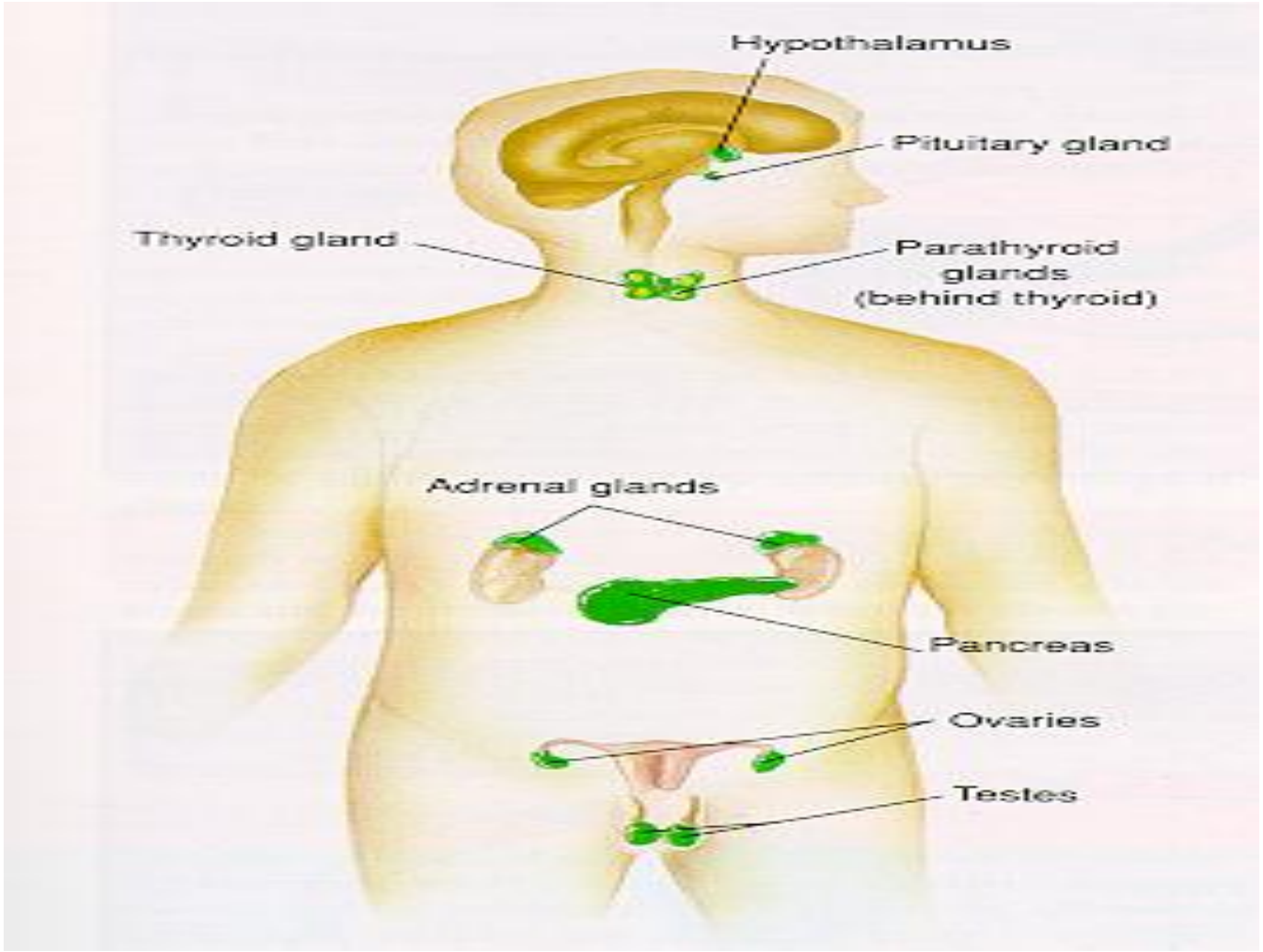
The Endocrine System



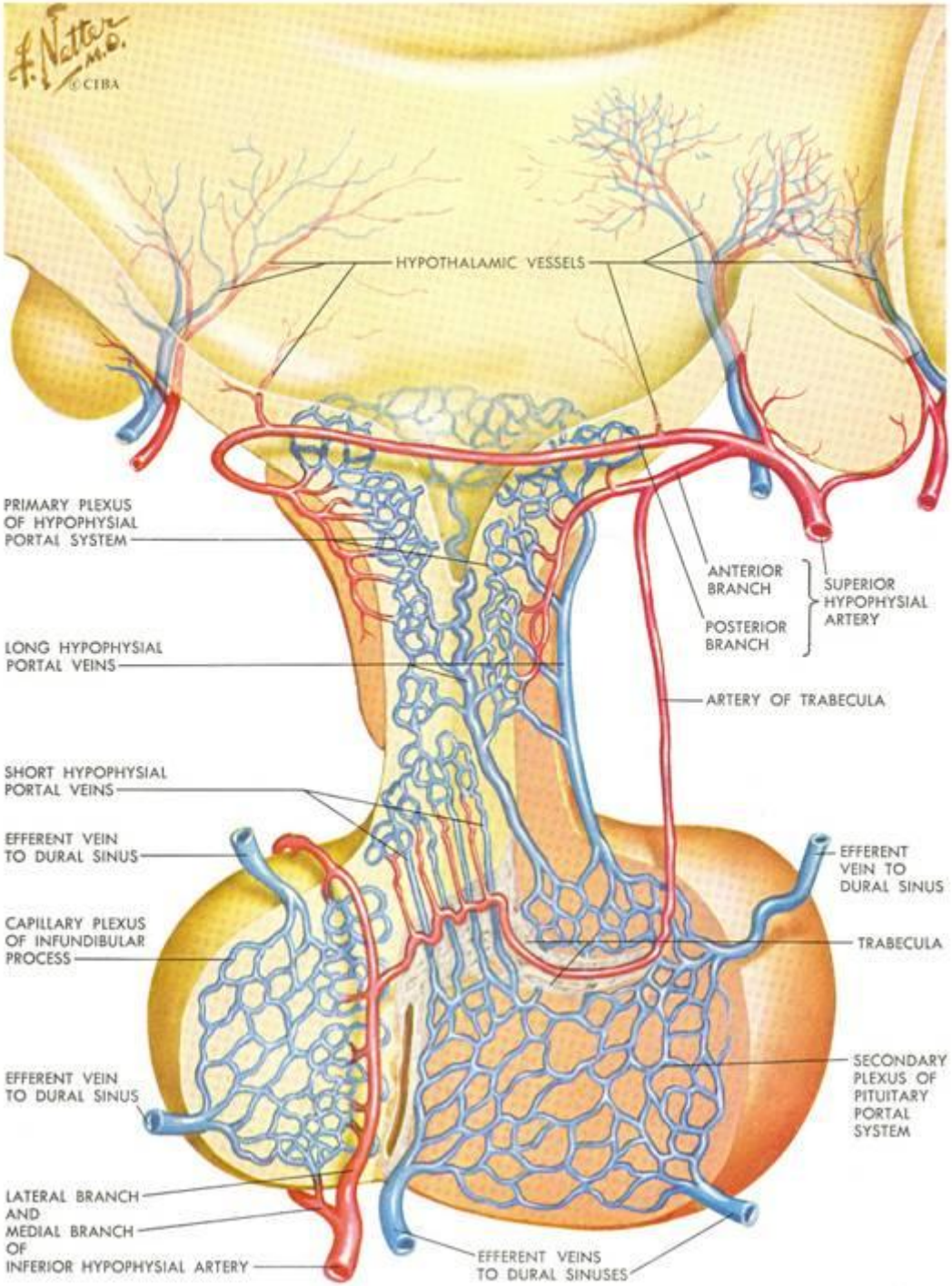
Resumen de lo publicado

- Sistemas secrecionales (endo, exo, auto y paracino
- Sistemas simples, complejos, más complejos
- Hormonas esteroides y no esteroides (proteicas, derivados de Aa, derivados de ácidos grasos)

Resumen de lo publicado II

- Ejes hipotálamo-hipofisarios (adrenal, gonadal, tiroideo)
- Psiconeuroinmunoendocrinología

THE PITUITARY GLAND


F. Netter M.D.
©CIBA
HYPOTHALAMIC VESSELS
PRIMARY PLEXUS OF HYPOPHYSIAL PORTAL SYSTEM
ANTERIOR BRANCH
POSTERIOR BRANCH
SUPERIOR HYPOPHYSIAL ARTERY
LONG HYPOPHYSIAL PORTAL VEINS
ARTERY OF TRABECULA
SHORT HYPOPHYSIAL PORTAL VEINS
EFFERENT VEIN TO DURAL SINUS
EFFERENT VEIN TO DURAL SINUS
CAPILLARY PLEXUS OF INFUNDIBULAR PROCESS
TRABECULA
SECONDARY PLEXUS OF PITUITARY PORTAL SYSTEM
EFFERENT VEIN TO DURAL SINUS
LATERAL BRANCH AND MEDIAL BRANCH OF INFERIOR HYPOPHYSIAL ARTERY
EFFERENT VEINS TO DURAL SINUSES

Hypothalamus	Anterior Pituitary
GHRH *(GH-releasing)*	GH *(growth hormone)*
SS *(somatostatin, GH-inhib)*	ñ
CRH *(corticotropin-rel)*	ACTH *(adrenocorticotropic)*
GnRH *(gonadotropin-rel)*	LH *(luteinizing hormone)*
ñ	FSH *(follicle-stimulating)*
PRH *(PRL-releasing)*	PRL *(prolactin)*
PIH *(PRL rel-inhibiting)*	ñ
TRH *(thyrotropin-rel)*	TSH *(thyroid stimulating)*

Hole's Human Anatomy and Physiology, 7th edition, by Shier, et al. copyright ©1996 TM Higher Education Group, Inc.

What do these anterior pituitary hormones do?

<u>Growth Hormone</u>:

