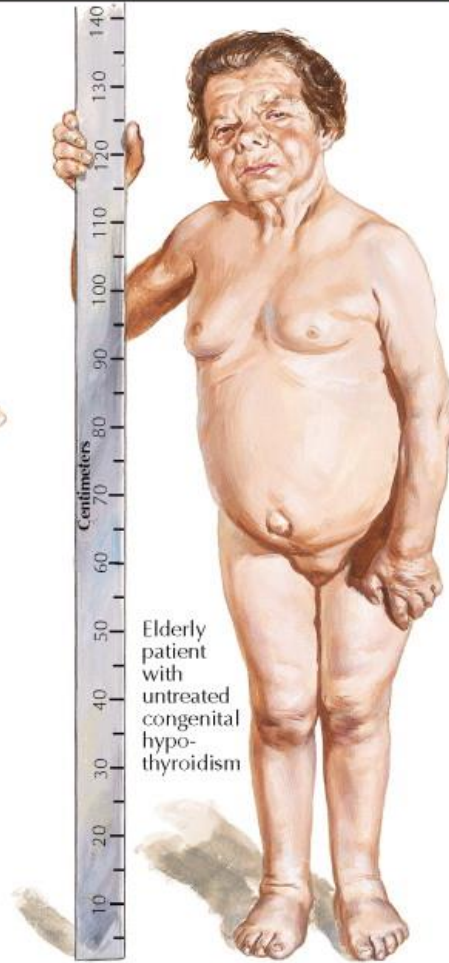


Infant with only mild stigmata of congenital hypothyroidism

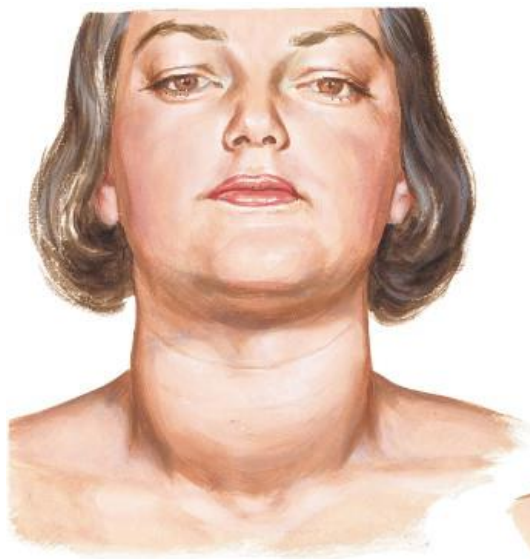


Young child with marked stigmata of untreated congenital hypothyroidism

*F. Netter M.D.*



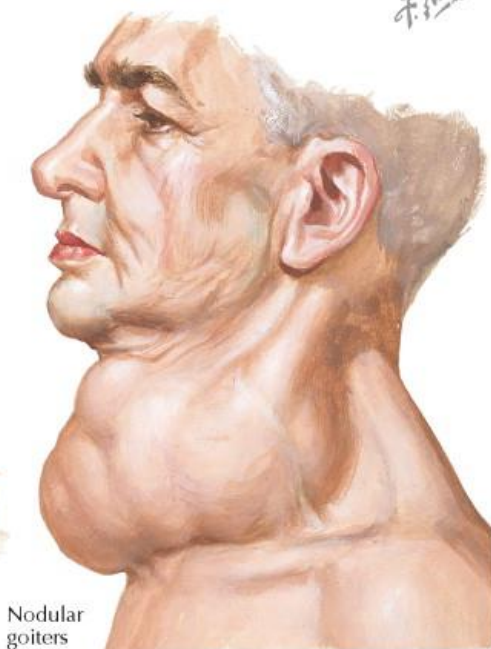
Elderly patient with untreated congenital hypothyroidism



Moderate size nontoxic diffuse goiter

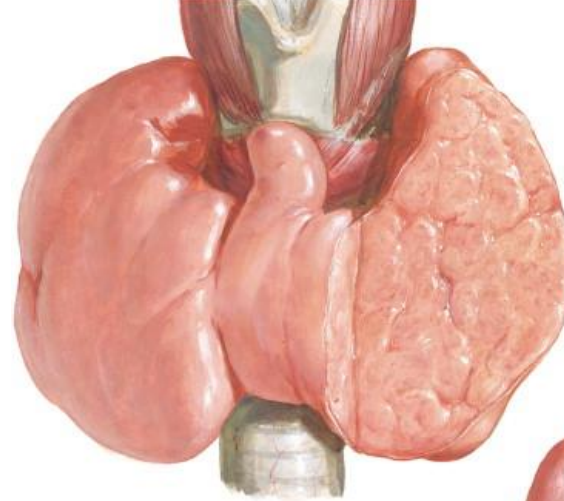


Large diffuse goiter

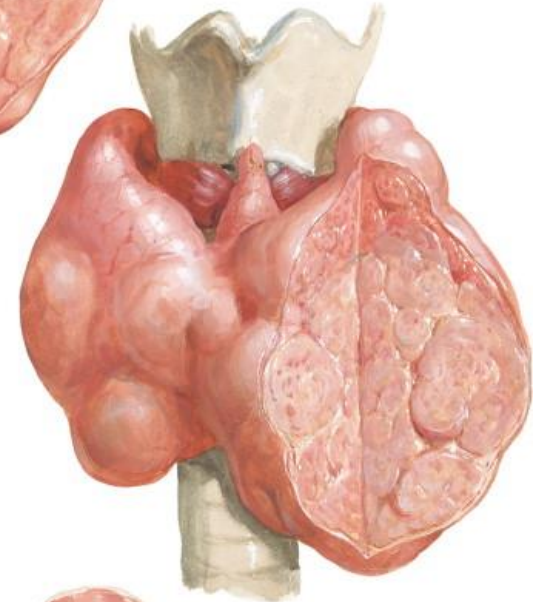


Nodular goiters

- Nodules
  - Hot
  - Warm
  - Cold



Diffuse colloid goiter



Nodular goiter; variation in size and structure of nodules



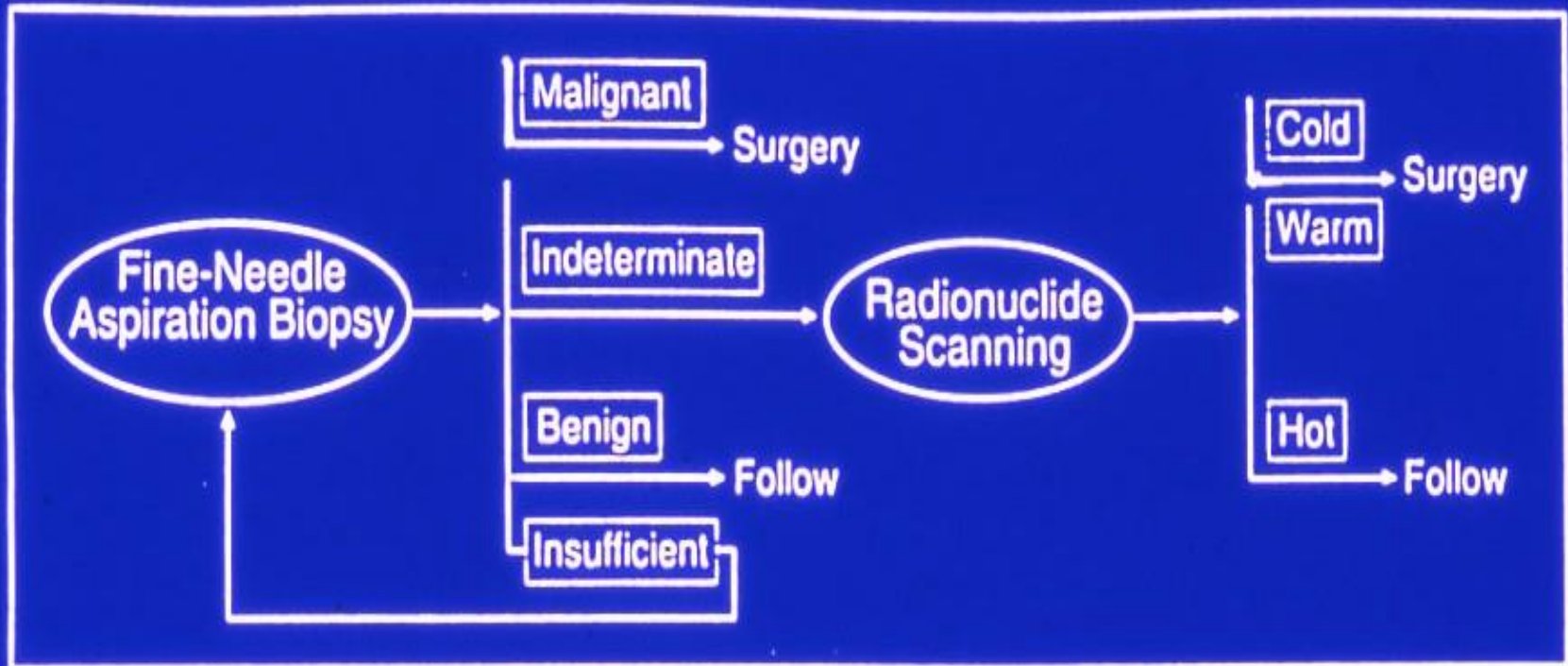
Long-standing nodular goiter with hemorrhages, cyst formation, fibrosis, and calcification

*F. Netter M.D.*



# Diagnostic Imaging

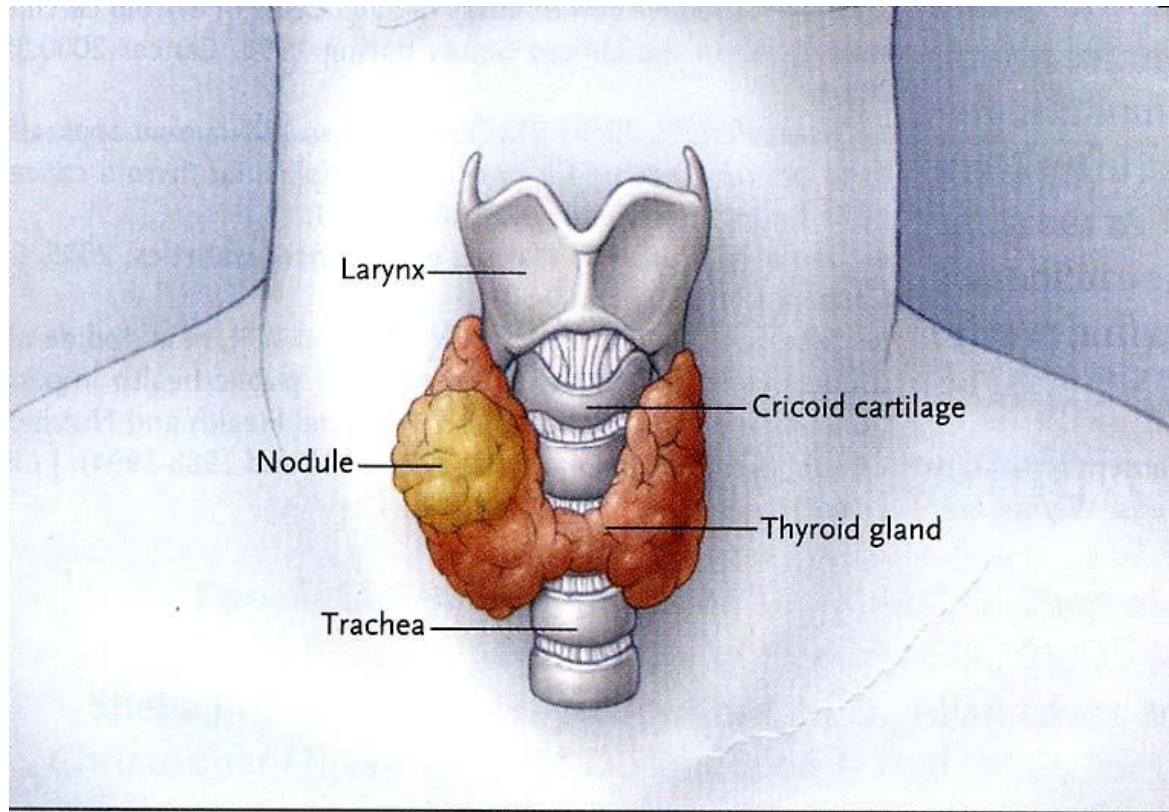
- Radioactive Iodine Uptake
  - quantitative uptake
  - distribution of uptake
- Technetium-99 Pertechnetate Uptake
  - Distinguishes high-uptake from low-uptake
  - Faster scan – only 30 minutes
- Thyroid ultrasonography
  - Identifies nodules
  - Doppler can distinguish high from low-uptake



### Sequence for the Evaluation of Patients with a Thyroid Nodule.

The results of radionuclide scanning are expressed as "hot," "warm," or "cold" to indicate the function of the nodule in relation to the normal thyroid tissue in the patient.

MAZZAFERRI




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**Benign Nodules (95%)**

Hyperplastic nodules (85%)  
 Adenomas (15%)  
 Cysts (<1%)

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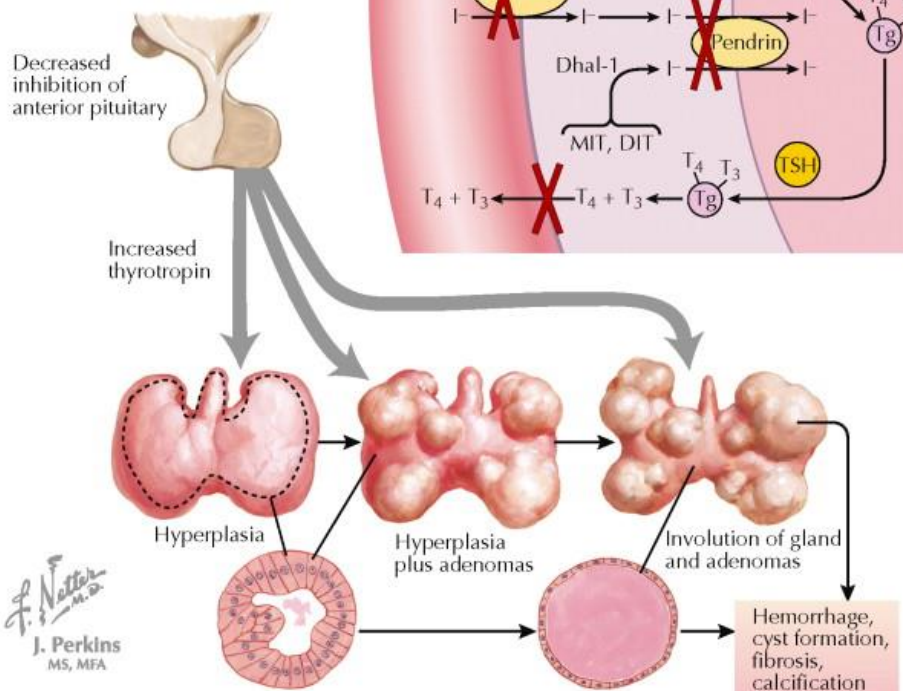
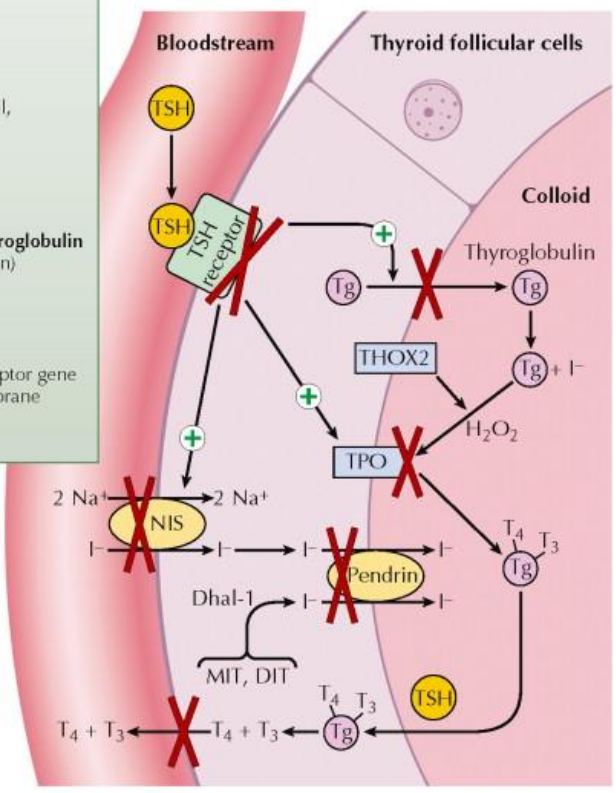
**Carcinomas (5%)**

Papillary (81%)  
 Follicular and Hürthle-cell (14%)  
 Medullary (3%)  
 Anaplastic (2%)

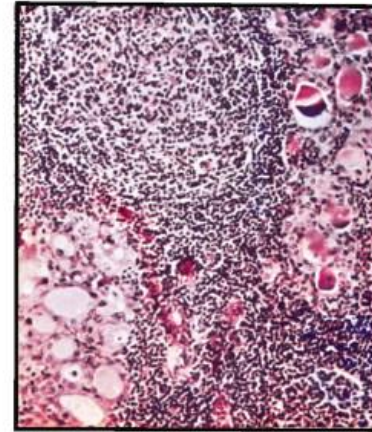
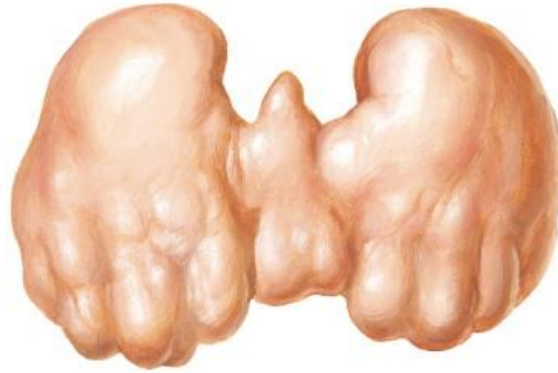
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**Common Varieties of Thyroid Nodules.**

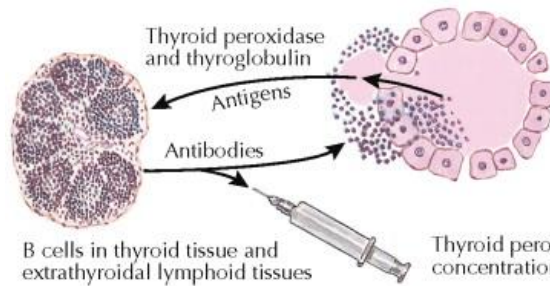
- Etiologic factors of nontoxic goiter**
- Iodine deficiency**
  - Nutritional
- Thyrotropin (TSH) receptor dysfunction**
  - TSH receptor mutations
- Block of sodium-iodide symporter (NIS)**
  - Iodine
  - Thiocyanate (e.g., millet, cassava)
  - Perchlorate
  - NIS gene mutations
- Pendrin dysfunction**
  - Pendred syndrome
- Inhibition of thyroid peroxidase (TPO)**
  - Antithyroid drugs (e.g., propylthiouracil, methimazole, carbimazole)
  - Thiourea
  - Phenols
  - Babassu coconut
  - TPO gene mutations
- Inhibition of synthesis and function of thyroglobulin**
  - Bacterial pollution (progoitrin activation)
  - Tg gene mutations
- Inhibition of release of thyroid hormones**
  - Iodine (e.g., seaweed)
- Reduced sensitivity to thyroid hormone**
  - Mutations in the thyroid hormone receptor gene
  - Defects in thyroid hormone transmembrane transporters
  - Defects in deiodinases



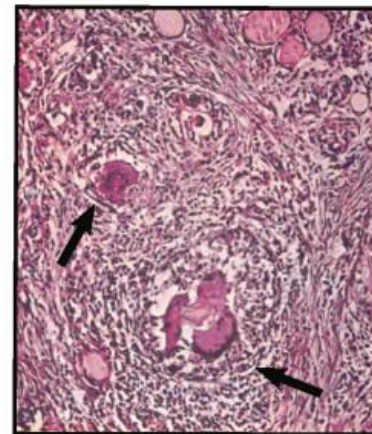
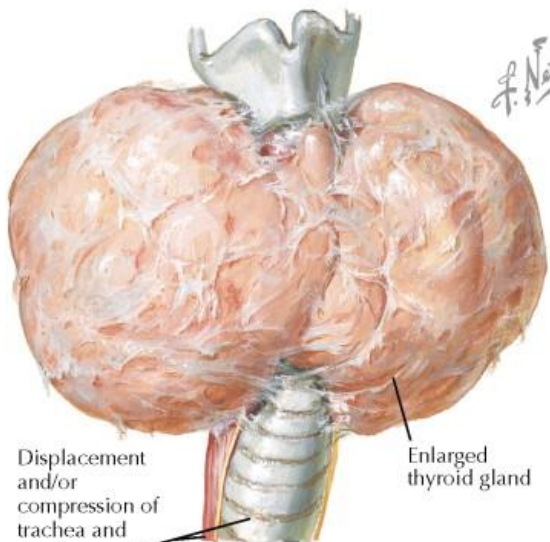
**Hashimoto thyroiditis**



**Microscopy of Hashimoto Thyroiditis**  
Mixture of hyperplastic and atrophic follicles with diffuse lymphocytic infiltration

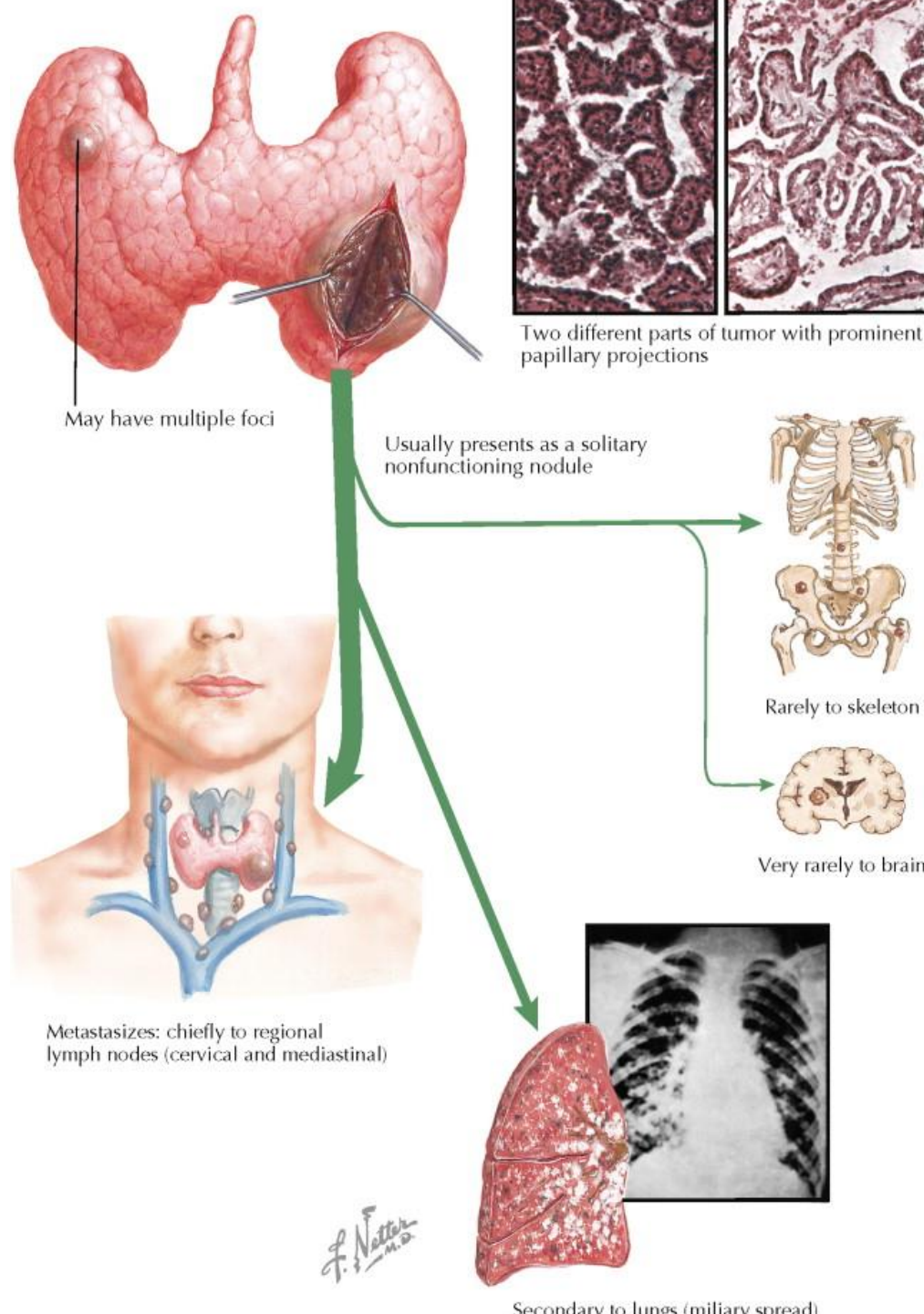


**Riedel thyroiditis**

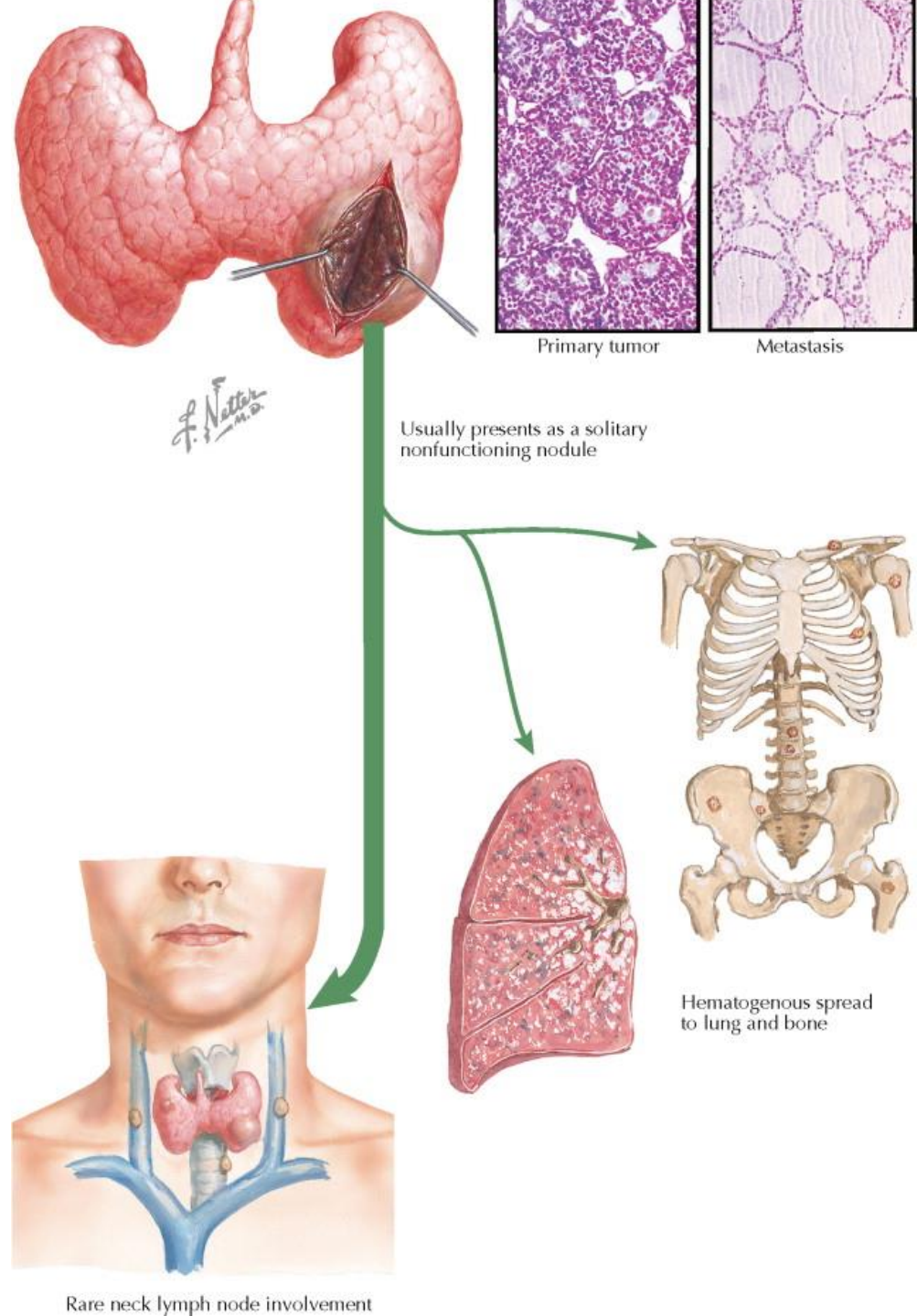


**Microscopy of Riedel Thyroiditis**  
Macrophage and eosinophilic infiltration with atrophy of follicles (arrows) and marked diffuse fibrosis

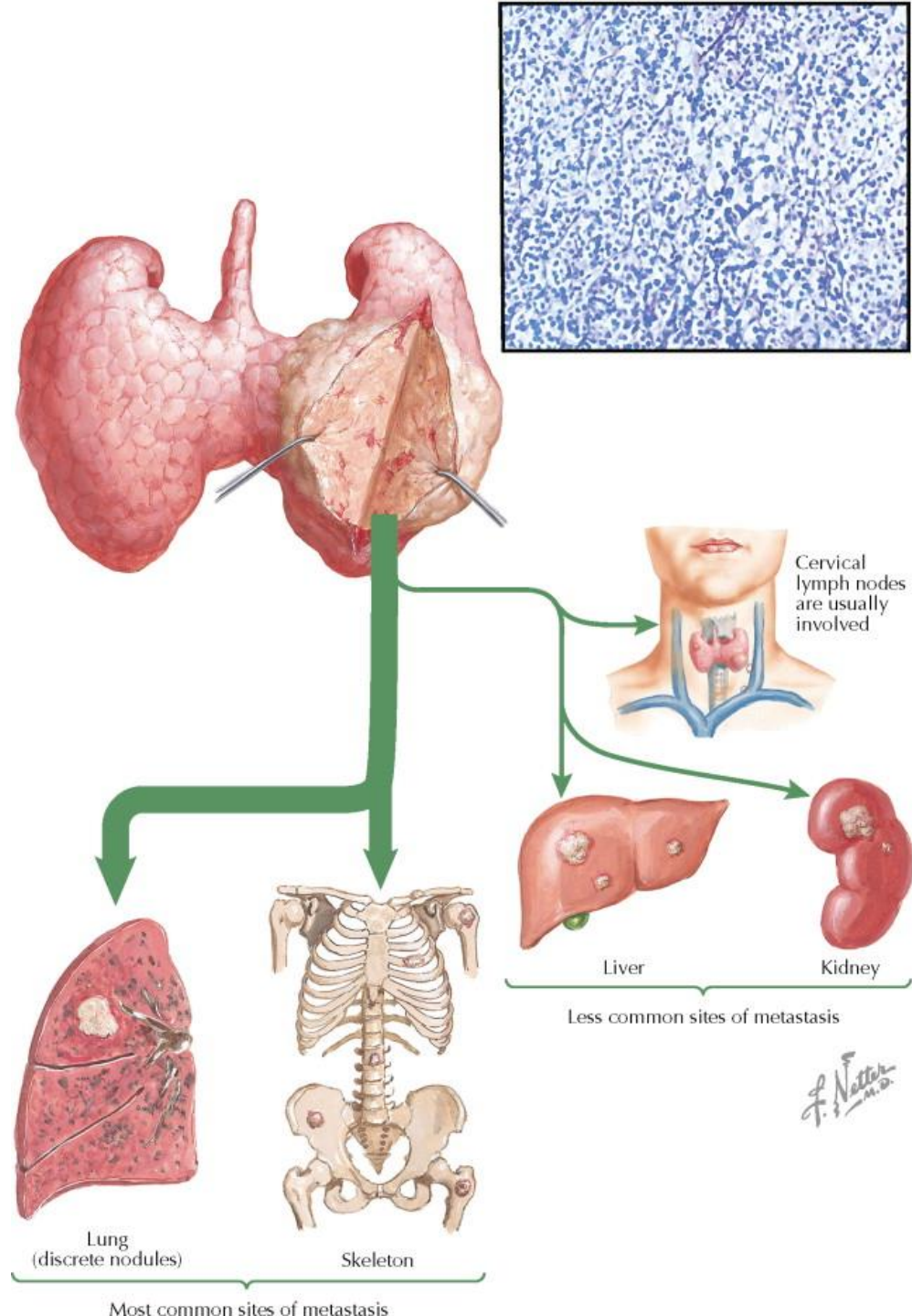
# Papillary TC



# Follicular TC

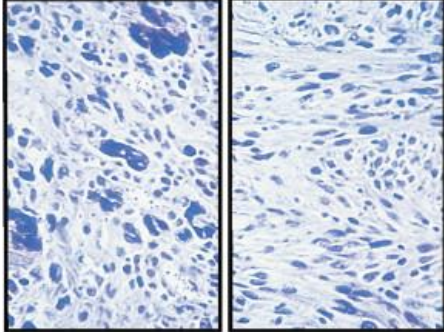
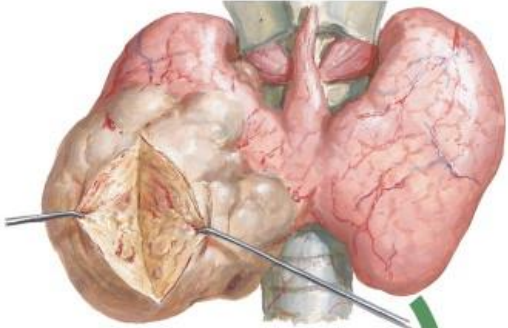