- Å stimulates cells to grow and divide
- Å increases amino acid transport rate and protein synthesis
- Å increases fat metabolism

Typically, GH is secreted during sleep.

GH secretion increases when malnourished

GH influences bone growth via somatomedin:

GH in blood

GH arrives in liver

liver secretes **somatomedin**

cartilage divides

bones grow!

Problems with GH

- ÅToo much GH in children leads to gigantism
- ÅToo much GH in adults leads to acromegaly
- ÅToo little GH in children leads to dwarfism

Somatostatina o octreotide se usan en acromegalia.

Other Anterior Pituitary Hormone Functions

ACTH:

- works on the cortex of the adrenal gland, influencing the release of cortisol
- stress can increase CRH secretion which will increase ACTH secretion
- negative feedback when adrenal cortex hormones in blood decrease CRH secretion

LH & FSH:

- LH in females and in males leads to sex hormone secretion
- FSH in females causes growth and development of egg cell-containing follicles in the ovary, and causes estrogen secretion
- FSH in males instigates sperm production
- both hormones are regulated by GnRH, which is not significant in concentration until puberty

ACTH:
Desde la aparición de adrenocorticoides sintéticos, el uso farmacológico de la ACTH se restringe al diagnóstico diferencial de insuficiencia adrenal primaria (enfermedad de Addington) de insuficiencia adrenal secundaria (secreción inadecuada de ACTH hipofisaria).
Se usan ACTHs purificadas de animales o cosintropina, una ACTH humana sintética.

More Anterior Pituitary Hormone Functions

PRL:

- In females, PRL promotes lactation
- In males, PRL decreases LH secretion *(note that too much PRL would then decrease androgen levels and cause sterility)*
- Controlled by both PRH and PIH

TSH:

- works on thyroid gland to either cause or inhibit its secretion of hormones
- works on thyroid gland to affect its growth *(too much TSH leads to a goiter)*
- negative feedback via thyroid hormones in blood
- stress or cold temperatures can change TSH secretion

The Posterior Pituitary Lobe

No hormones are *made* here. They are made in the hypothalamus and just released here.

Two peptide hormones are released from the posterior pituitary lobe (the neurohypophysis):

ÅADH *(antidiuretic hormone or vasopressin)*

ÅOT *(oxytocin)*

Function of Posterior Pituitary Lobe Hormones

ADH:

- Also known as antidiuretic hormone (ADH) decreases urine formation by having kidneys conserve water
- also can contract smooth muscle cells, as found in blood vessels--this causes an increase in blood pressure
- ADH release triggered by osmoreceptors and inhibited by stretch receptors in blood vessels

OT:

- In females, contracts the uterine wall smooth muscles
- In females, helps to eject milk when lactating
- No known function in males, although in both males and females, OT can have some antidiuretic effects

Oxitocina: iv para inducción de contracciones uterinas
spray nasal para eyección de leche materna
usos como feromona?

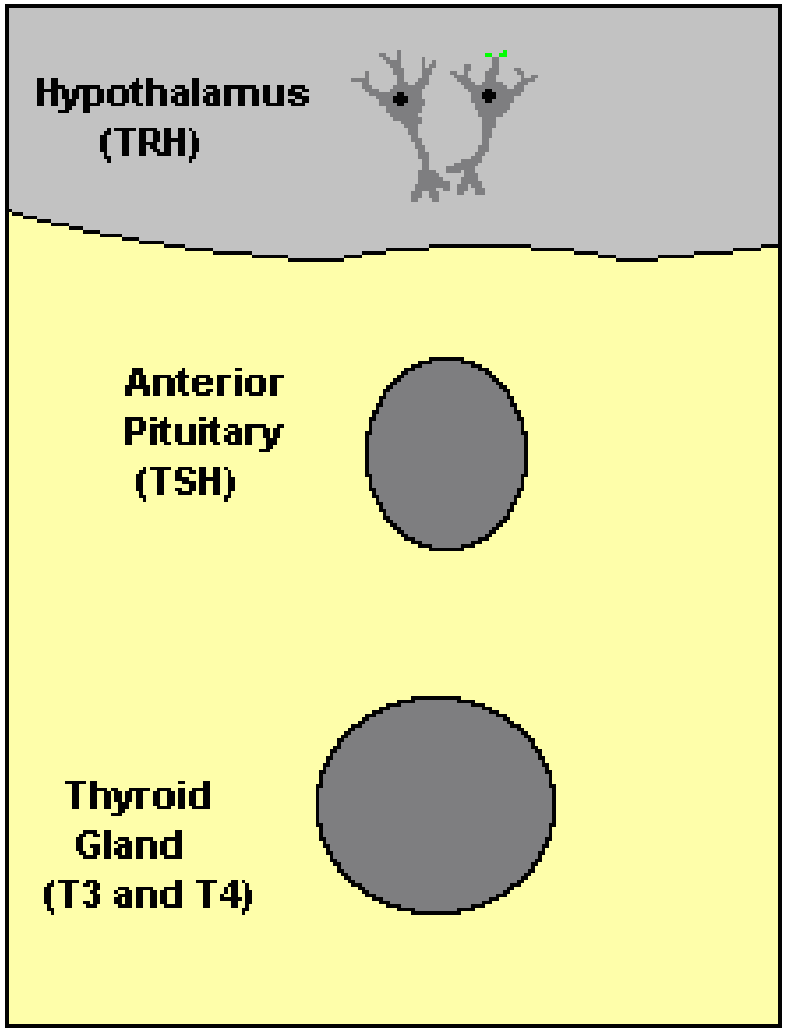
ADH/Vasopresina:
diabetes insípida
desmopresina para diabetes, sin efectos sobre presión arterial