# Medullary TC



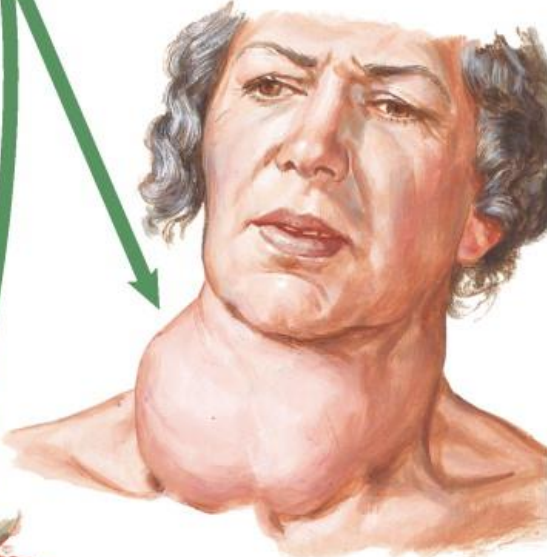


# Anaplastic TC

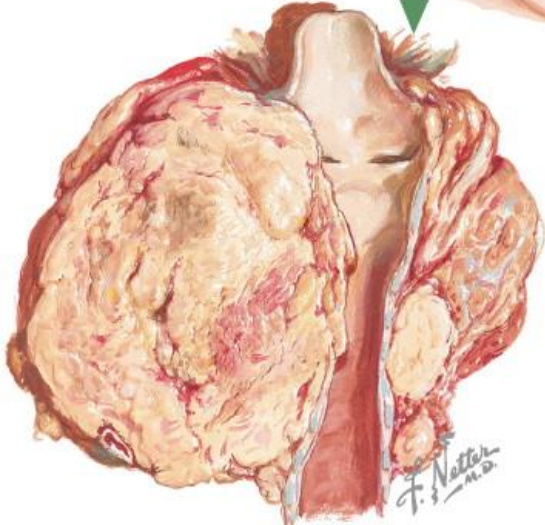


Giant cells

Spindle cells



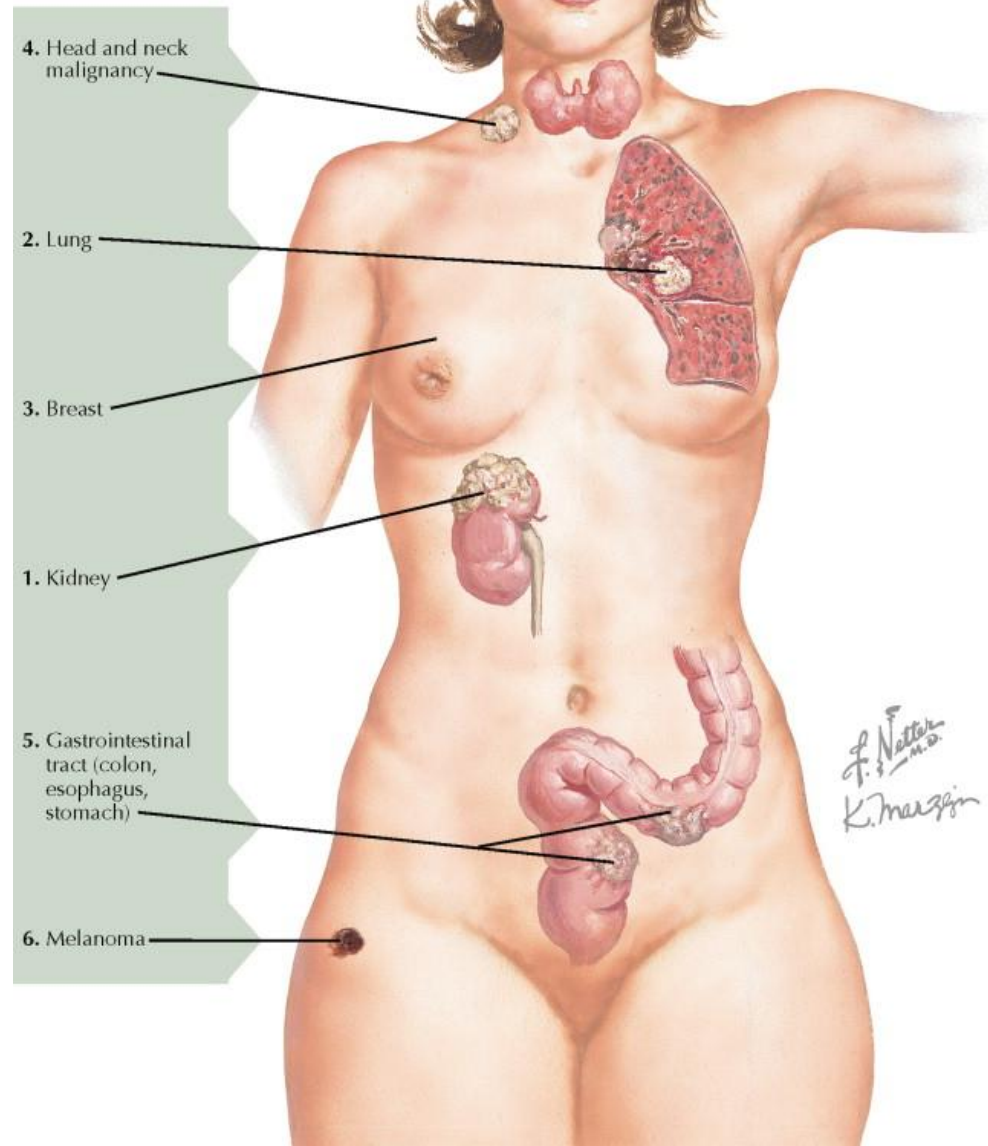
Rapidly growing tender tumor of neck



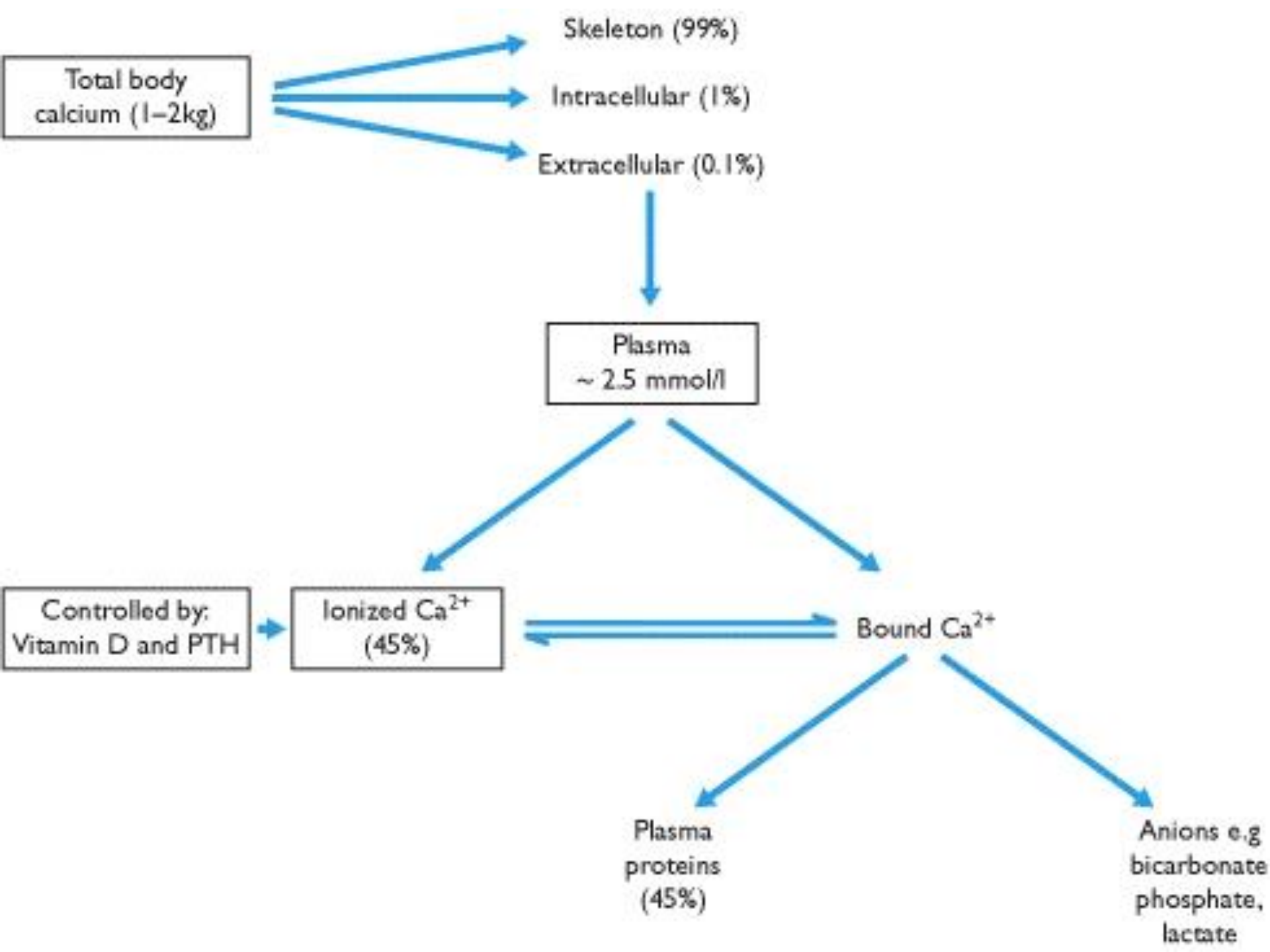
Compression and invasion of trachea

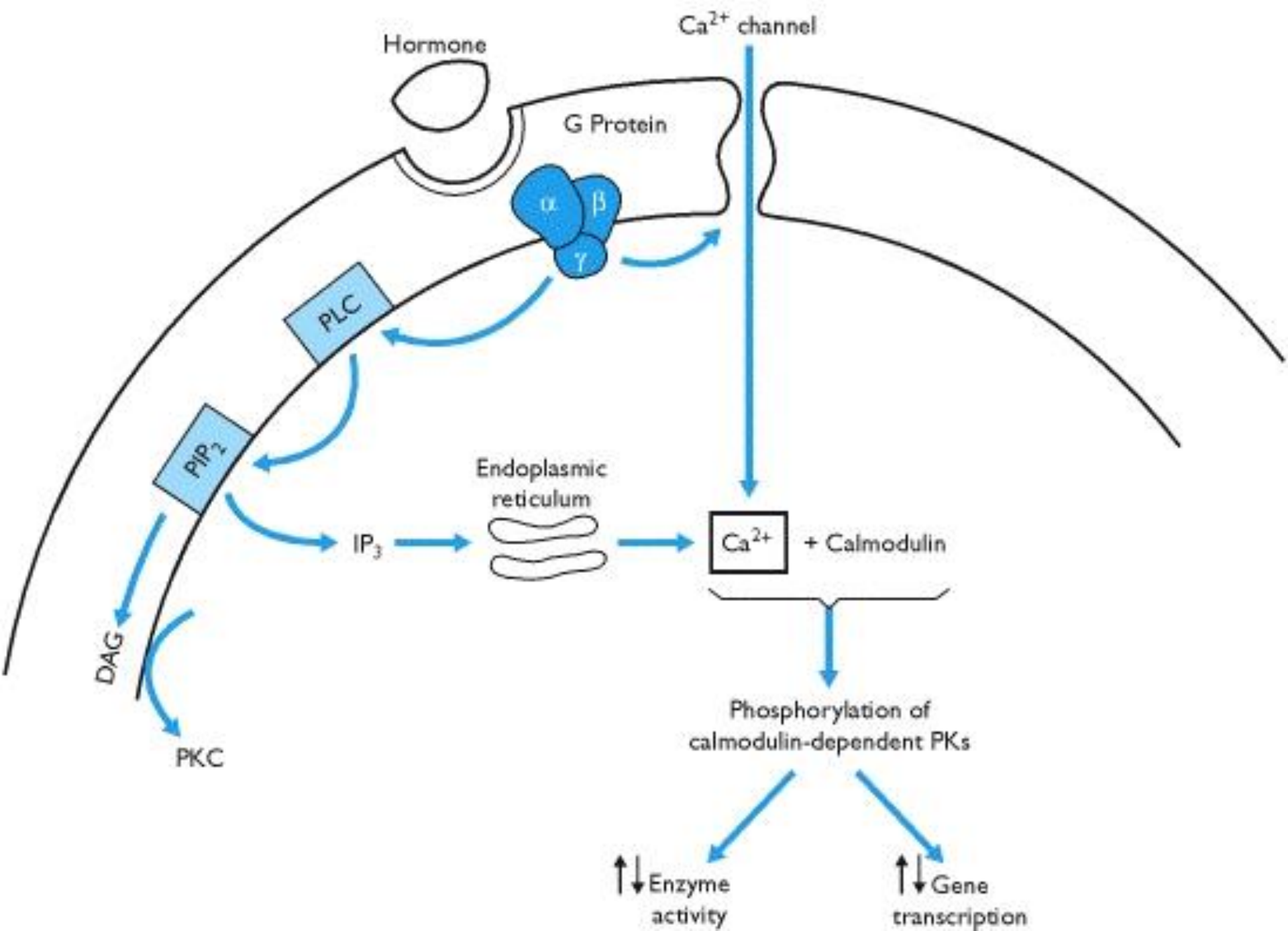
*F. Netter M.D.*

# MTS to the thyroid

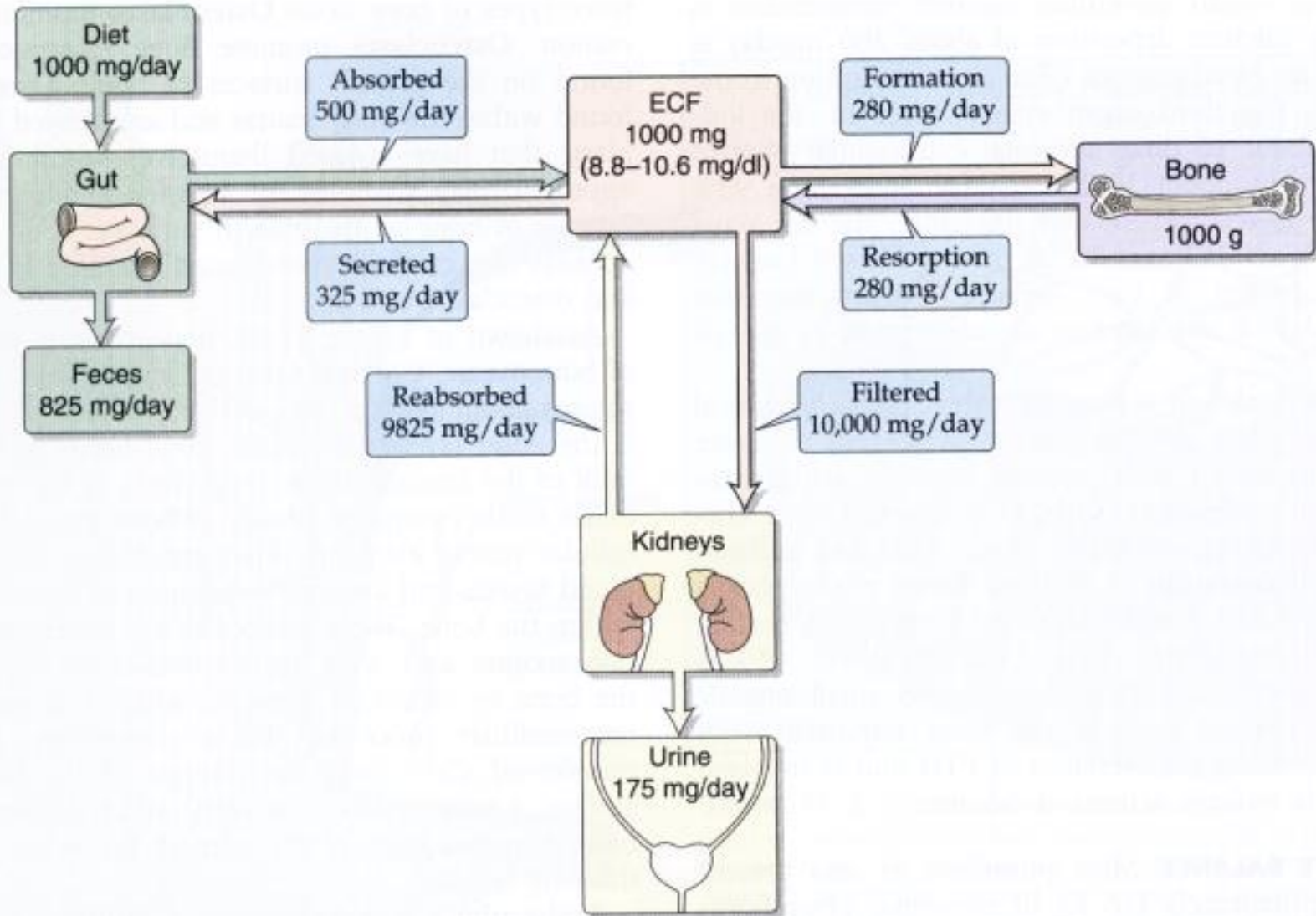


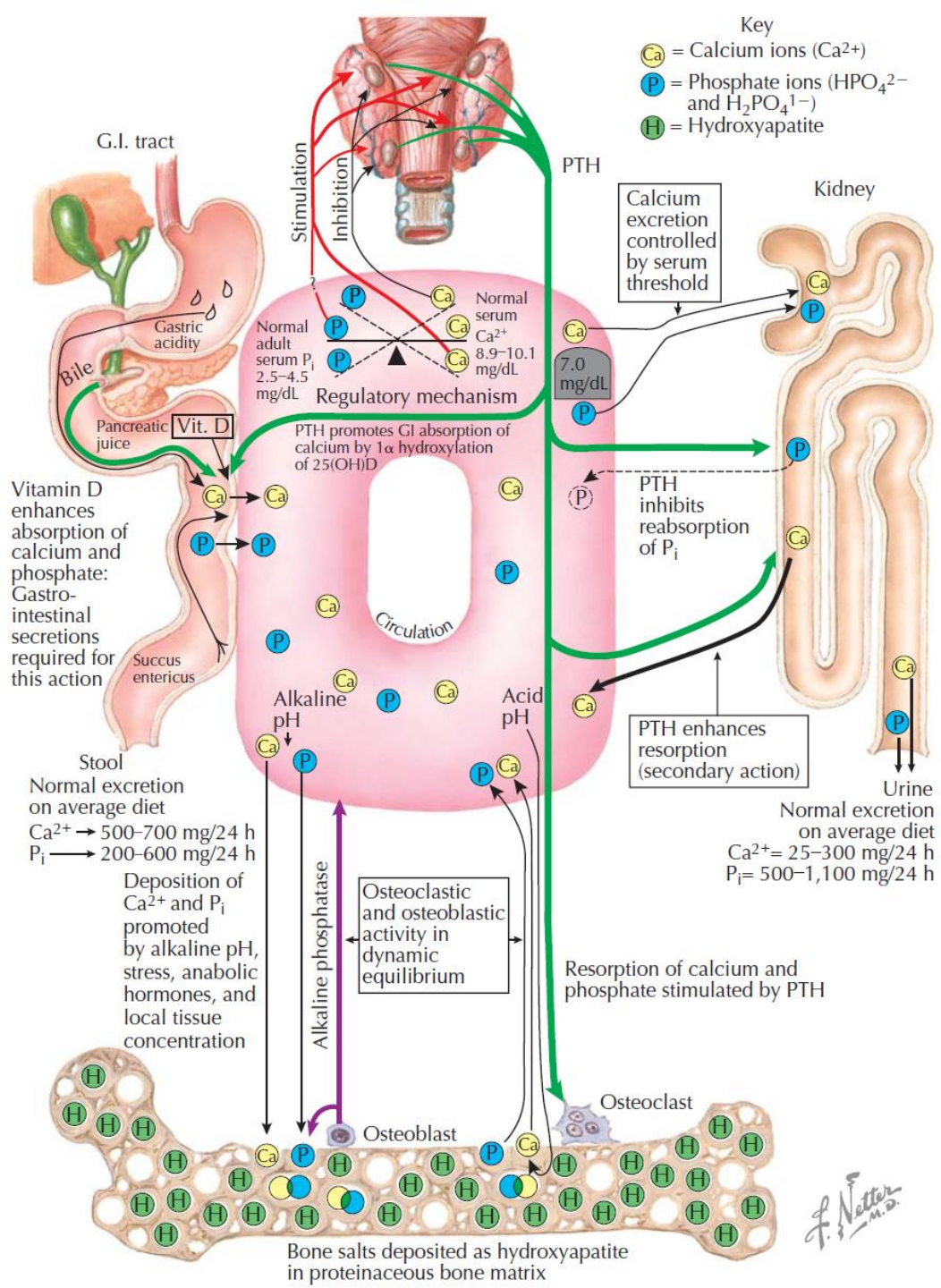