Pituitary Diseases

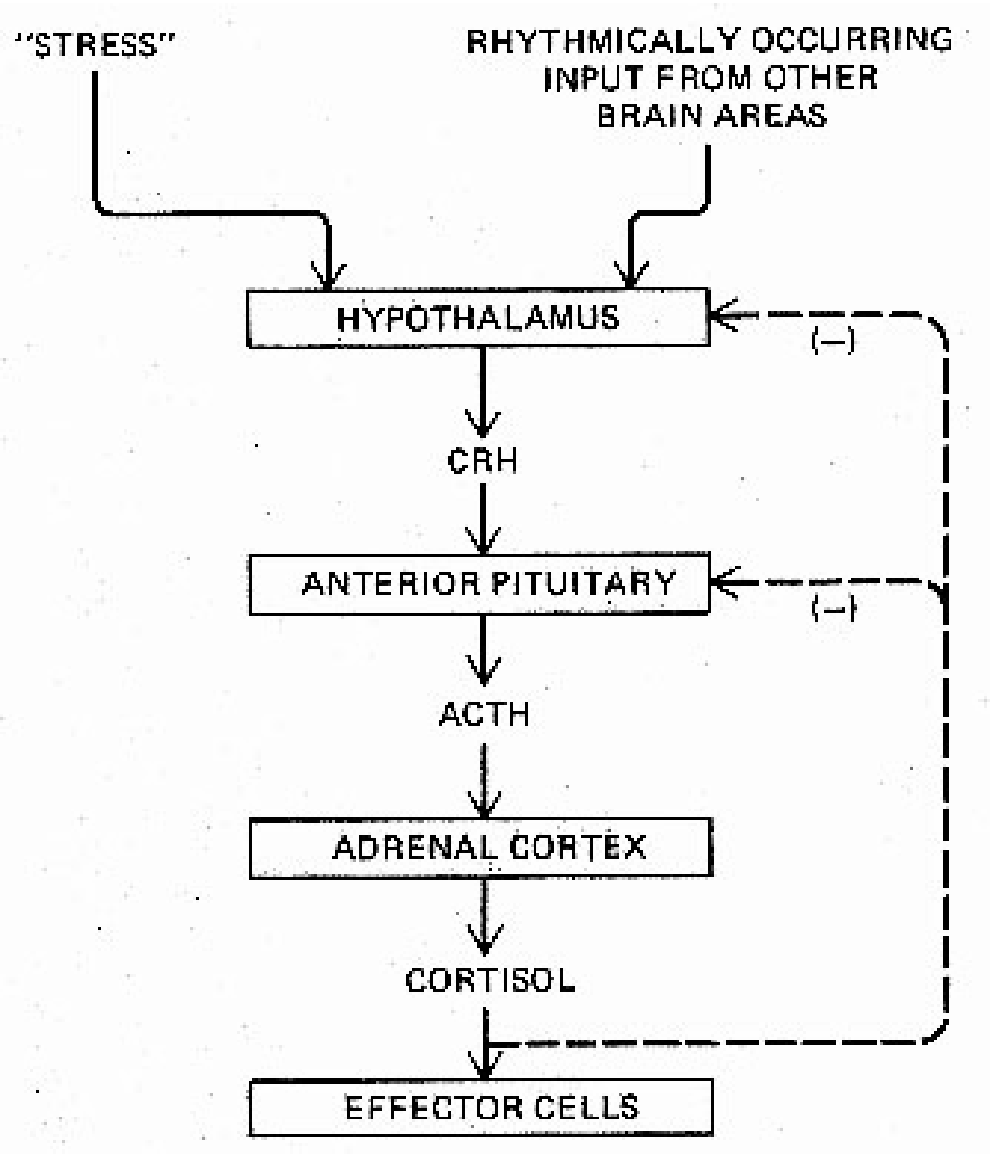
- Primary Tumors
  - Adenomas
  - Craniopharyngioma
- Metastasis
- Empty Sella
  - Surgical, post-Sheehandôs
- Hemorrhage
  - Sheehandôs syndrome
- Hyperfunction
  - Prolactin
- Insufficiency

Feedback Control of Hormone Production

Feedback loops are used extensively to regulate secretion of hormones in the hypothalamic-pituitary axis. An important example of a negative feedback loop is seen in control of thyroid hormone secretion



Negative feedback effects of cortisol



Physiological importance of pulsatile hormone release

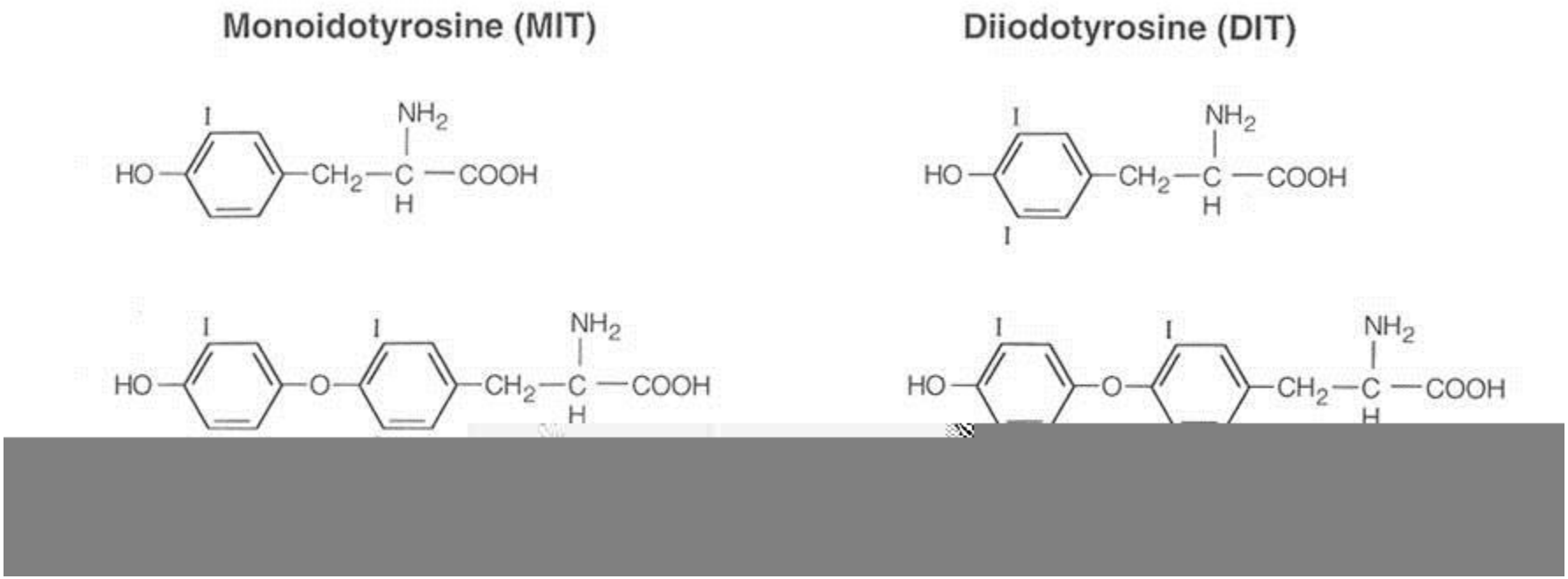
- Demonstrated by GnRH infusion
- If given once hourly, gonadotropin secretion and gonadal function are maintained normally
- A slower frequency won't function
- Faster, or continuous infusion inhibits gonadotropin secretion and blocks gonadal steroid production

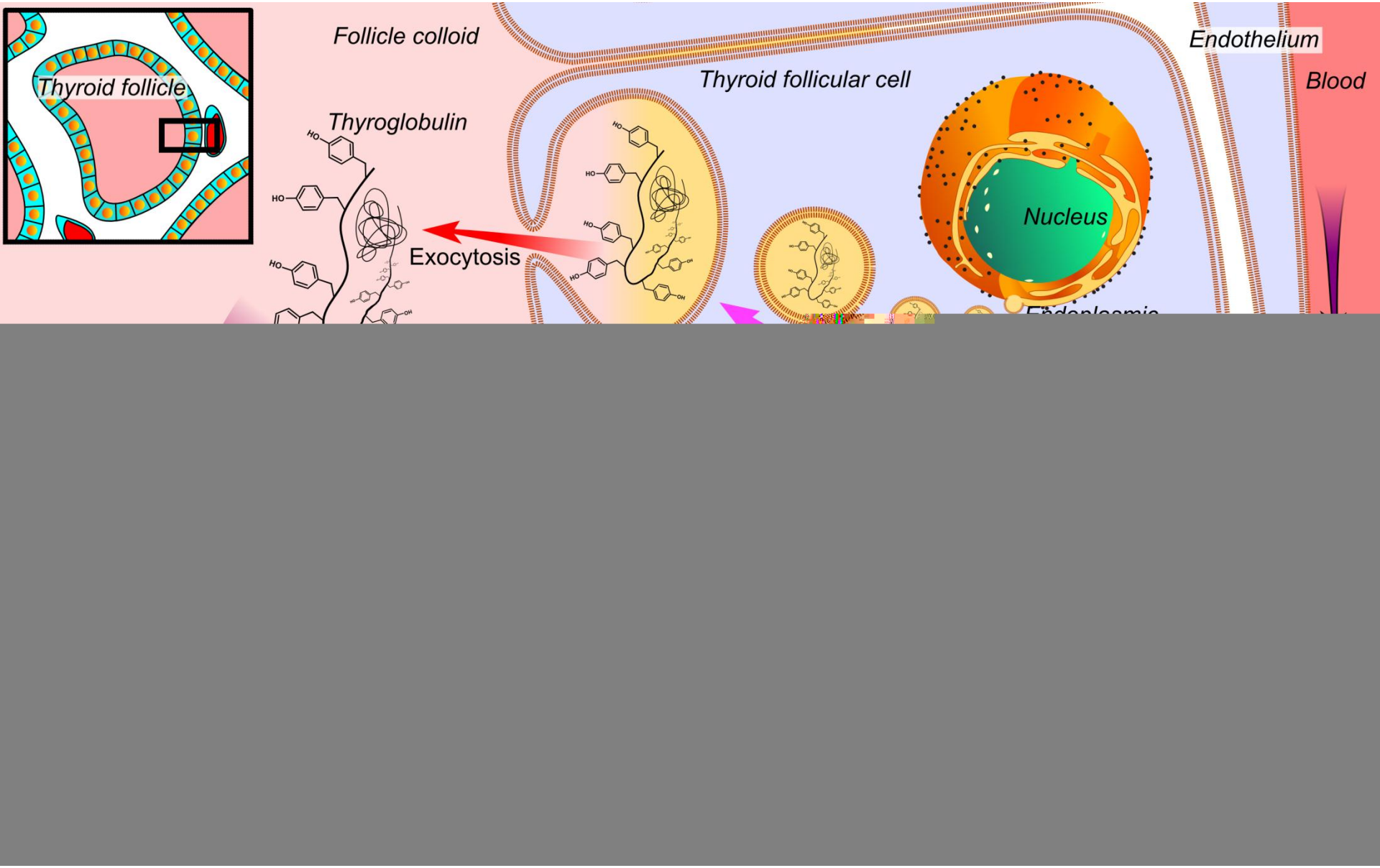
The Endocrine Glands and Their Hormones

- Thyroid Gland
  - Located along the midline of the neck
  - Secretes two nonsteroid hormones
    - Triiodothyronine (T3)
    - Thyroxine (T4)
  - Regulates metabolism
    - increases protein synthesis
    - promotes glycolysis, gluconeogenesis, glucose uptake
    - Calcitonin: calcium metabolism

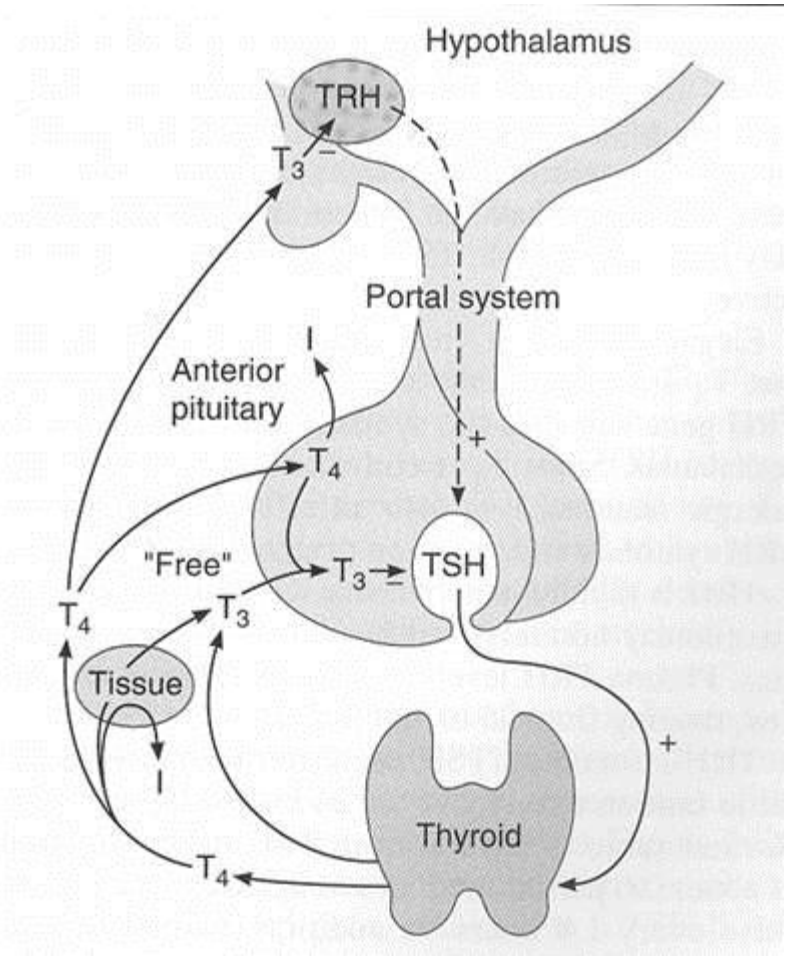
EXTERNAL CAROTID ARTERY
DESCENDENS HYPOGLOSSI
SUPERIOR THY
HYOID BONE
SUPERIOR LARYNGEAL NERVE