Calcium



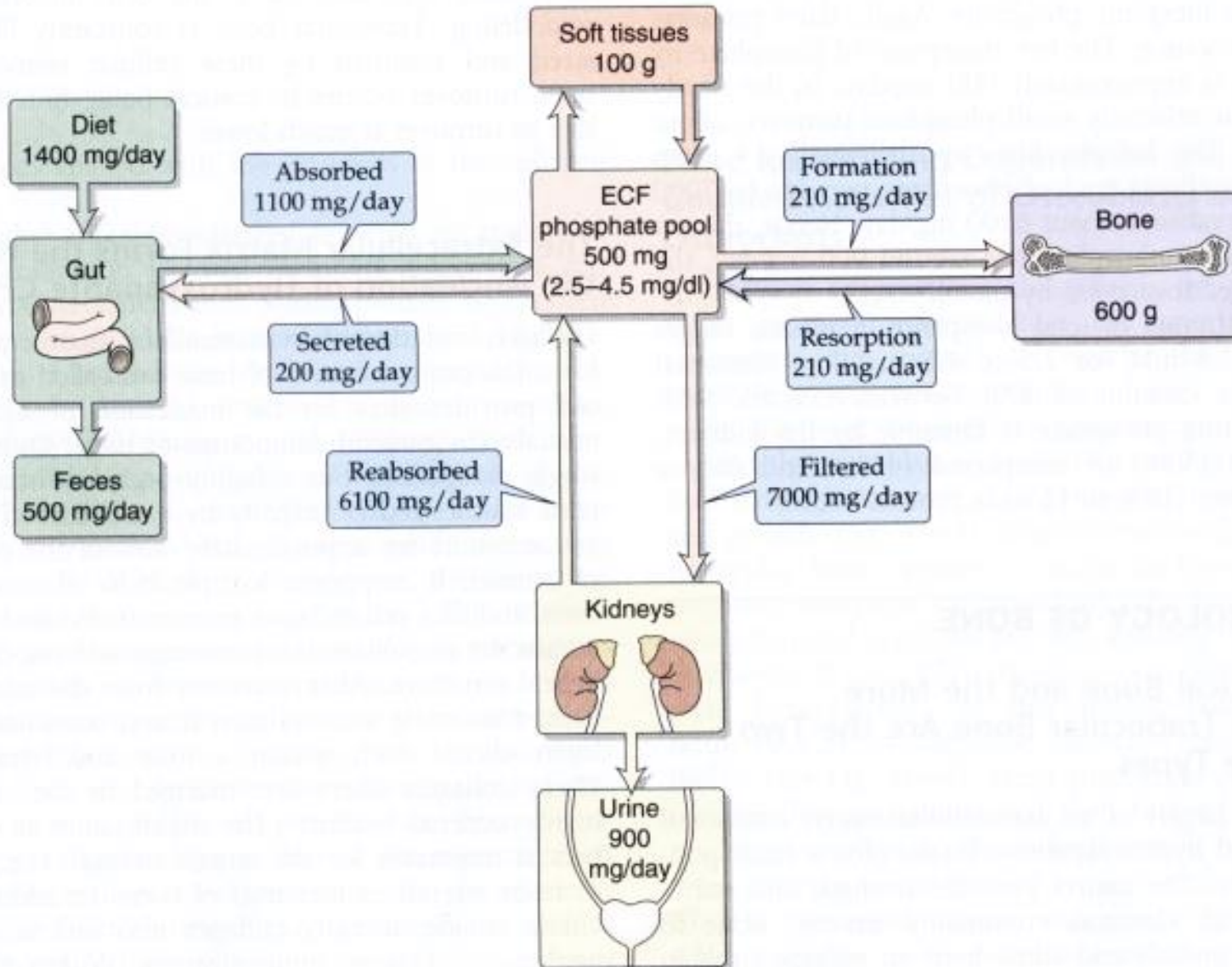


# Calcium

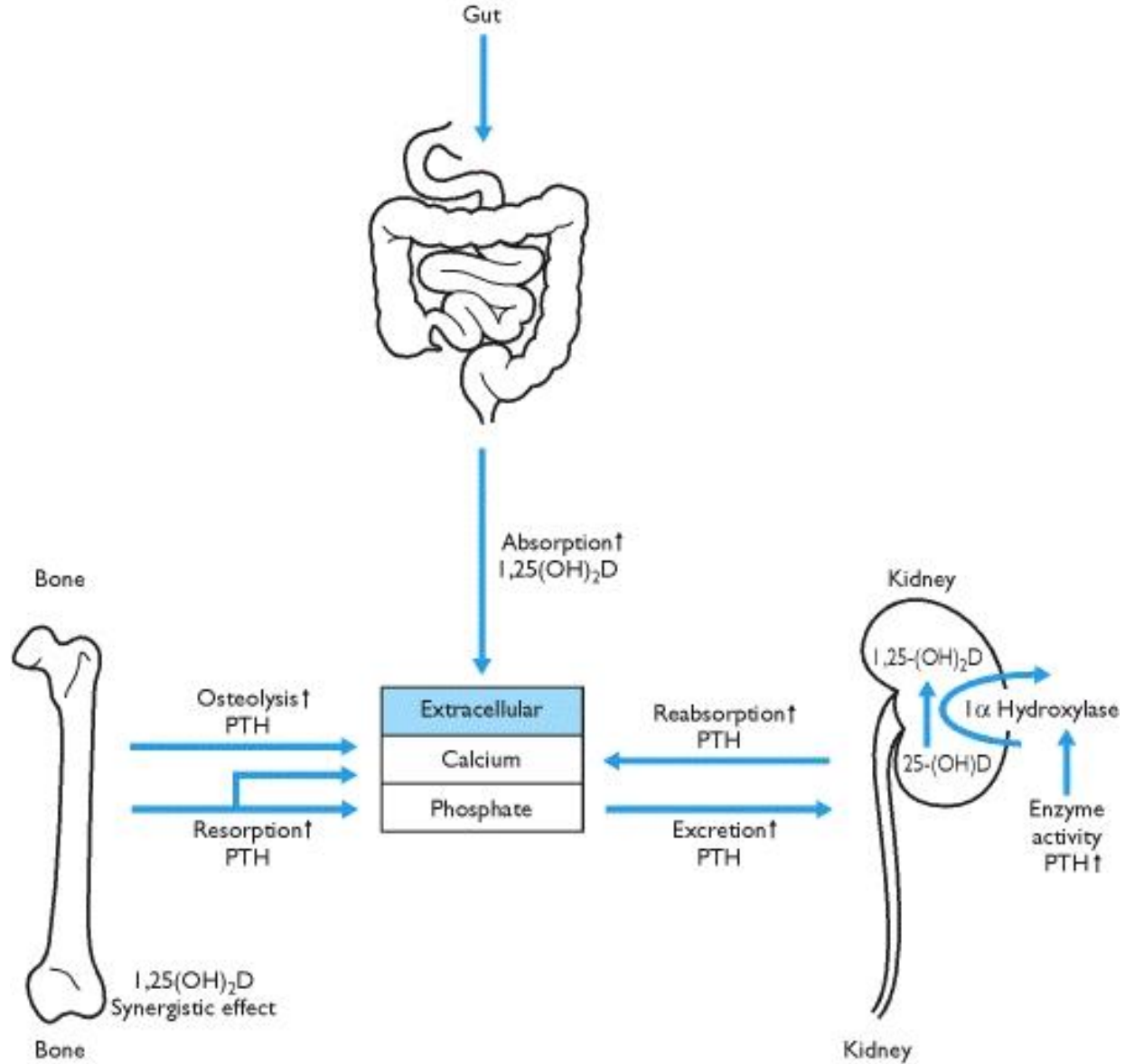




# Phosphate



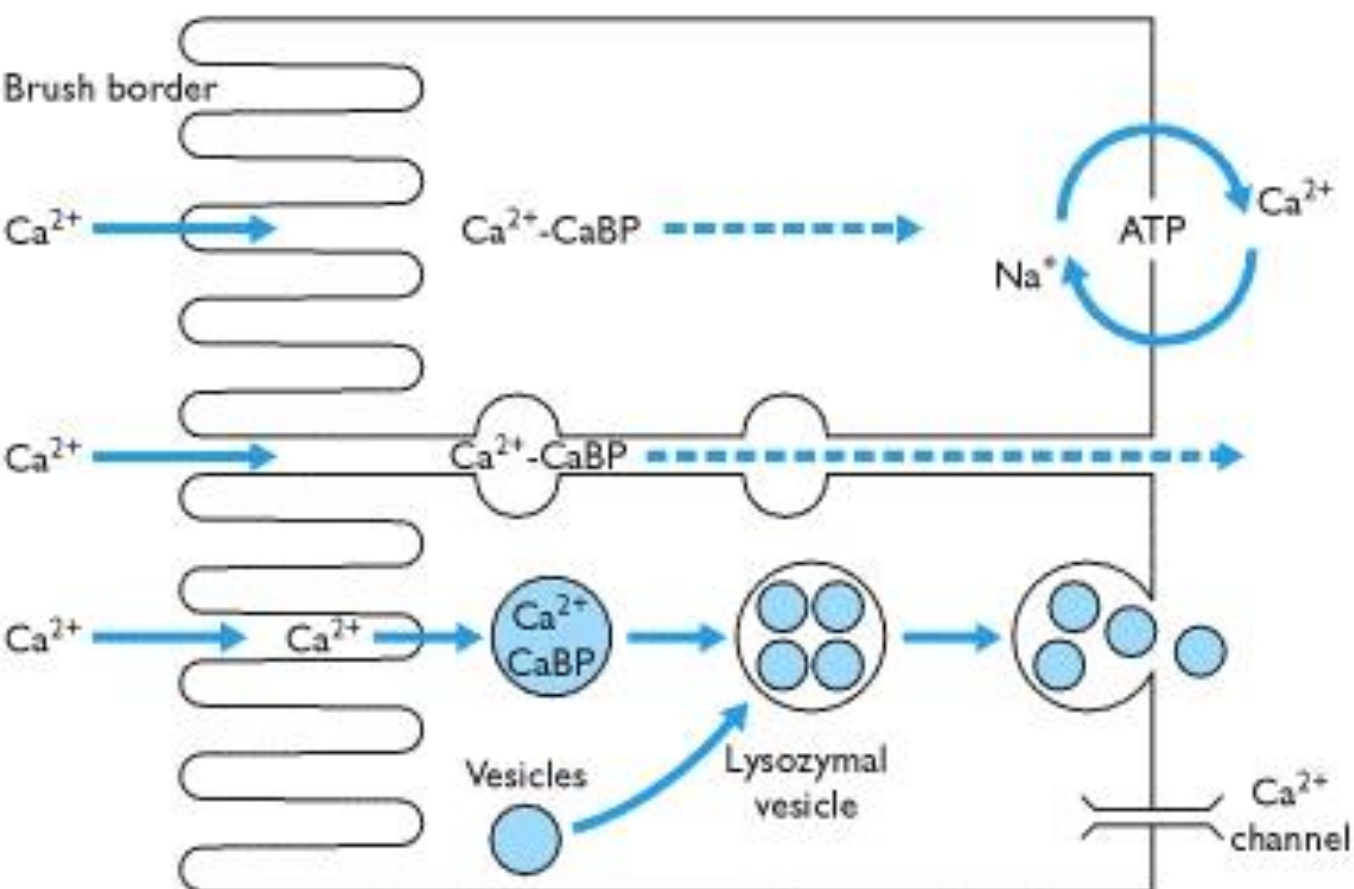




Hormone	Effect	Control
PTH	↑ Calcium ↓ phosphate	↓ Ca <sup>2+</sup>
Vitamin D	↑ Calcium ↓ phosphate	↓ Phosphate
		↑ PTH

Luminal surface

Basolateral surface



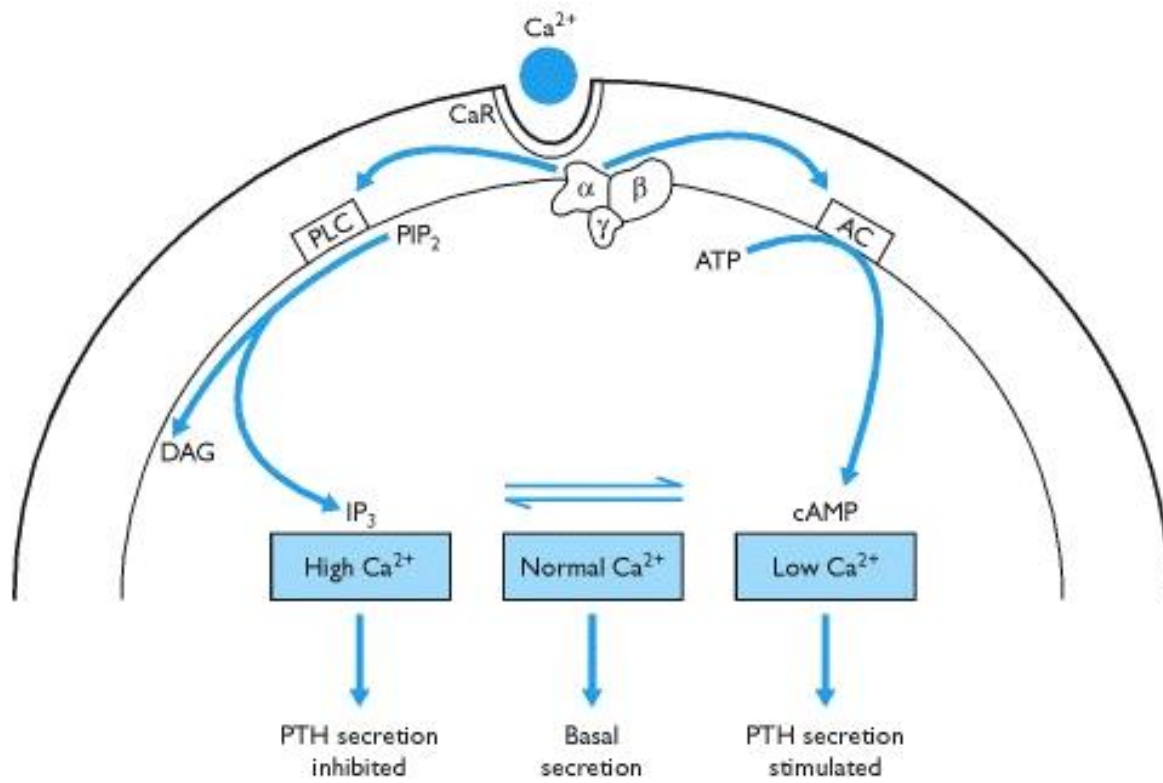
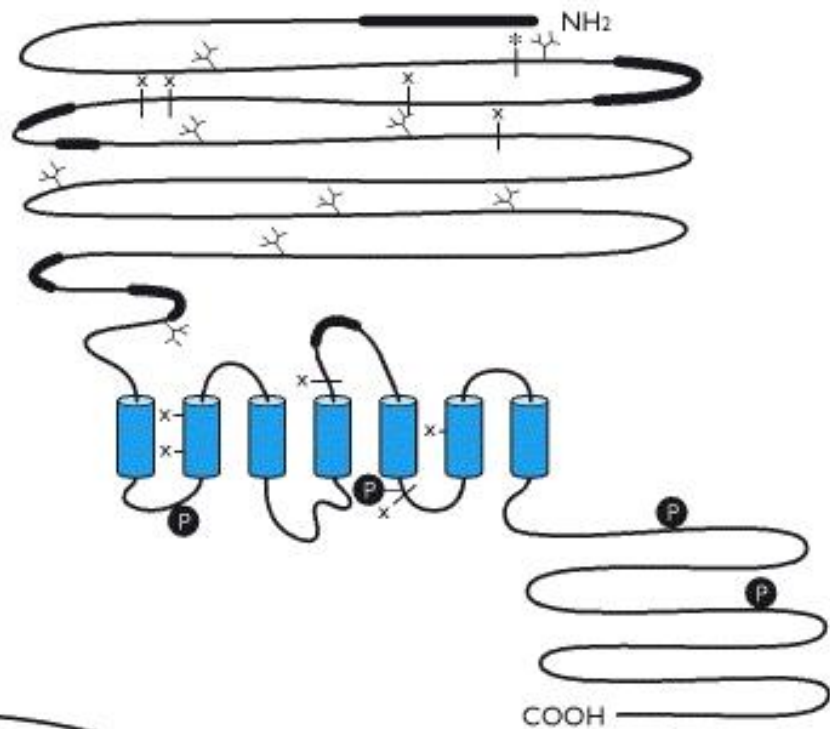
① Active uptake and extrusion of  $\text{Ca}^{2+}$  ions

② Transcellular transport

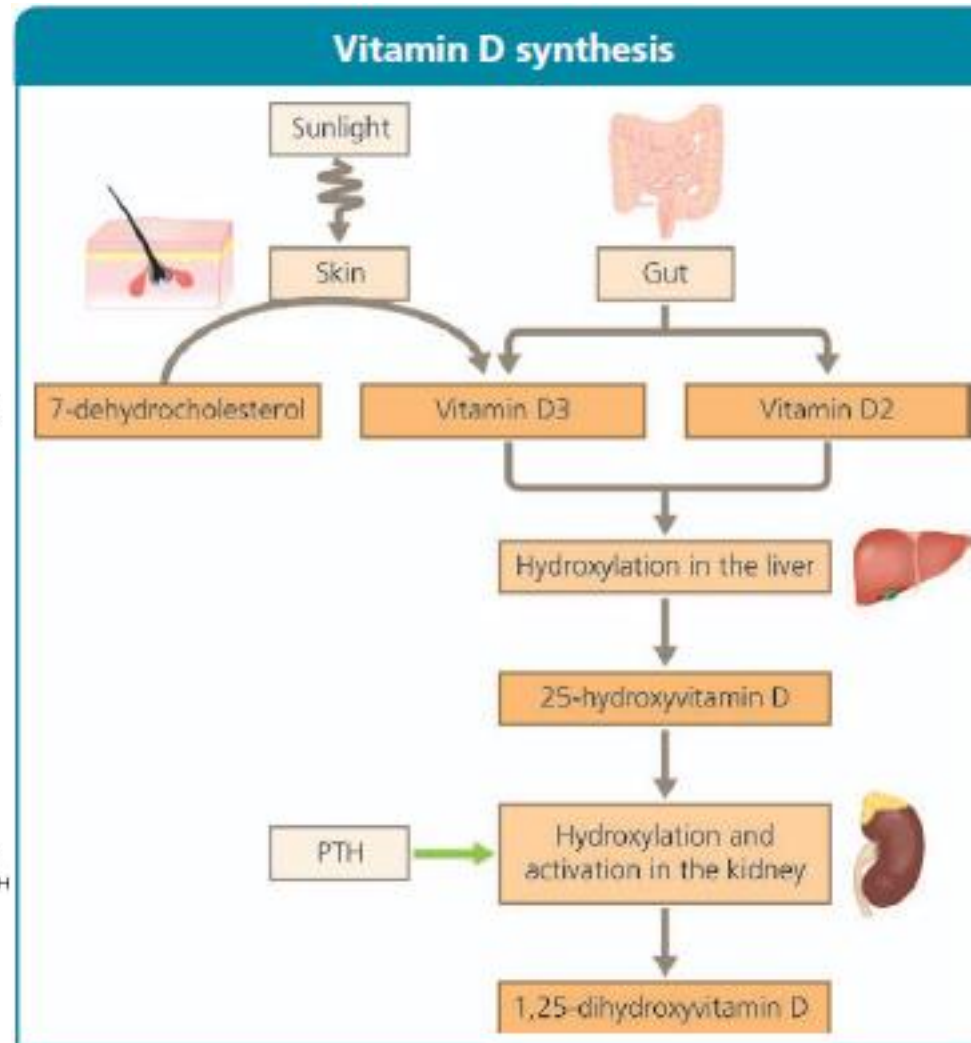
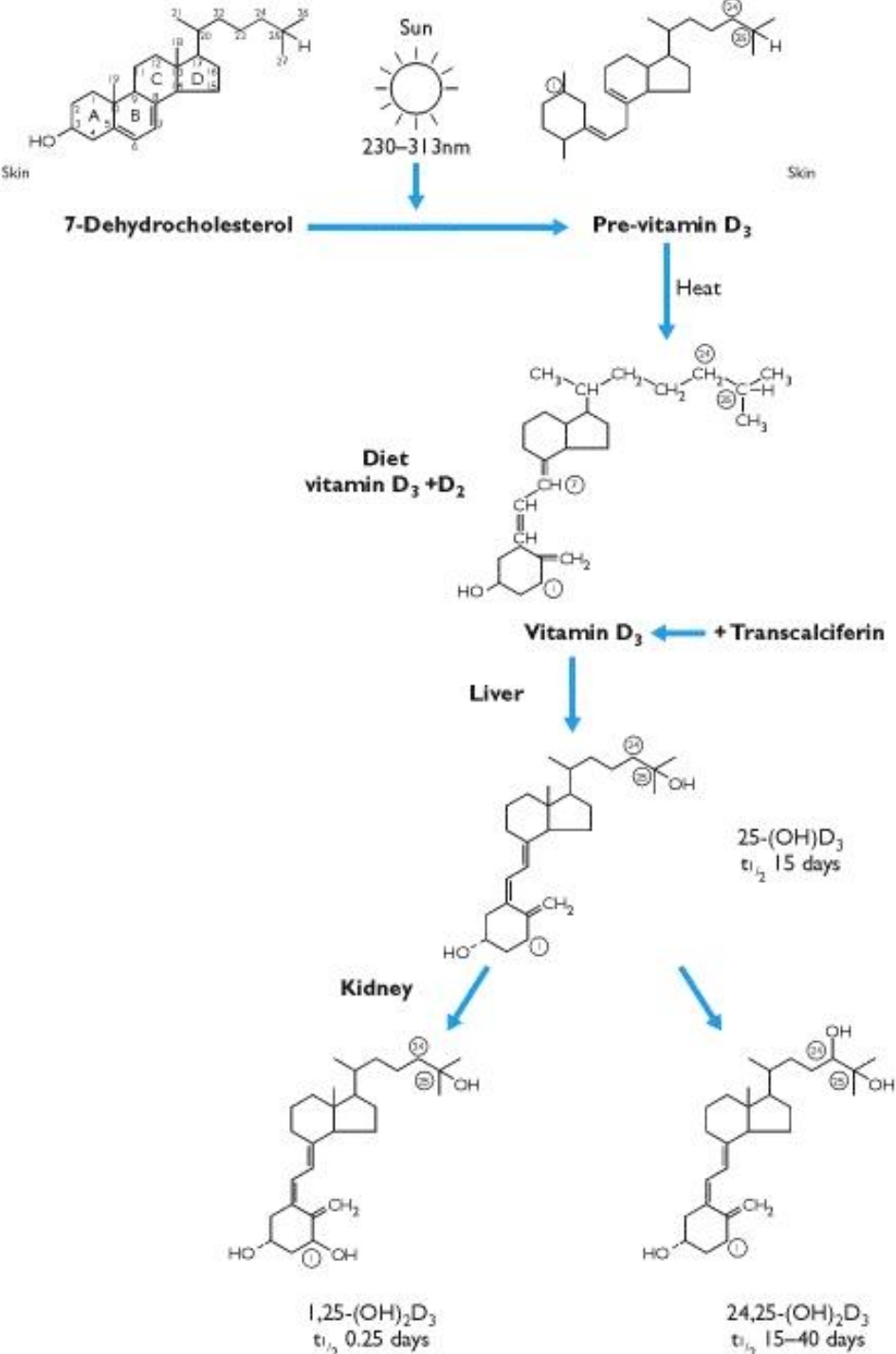
③ Endocytosis and exocytosis of  $\text{Ca}^{2+}$ -CaBP complex

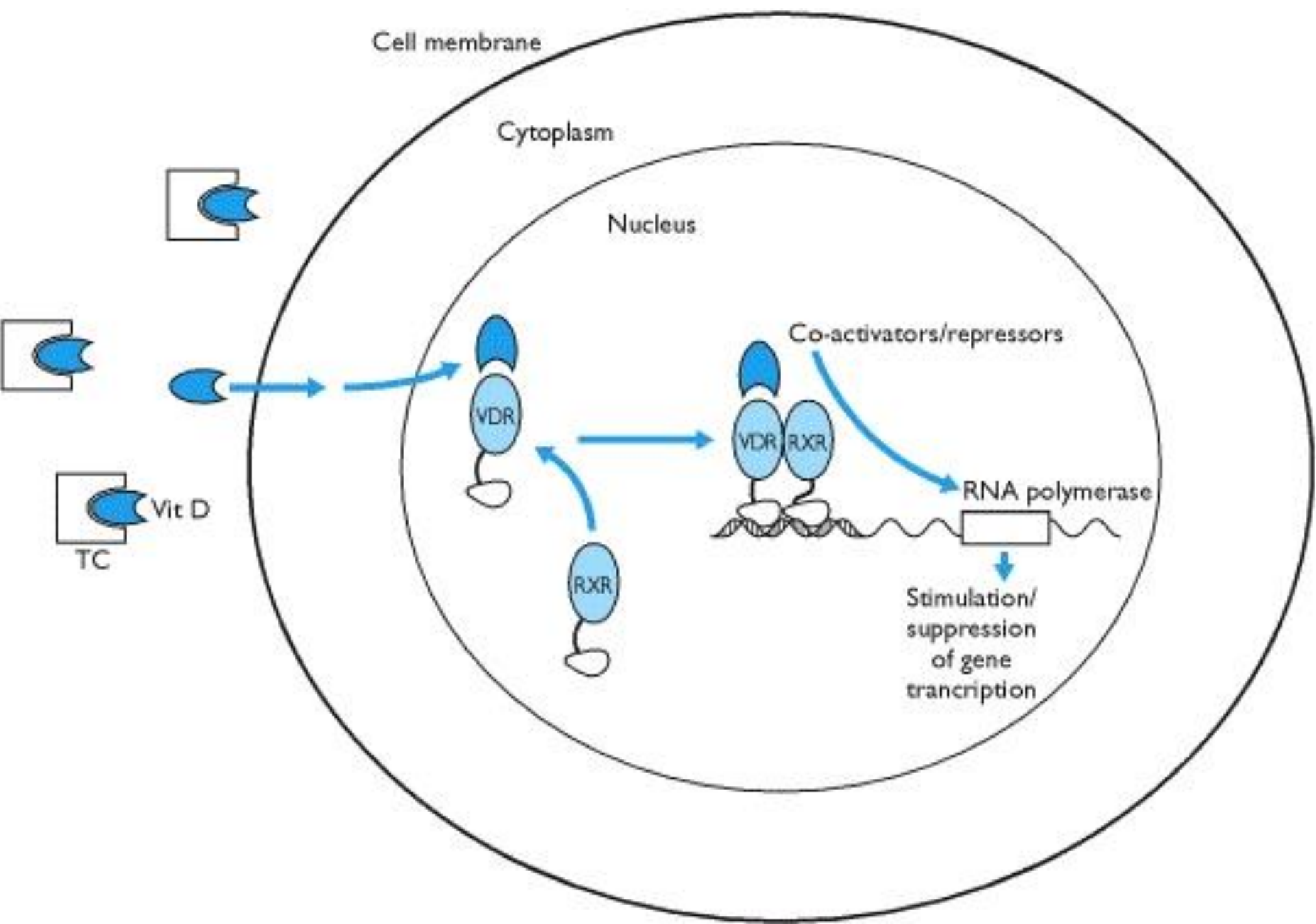
## Structural features of the $\text{Ca}^{2+}$ receptor

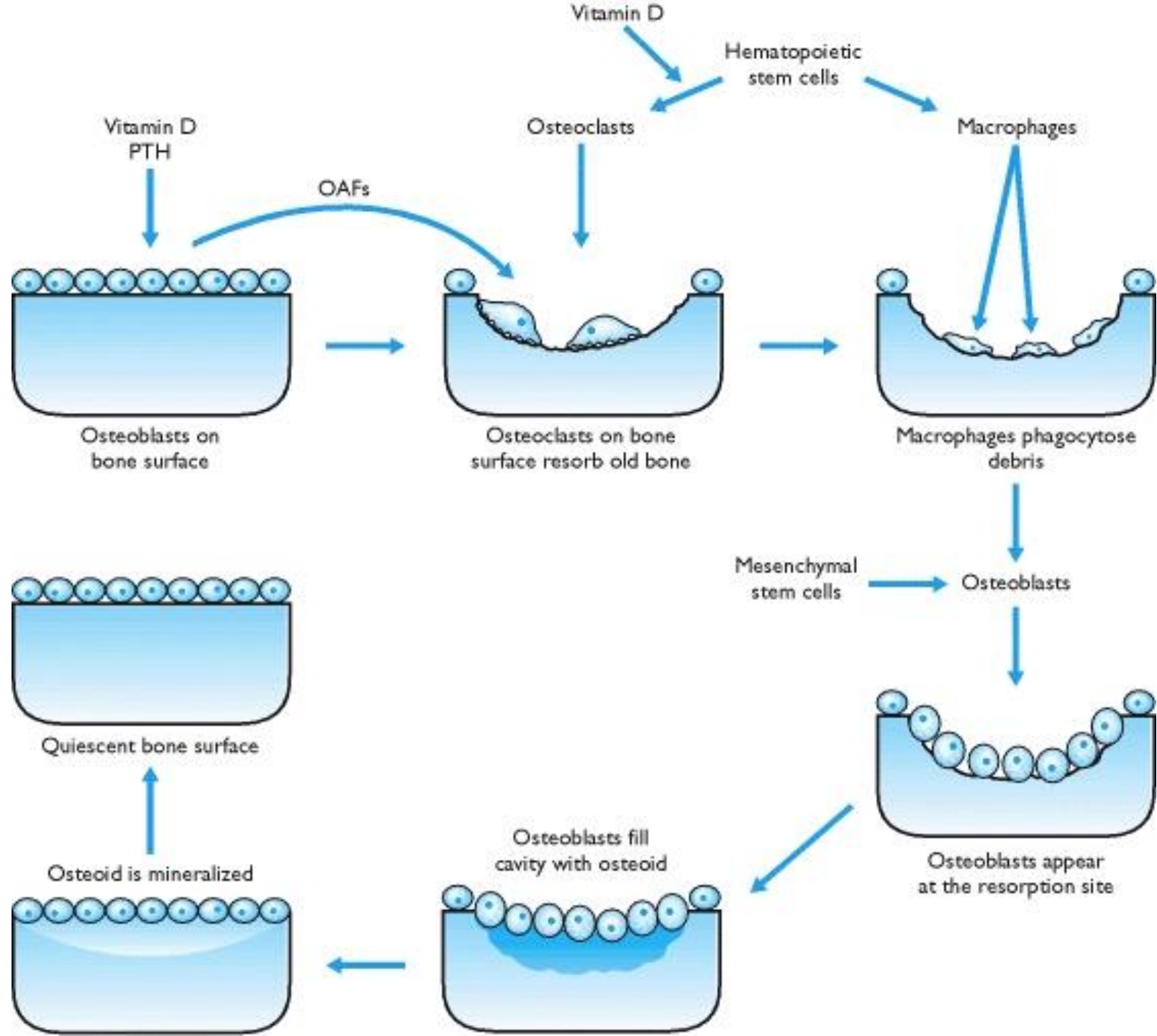
- P Protein kinase C phosphorylation sites
- x Location of inactivating mutations of the receptor
- \* Location of activating mutations of the receptor
- X Glycosylation sites