Thyroid Hormones




Thyroid follicle
Follicle colloid
Thyroglobulin
Exocytosis
Thyroid follicular cell
Nucleus
Endothelium
Blood

Thyroid Hormone Control



About the Thyroid Hormones...

T_3 and T_4:

- Function: metabolism regulation (break down carbohydrates and fats, synthesize proteins)
- Can only be made by follicular cells when iodides are available
- Somewhat hydrophobic and get carried by proteins in the blood.
- Controlled by anterior pituitary lobe TSH
- T_3 more effective, T_4 more abundant

Calcitonin:

- Function: decrease blood calcium levels and blood phosphate levels (by helping them get deposited in bone, and by stimulating excretion of them by kidneys)
- Controlled by blood calcium levels and digestive chemicals

Problems with the Thyroid Gland

Hyperthyroidism:

- high metabolic rate, hyperactivity, sensitivity to heat, protruding eyes
- **Graveôs disease**: when hyperthyroidism is due to an autoimmune problem (TSH is mimicked by autoantibodies)

Hypothyroidism:

- in the adult: low metabolic rate, sensitivity to cold, sluggishness
- in an infant: **cretinism**-- stunted growth, mental retardation, abnormal bone formation
- **Hashimotoôs disease**: when hypothyroidism is due to an autoimmune problem (autoantibodies attack and destroy follicular cells)
- **goiter**: no T3 and T4 can be made because not enough iodides were ingested.

HIPOTIROIDISIMO:
Se trata con levotiroxina (1 dosis diaria)

HIPERTIROIDISIMO
Se trata con cirugía, con inhibidores de síntesis de T3/T4 (como propiltiouracilo o metimazol), con propranolol (beta-bloqueante) o inhibición de la secreción de hormonas tiroideas (con ioduro)

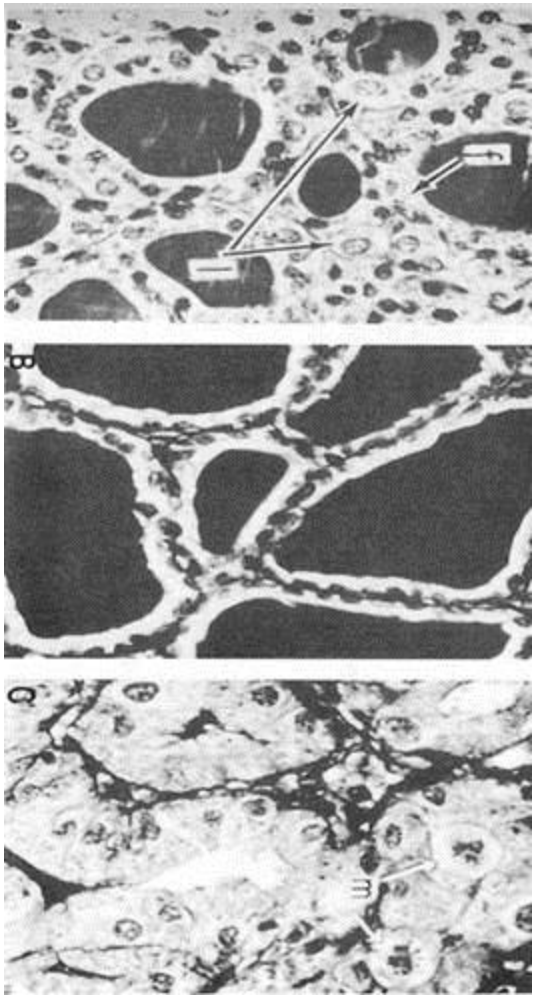
Thyroid Lab Evaluation

- TRH
- TSH
- TT_3, TT_4
- FT_3, FT_4
- RAIU
- Thyroglobulin, Thyroglobulin Ab
- Perchlorate Test
- Stimulation Tests

RAIU

- Scintillation counter measures radioactivity 6 & 24 hours after I^{123} administration.
- Uptake varies greatly by iodine status
  - Indigenous diet (normal uptake 10% vs. 90%)
  - Amiodarone, Contrast study, Topical betadine
- Symptomatic elevated RAIU
  - Graves
  - Toxic goiter
- Symptomatic low RAIU
  - Thyroiditis (Subacute, Active
  - Hormone ingestion (Thyrotoxicosis factitia, Hamburger Thyrotoxicosis)
  - Excess I^- intake (Jod-Basedow effect)
  - Ectopic thyroid carcinoma (Struma ovarii)