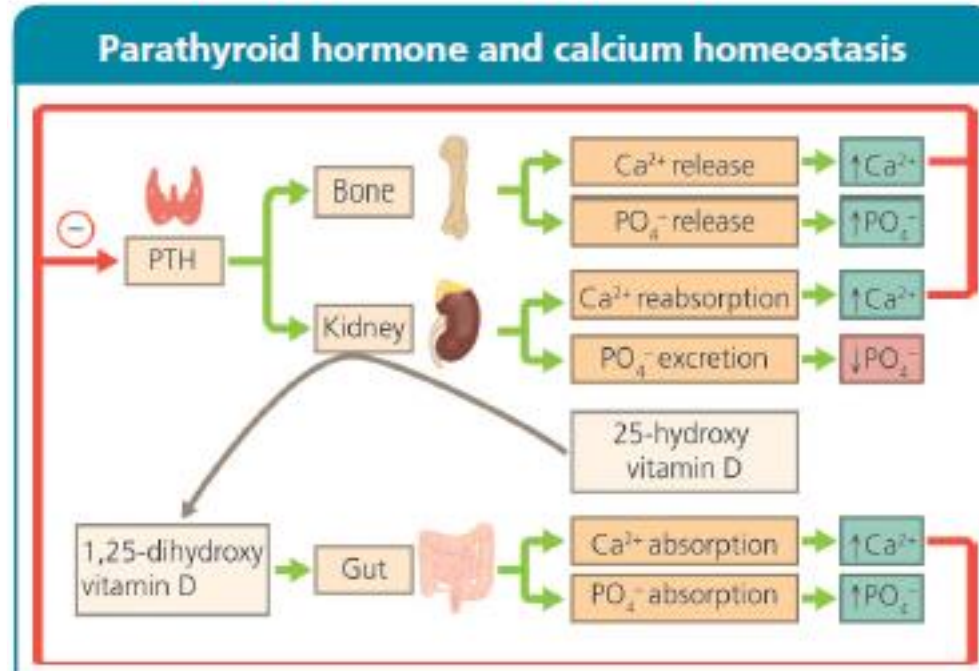
# Vitamin D







# Parathyroid hormone

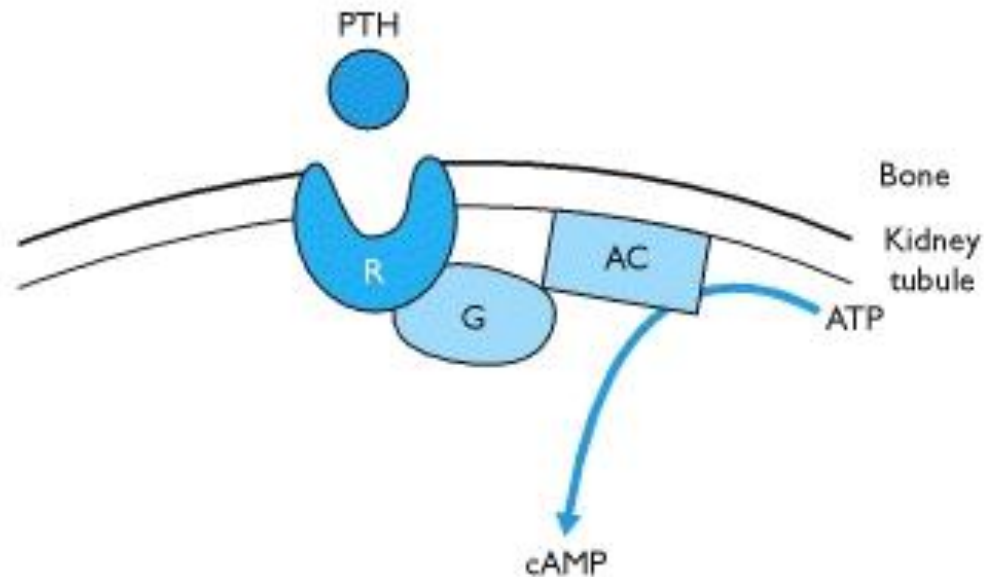




# Parathyroid hormone

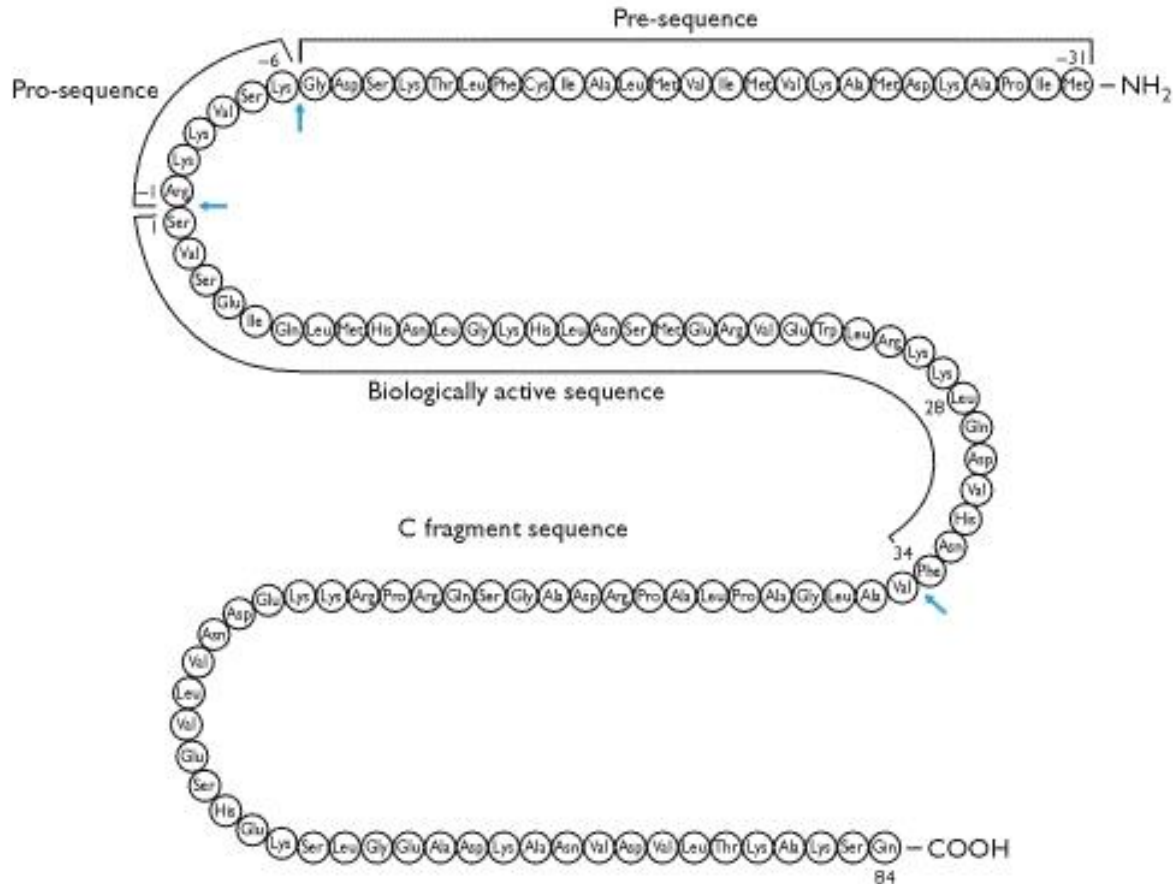
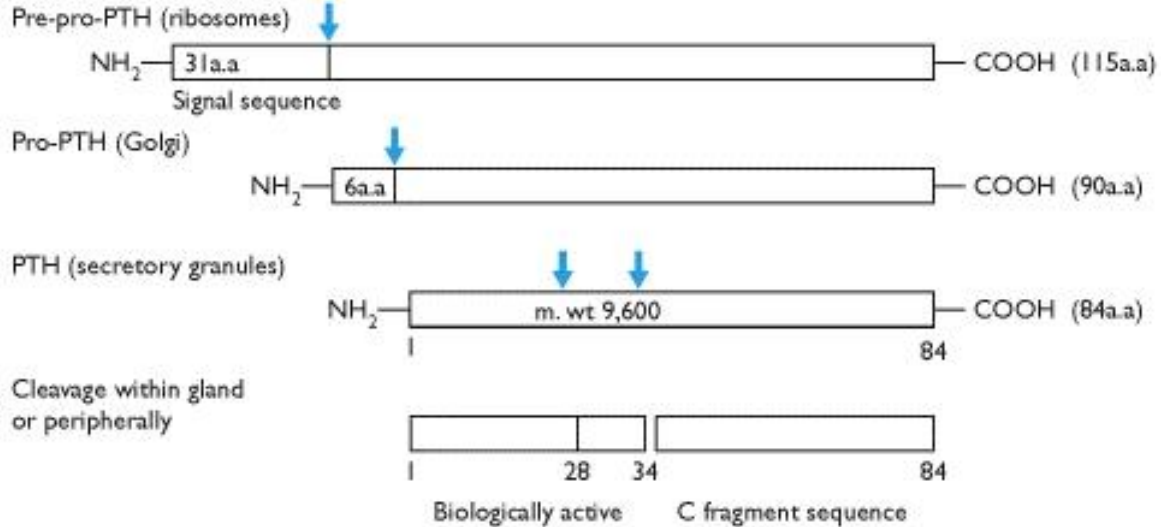
## Bone

- Osteolysis
- Differentiation of osteoclasts
- Regulation of osteoblasts → bone remodelling
- Bone resorption



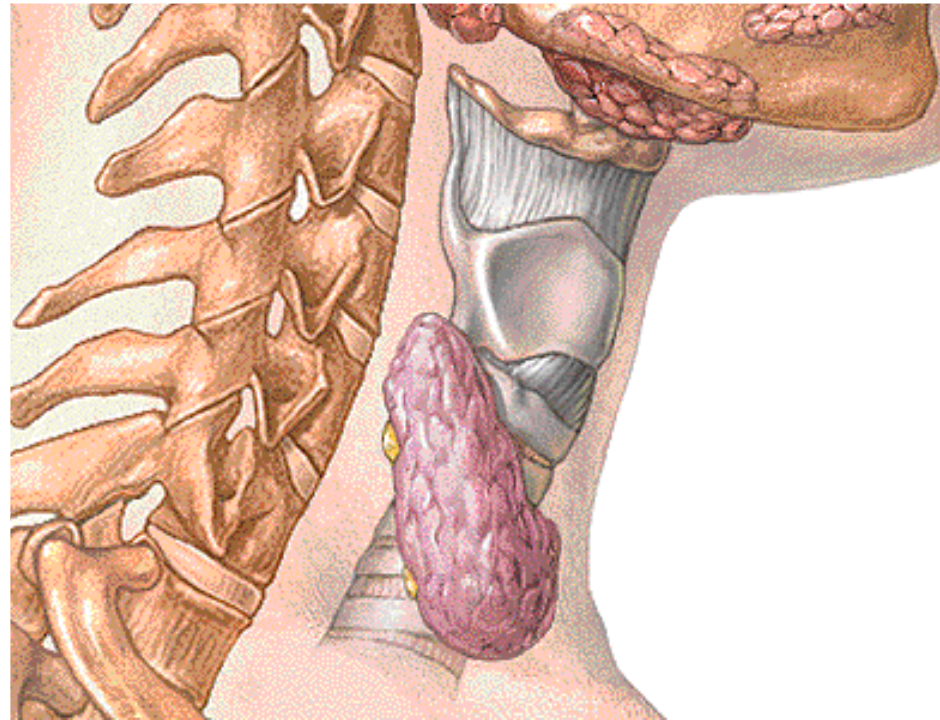
## Kidney

- Reabsorption of  $\text{Ca}^{2+}$
- Inhibition of phosphate reabsorption
- Hydroxylation of 25-(OH) vitamin D

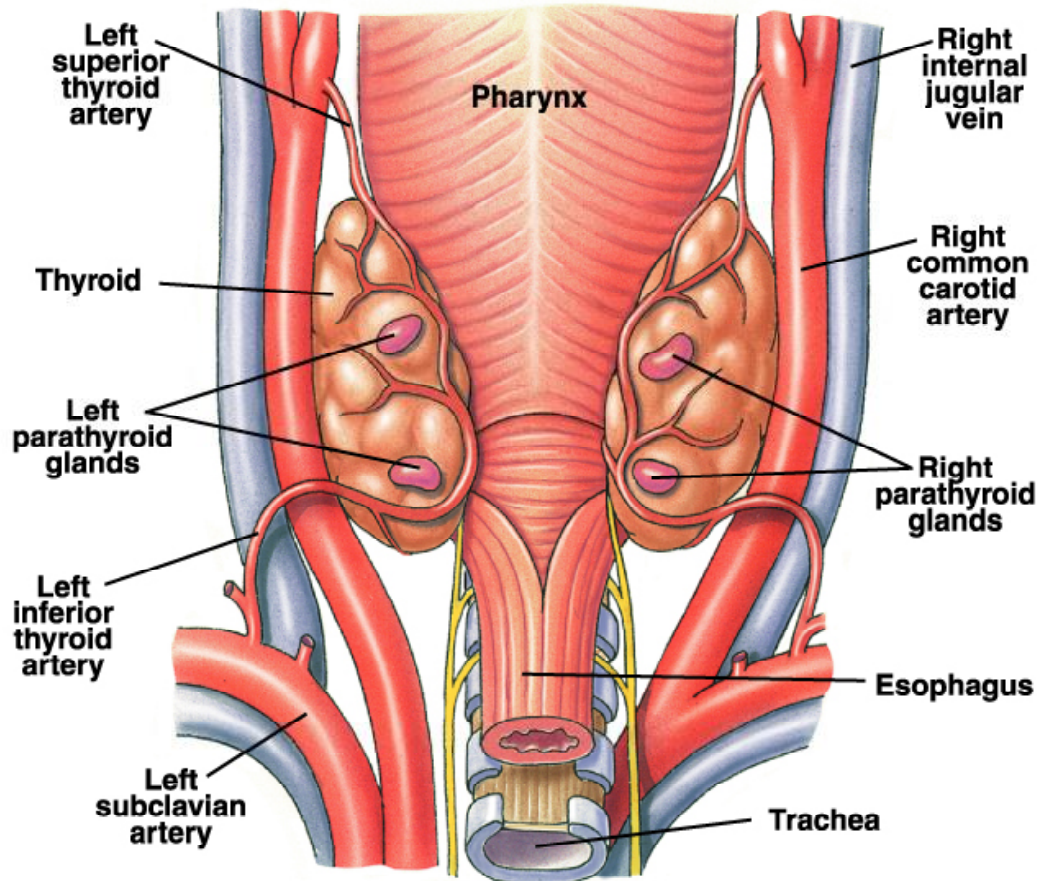


# Parathyroid glands

- Parathyroid hormone
  - An antagonist of calcitonin
  - Increase in plasma  $\text{Ca}^{2+}$



# Parathyroid glands

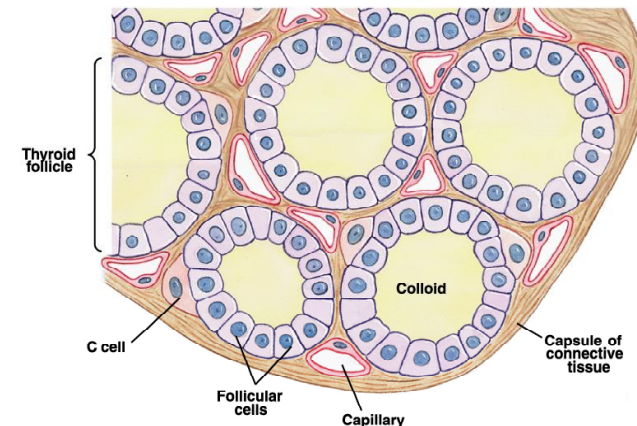


# Calcitonin

Actions of calcitonin	
Organ	Action
Bone	Inhibits bone breakdown by osteoclasts
	Simulates bone formation by osteoblasts
Intestine	Inhibits calcium absorption
Kidney	Inhibits calcium reabsorption by the renal tubules

- Parafofollicular C cells in the thyroid gland
- Unknown physiological functions
  - Inhibits absorption from the gut
  - Inhibits osteoclasts
  - Inhibits food intake (satiety hormone?)
  - Inhibits phosphate reabsorption
- Procalcitonin
  - Marker of sepsis

Section of thyroid gland



# Pathology

# Hypercalcemia

- Symptoms
  - Renal (stones, polydipsia, polyuria)
  - Bones (pain)
  - Gut (constipation)
  - Brain (depression, fatigue, anorexia)
- Signs
  - Hypertension, cognitive impairment, joint swelling, bone deformities

# Hypercalcemia

- Causes

- Primary (tertiary) hyperparathyroidism
- Malignancies (parathyroid hormone-related protein)
- Hypervitaminosis D
- Renal failure

- Therapy

- Diuretics
- Bisphosphonates
- Calcitonin

Causes of hypercalcaemia	
Mechanism	Parathyroid hormone
Hyperparathyroidism	
Primary	↑ or normal
Tertiary	↑
Malignancy (bony metastases and tumours secreting parathyroid hormone-related peptide)	↓
Multiple myeloma	↓
Bone diseases (rarely hypercalcaemia occurs when a patient with Paget's disease is immobilised)	↓ or normal
Familial hypocalciuric hypercalcaemia	Mildly elevated or high-normal
Vitamin D toxicity	↓
Certain drugs (lithium and thiazides)	↓ (but may be normal in lithium-induced hypercalcaemia)
Sarcoidosis	↓

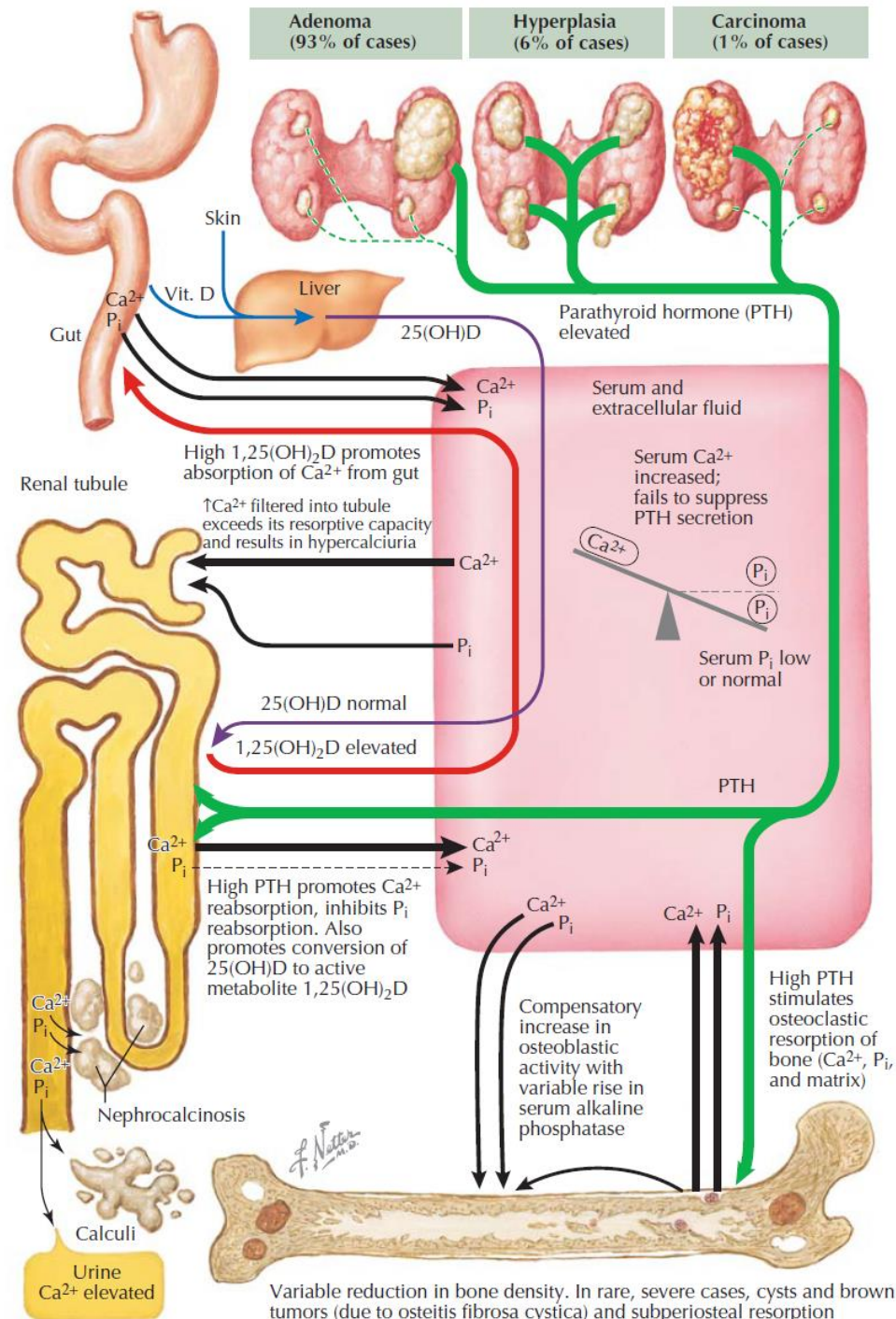


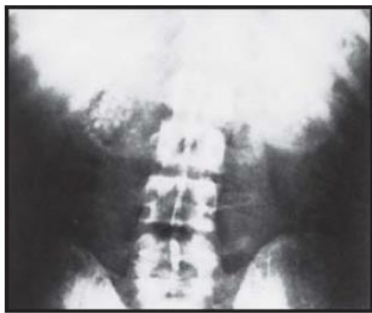
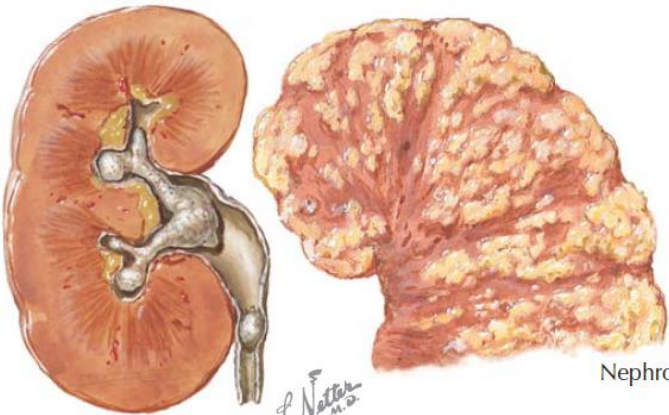
# Hyperparathyroidism

- Primary (4/100000; women; age>45)
  - Parathyroid glands
- Secondary
  - Kidneys
- Tertiary
  - From secondary – autonomy of the parathyroid glands
- Bone resorption

## Pathologies underlying hyperparathyroidism

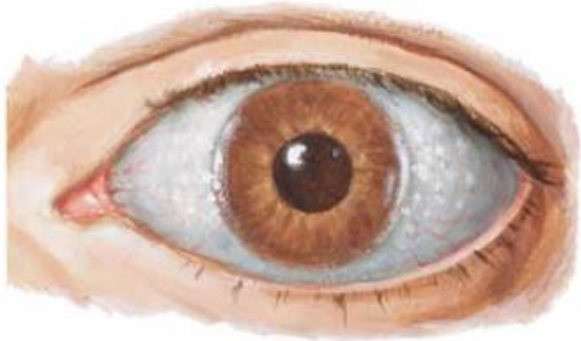
Type of hyperparathyroidism	Pathology
Primary	Autonomous production of excessive parathyroid hormone by an adenoma of a single parathyroid gland (sporadic cases or as part of genetic syndromes such as MEN type 1 and 2a)
	Multiple parathyroid gland hyperplasia (sporadic cases or as part of genetic syndromes such as MEN type 1 and 2a)
Secondary	Renal failure increasing serum phosphate concentration
	Renal failure or vitamin D deficiency resulting in a deficiency in activated vitamin D, which causes a compensatory increase in parathyroid hormone production to maintain serum calcium concentration (calcium concentration is usually low or normal)
Tertiary	Autonomous hypersecretion of parathyroid hormone in some cases of persistent secondary hyperparathyroidism, which results in hypercalcaemia and often hyperplasia of all four parathyroid glands



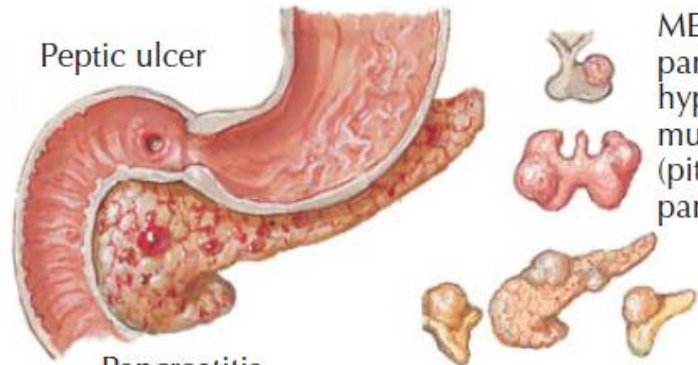


Nephrocalcinosis

Nephrolithiasis



Limbus keratopathy



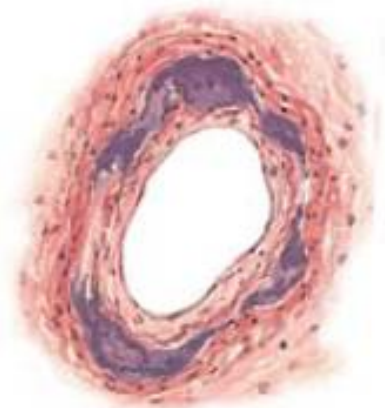
Peptic ulcer

Pancreatitis

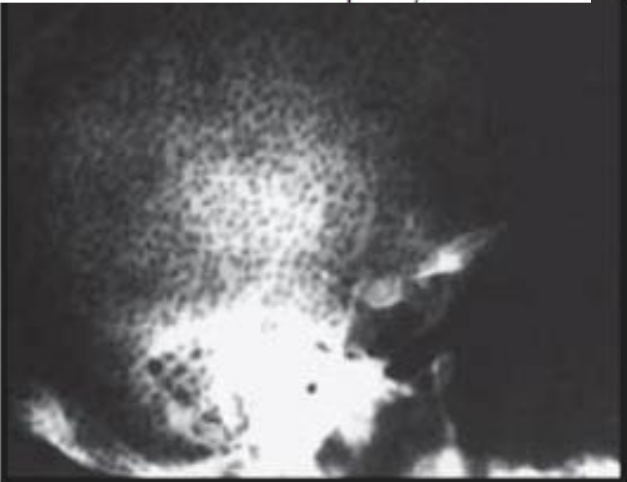
MEN 1 with parathyroid gland hyperplasia and multiple adenomas (pituitary, thyroid, pancreas, adrenals)



"Codfishing" of vertebrae













Calicum deposits in blood vessels; hypertension



"Salt and pepper" skull

**DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIC STATES**

Condition	Serum Ca <sup>2+</sup>	Serum P <sub>i</sub>	Serum PTH	Serum 25(OH)D	Serum 1,25(OH) <sub>2</sub> D	Associated findings
 Primary hyperparathyroidism	↑	N or ↓	High N or ↑	N	N or ↑	80% Asymptomatic Nephrolithiasis Osteoporosis Hypercalcemic sx
 Cancer with extensive bone metastases	↑	N or ↑	↓	N	↓ or N	History of primary tumor, destructive lesions on radiograph, bone scan
 Multiple myeloma and lymphoma	↑	N or ↑	↓	N	↓ or N	Abnormal serum or urine protein electrophoresis, abnormal bone radiographs
 Humoral hypercalcemia of malignancy	↑	N or ↓	↓	N	↓ or N	↑PTHrP Solid malignancy usually evident
 Sarcoidosis and other granulomatous diseases	↑	N or ↑	↓	N	↑	Hilar adenopathy interstitial lung disease, elevated angiotensin-converting enzyme
 Hyperthyroidism	↑	N	↓	N	N	Symptoms of hyperthyroidism, elevated serum thyroxine
 Vitamin D intoxication 	↑	N or ↑	↓	Very ↑	N or ↑	History of excessive vitamin D intake
 Milk—alkali syndrome	↑	N or ↑	↓	N	N or ↓	History of excessive calcium and alkali ingestion, heavy use of over-the-counter calcium-containing antacids
 Total body immobilization	↑	N or ↑	↓	N	↓ or N	Multiple fractures, paralysis (children, adolescents, patients with Paget disease of bone)

Key  
 Ca = Calcium ( $\text{Ca}^{2+}$ )  
 P = Phosphate ( $\text{HPO}_4^{2-}$ )  
 H = Hydroxyapatite

Parathyroids secondarily stimulated by low serum  $\text{Ca}^{2+}$  and lack of negative feedback from  $1,25(\text{OH})_2\text{D}$

Phosphate filtration blocked by glomerular disease

PTH secondarily increased

Hyperplasia of all parathyroid glands

High serum  $\text{P}_i$  depresses serum  $\text{Ca}^{2+}$

Creatinine

7.0 mg/dL

Acidosis

Circulation

PTH inhibits  $\text{P}_i$  reabsorption and promotes  $\text{Ca}^{2+}$  reabsorption but to no avail because little filters through glomerulus

$\text{P}_i$  absorption not impaired

$\text{Ca}^{2+}$  bound in gut by high  $\text{P}_i$

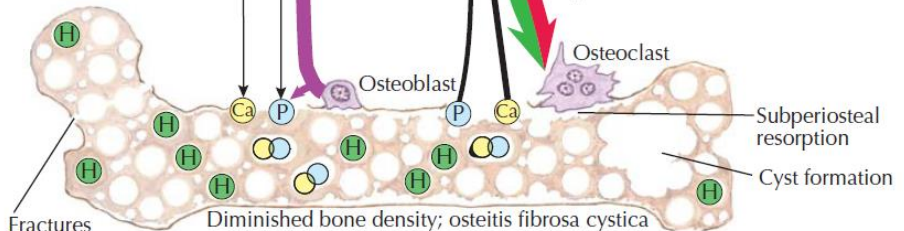
Deposition of  $\text{Ca}^{2+}$  and  $\text{P}_i$  normal or enhanced: also in ectopic sites

Compensatory increase in osteoblastic activity with variable rise of serum alkaline phosphatase

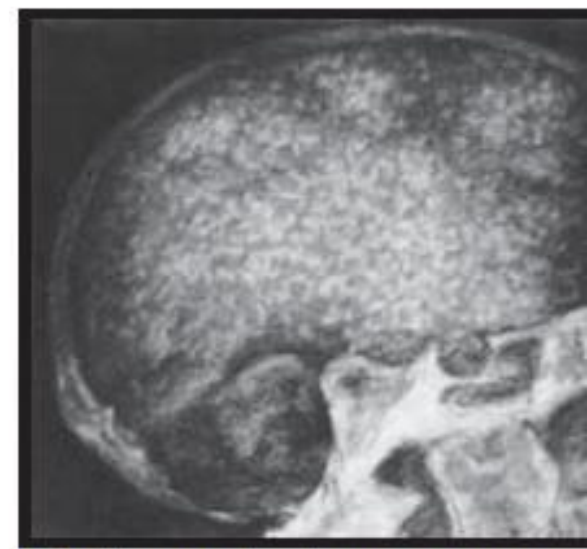
Increased stimulation of osteoclastic activity by PTH: resorption of  $\text{Ca}^{2+}$  and  $\text{P}_i$  enhanced by acidosis

Urine  
 $\text{Ca}^{2+}$  } Very low  
 $\text{P}_i$  } low

*F. Netter M.D.*

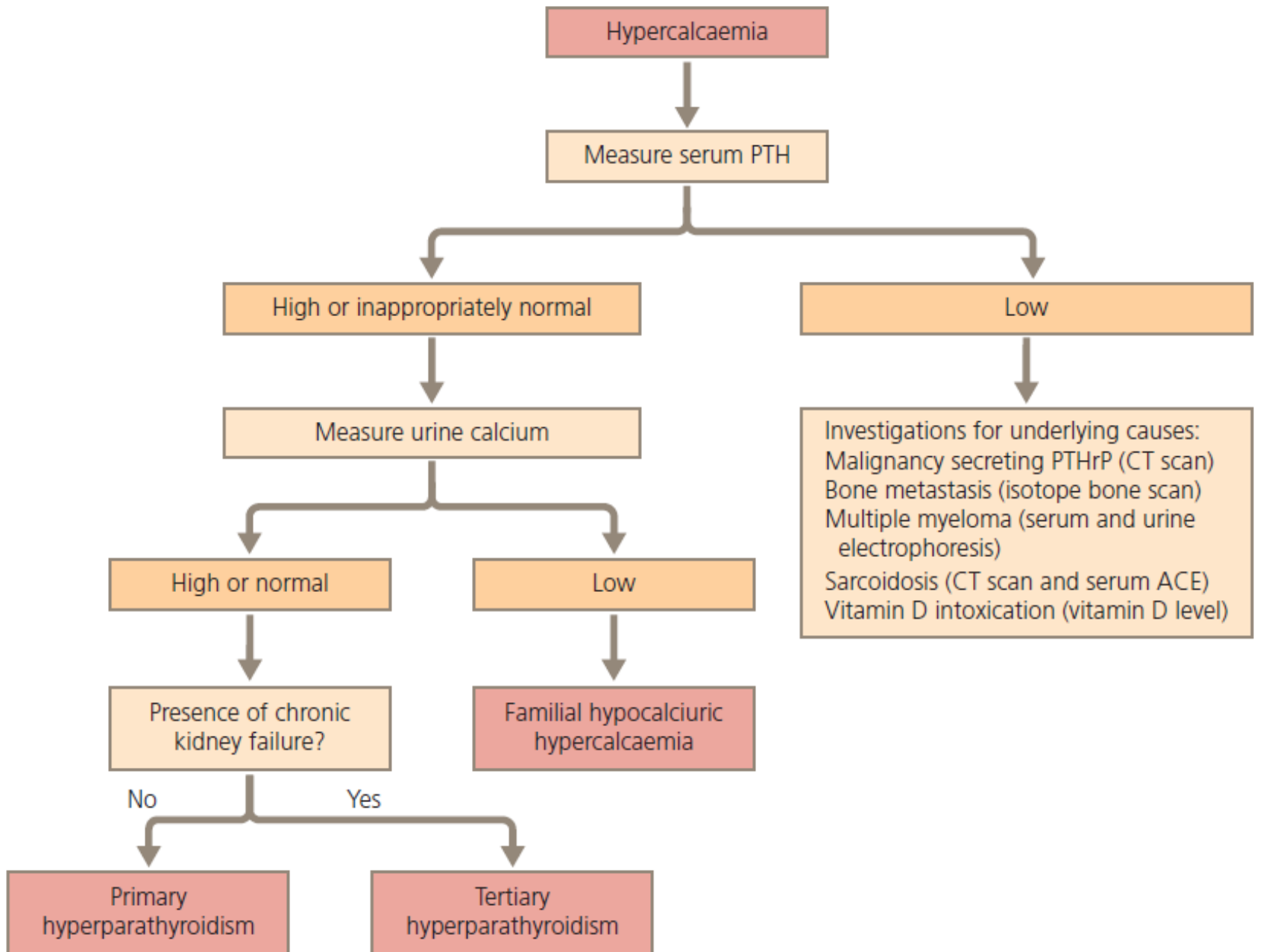


Fracture of long bones



Radiograph shows spotty decalcification of skull ("salt-and-pepper" skull)

# Investigating hypercalcaemia



# Hypocalcemia

- Symptoms & Signs
  - Tetany, paresthesia, ECG changes
- Causes
  - Hypoparathyroidism (inborn, post surgery), low calcium intake, hypovitaminosis D, renal failure
- Therapy
  - Calcium, vitamin D



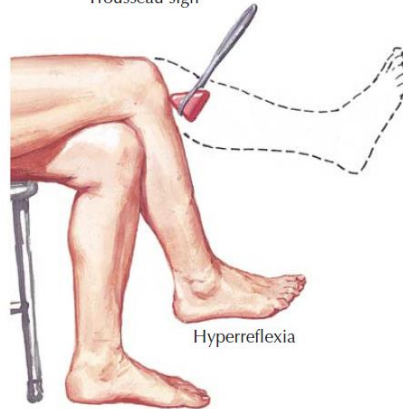
# Hypocalcemia



Trousseau sign

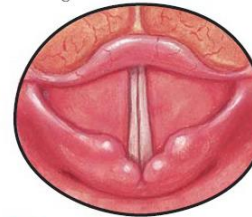


Chvostek sign

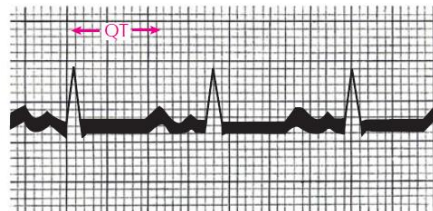


Hyperreflexia

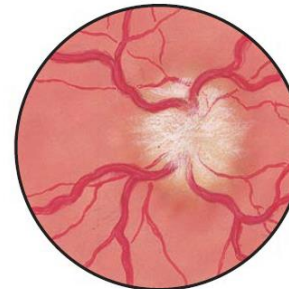
Laryngeal spasm (stridor)