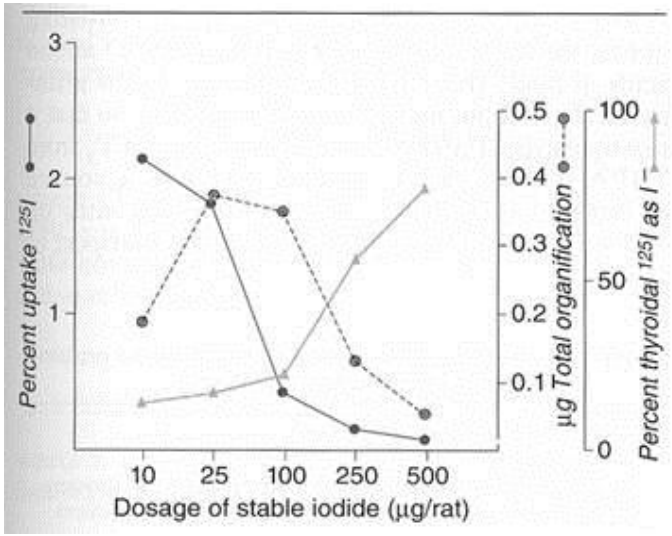
Iodine states



- Normal Thyroid
- Inactive Thyroid
- Hyperactive Thyroid

Wolff-Chaikoff

- Increasing doses of I^- increase hormone synthesis initially
- Higher doses cause cessation of hormone formation.
- This effect is countered by the Iodide leak from normal thyroid tissue.
- Patients with autoimmune thyroiditis may fail to adapt and become hypothyroid.



Jod-Basedow

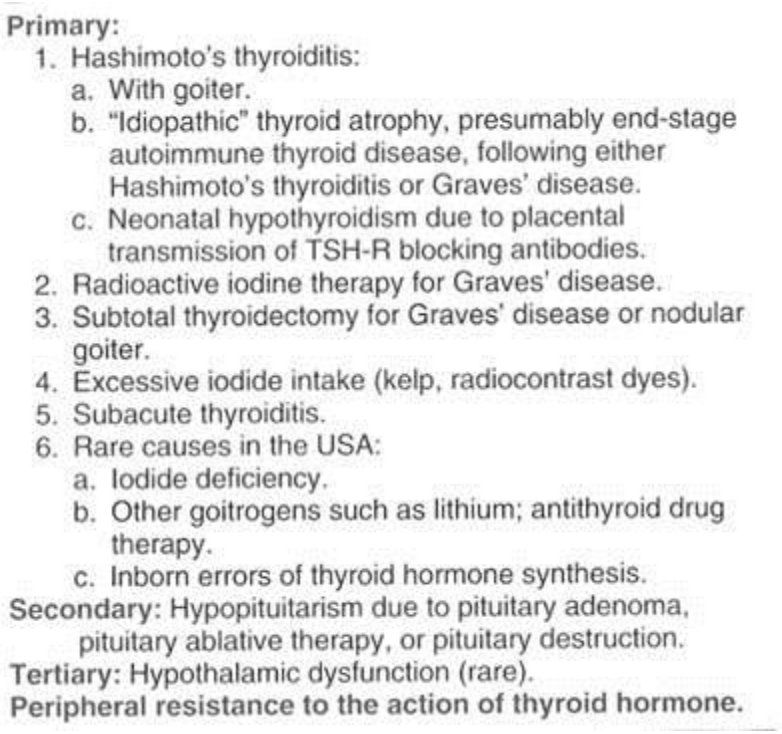
- Aberration of the Wolff-Chaikoff effect
- Excessive iodine loads induce hyperthyroidism
- Observed in several disease processes
  - Graveso disease
  - Multinodular goiter

Hypothyroid

- Symptoms – fatigability, coldness, weight gain, constipation, low voice
- Signs – Cool skin, dry skin, swelling of face/hands/legs, slow reflexes, myxedema
- Newborn – Retardation, short stature, swelling of face/hands, possible deafness
- Types of Hypothyroidism
  - Primary – Thyroid gland failure
  - Secondary – Pituitary failure
  - Tertiary – Hypothalamic failure
  - Peripheral resistance

Hypothyroid

- Cause is determined by geography
- Diagnosis
  - Low FT_4, High TSH (Primary, check for antibodies)
  - Low FT_4, Low TSH (Secondary or Tertiary, TRH stimulation test, MRI)
- Treatment
  - Levothyroxine (T_4) due to longer half life
  - Treatment prevents bone loss, cardiomyopathy, myxedema



Primary:

1. Hashimoto's thyroiditis:
   a. With goiter.
   b. "Idiopathic" thyroid atrophy, presumably end-stage autoimmune thyroid disease, following either Hashimoto's thyroiditis or Graves' disease.
   c. Neonatal hypothyroidism due to placental transmission of TSH-R blocking antibodies.
2. Radioactive iodine therapy for Graves' disease.
3. Subtotal thyroidectomy for Graves' disease or nodular goiter.
4. Excessive iodide intake (kelp, radiocontrast dyes).
5. Subacute thyroiditis.
6. Rare causes in the USA:
   a. Iodide deficiency.
   b. Other goitrogens such as lithium; antithyroid drug therapy.
   c. Inborn errors of thyroid hormone synthesis.

Secondary: Hypopituitarism due to pituitary adenoma, pituitary ablative therapy, or pituitary destruction.

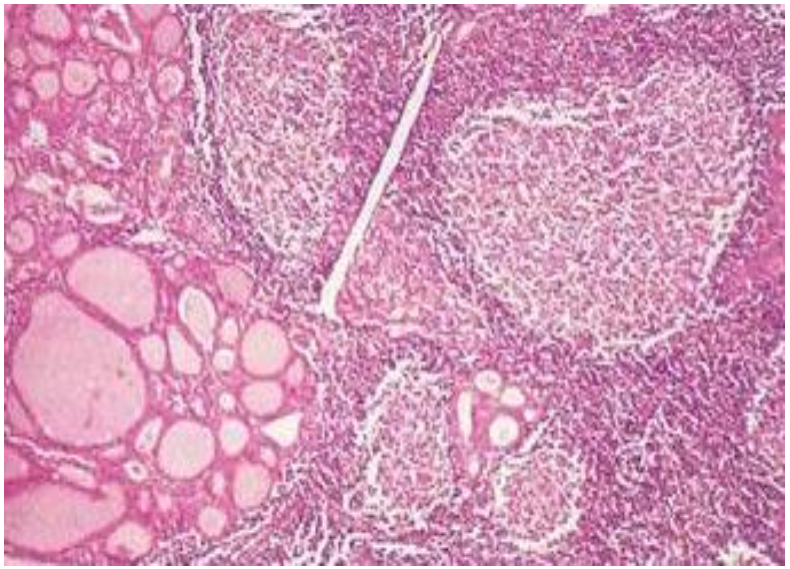
Tertiary: Hypothalamic dysfunction (rare).