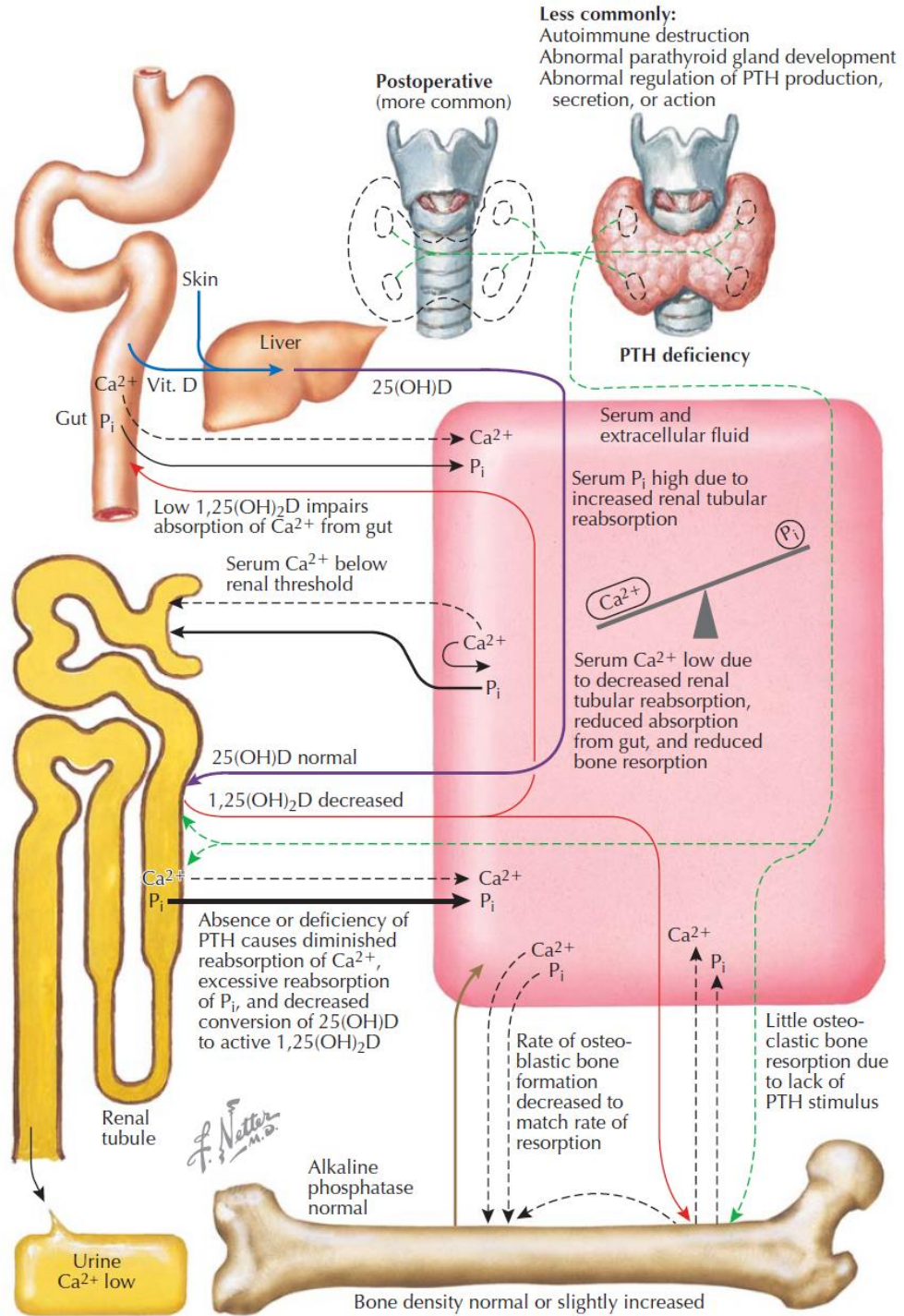
Convulsions

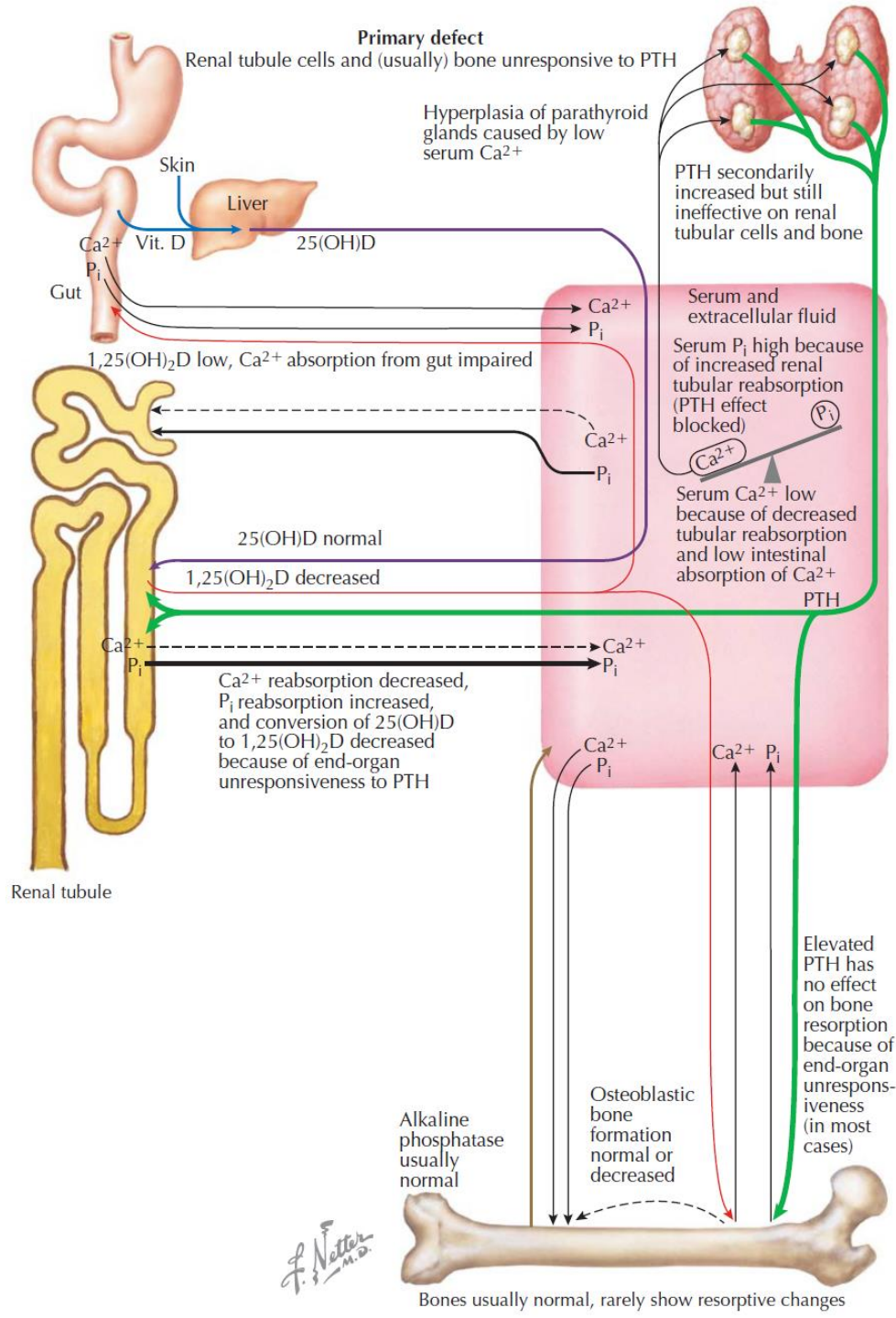


Electrocardiogram: prolonged Q-T interval



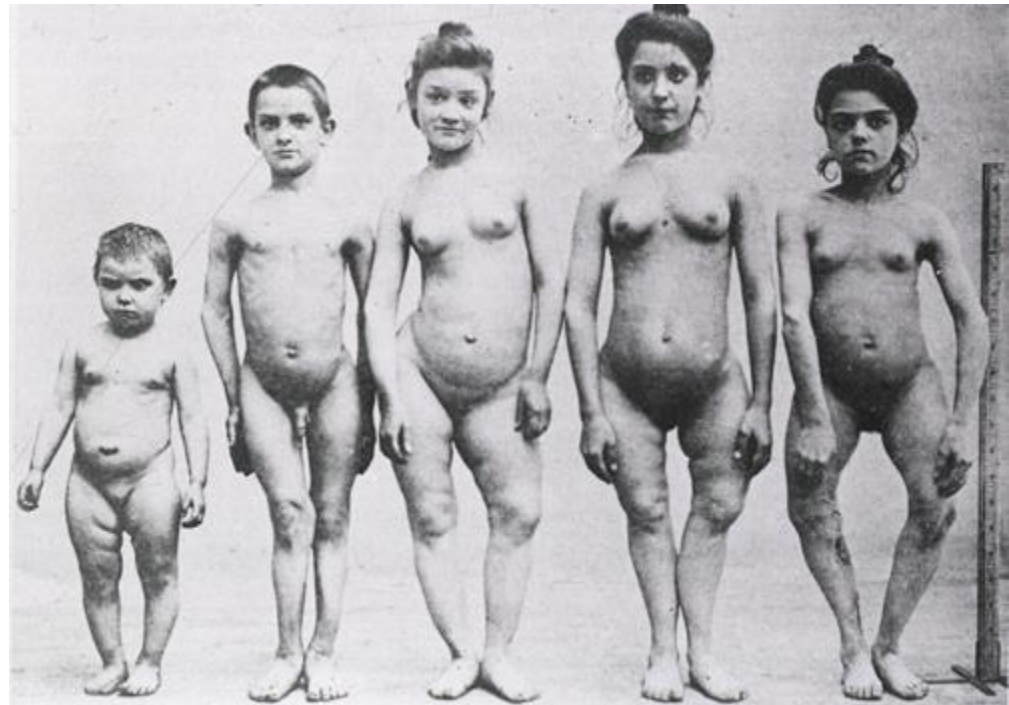
Choked disk





# Hypovitaminosis D

- Rickets
  - Long bone malformation in children
- Osteomalacia
  - In adults
  - „soft bone“ disease
- Osteoporosis
- Hypervitaminosis?




# Osteoporosis

- Increased fracture risk
- Decreased bone mineralization
- Postmenopausal, glucocorticoids, immobilization
- Therapy
  - Bisphosphonates
  - Estrogen replacement
  - Calcitonin

# RISK FACTORS FOR OSTEOPOROSIS

### Disuse



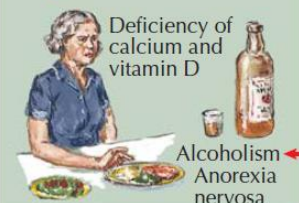
Prolonged casting or splinting (localized osteoporosis)

Paralysis (paraplegia, quadriplegia, hemiplegia, lower motor neuron disease)

Space travel (weightlessness)

Prolonged bed rest or general inactivity

### Diet



Deficiency of calcium and vitamin D

Alcoholism

Anorexia nervosa

### Drugs




Heparin

Methotrexate

Ethanol

Glucocorticoids

### Idiopathic



Adolescent (10-18 yr)

Middle-aged man

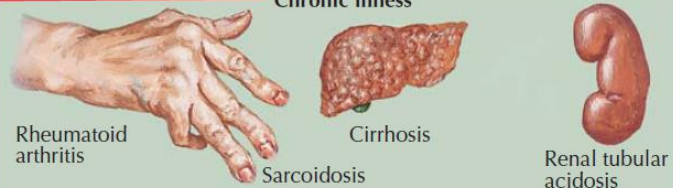
### Genetic disorders



Osteogenesis imperfecta

Homocystinuria

### Chronic illness




Rheumatoid arthritis

Sarcoidosis

Cirrhosis

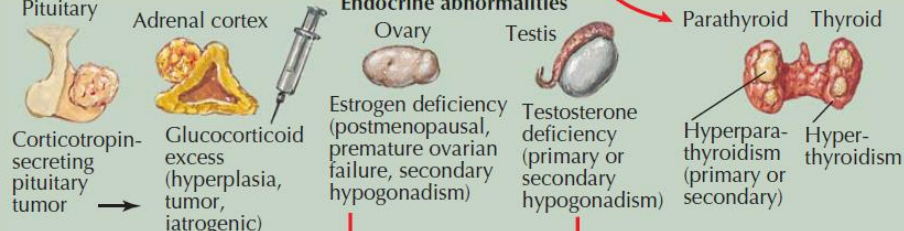
Renal tubular acidosis

### Neoplasms



Bone marrow tumors (myeloma, lymphoma, leukemia, mast cell)

### Endocrine abnormalities



Pituitary: Corticotropin-secreting pituitary tumor

Adrenal cortex: Glucocorticoid excess (hyperplasia, tumor, iatrogenic)

Ovary: Estrogen deficiency (postmenopausal, premature ovarian failure, secondary hypogonadism)

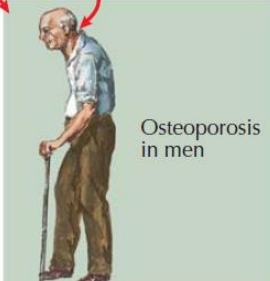
Testis: Testosterone deficiency (primary or secondary hypogonadism)

Parathyroid: Hyperparathyroidism (primary or secondary)

Thyroid: Hyperthyroidism



Osteoporosis in postmenopausal women



Osteoporosis in men

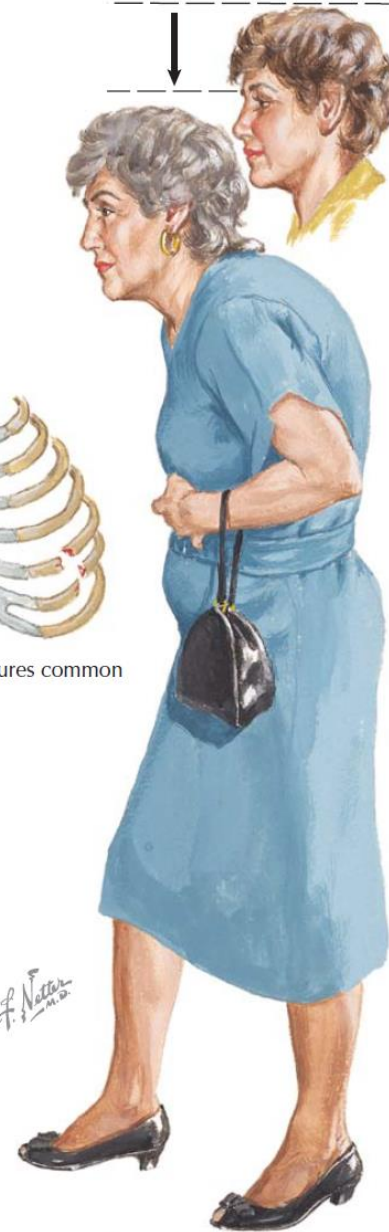
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Axial



Rib fractures common

Vertebral compression fractures cause continuous (acute) or intermittent (chronic) back pain from midthoracic to midlumbar region, occasionally to lower lumbar region



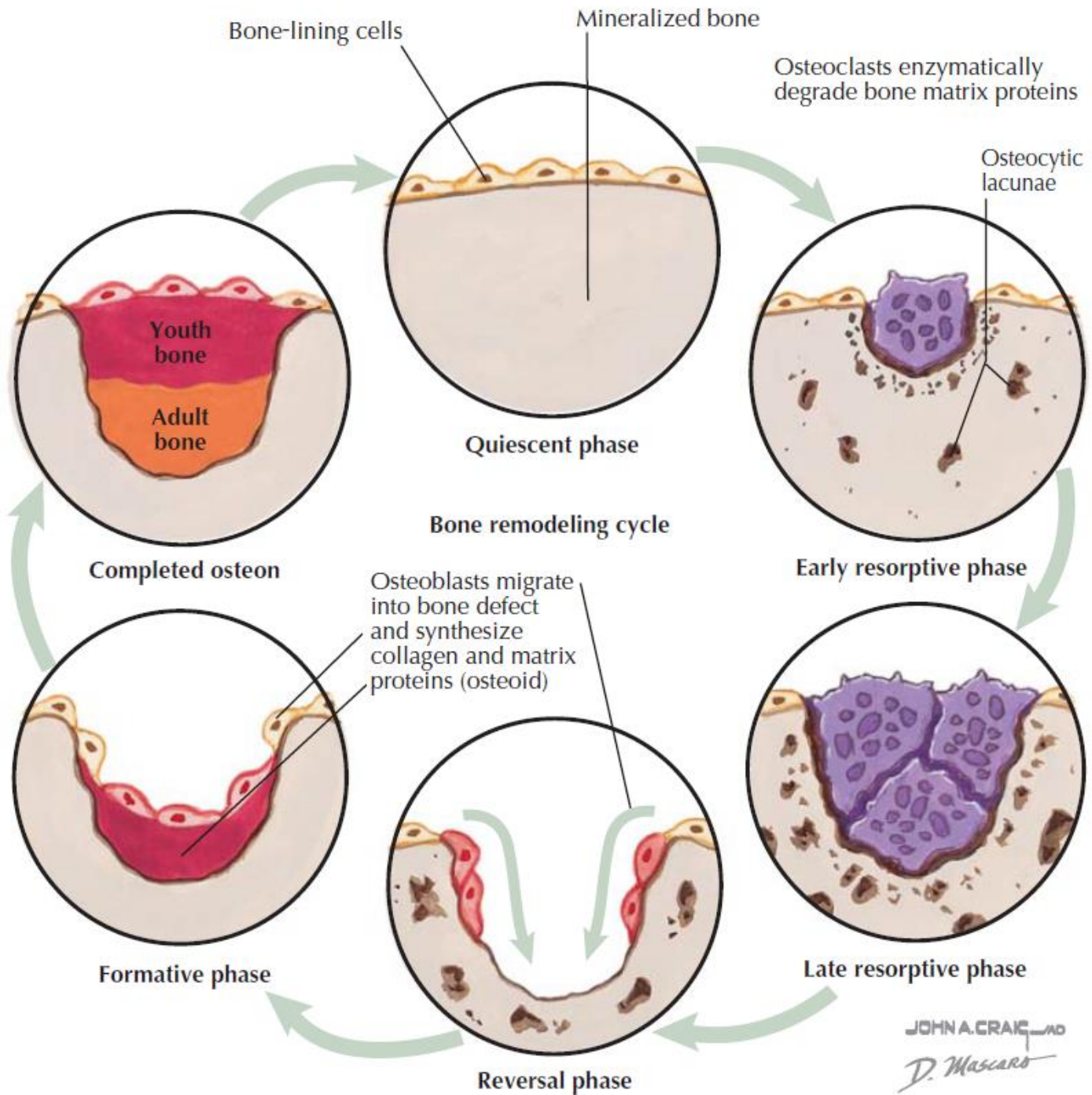
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Progressive thoracic kyphosis, or dowager's hump, with loss of height and abdominal protrusion

**Appendicular**  
Fractures caused by minimal trauma

Proximal femur (intertrochanteric or intracapsular)    Proximal humerus    Distal radius

Most common types



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