Peripheral resistance to the action of thyroid hormone.

H a s h i m o t o ô s

(Chronic, Lymphocytic)

- Most common cause of hypothyroidism
- Result of antibodies to TPO, TBG
- Commonly presents in females 30-50 yrs.
- Usually asymptomatic
- Lab values
  - ï High TSH
  - ï Low T_4
  - ï Anti-TPO Ab
  - ï Anti-TBG Ab
- Treat with Levothyroxine



Hyperthyroid

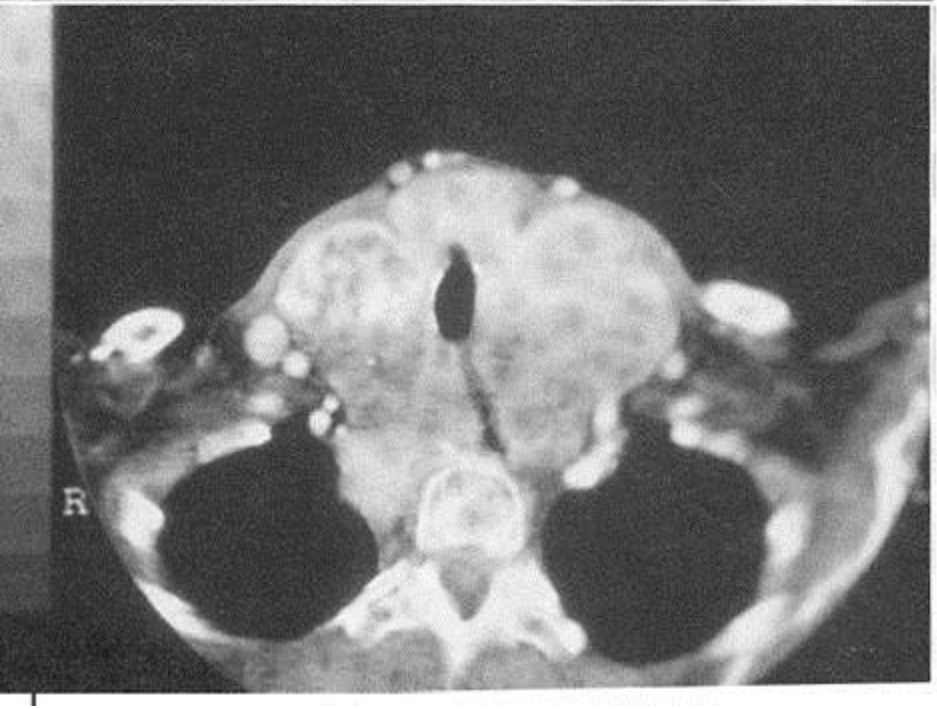
- Symptoms
  - Palpitations, nervousness, fatigue, diarrhea, sweating, heat intolerance
- Signs
  - Thyroid enlargement (?), tremor
- Lab workup
  - TSH
  - FT4
  - RAIU
- Other Labs
  - Anti-TSH-R Ab, Anti-TPO Ab, Anti-TBG Ab
  - FT3
  - FNA
  - MRI, US

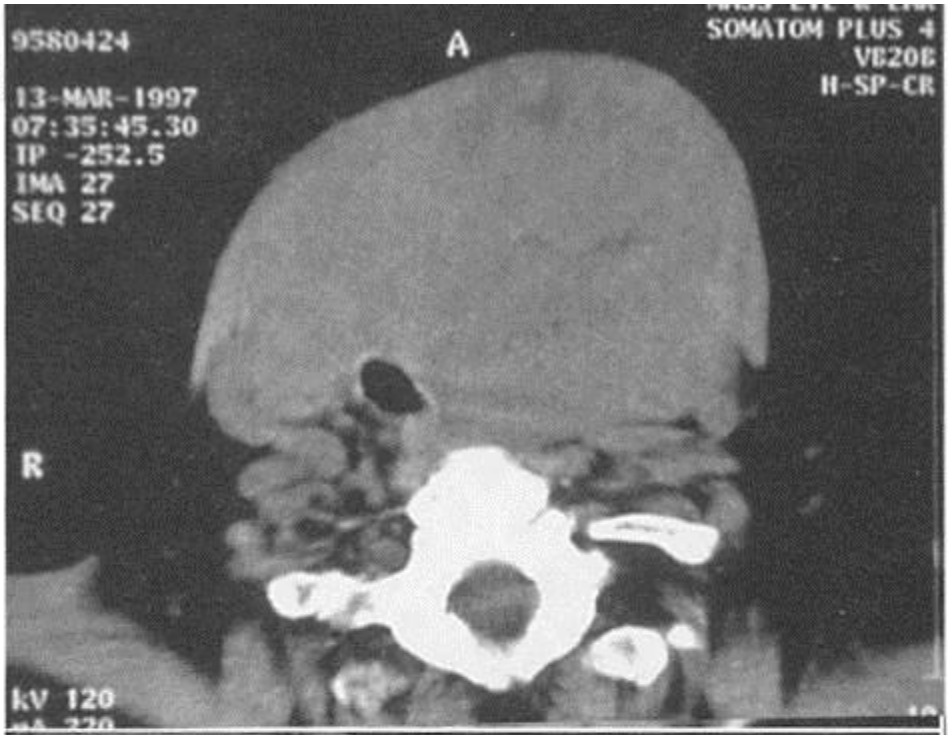
Hyperthyroid

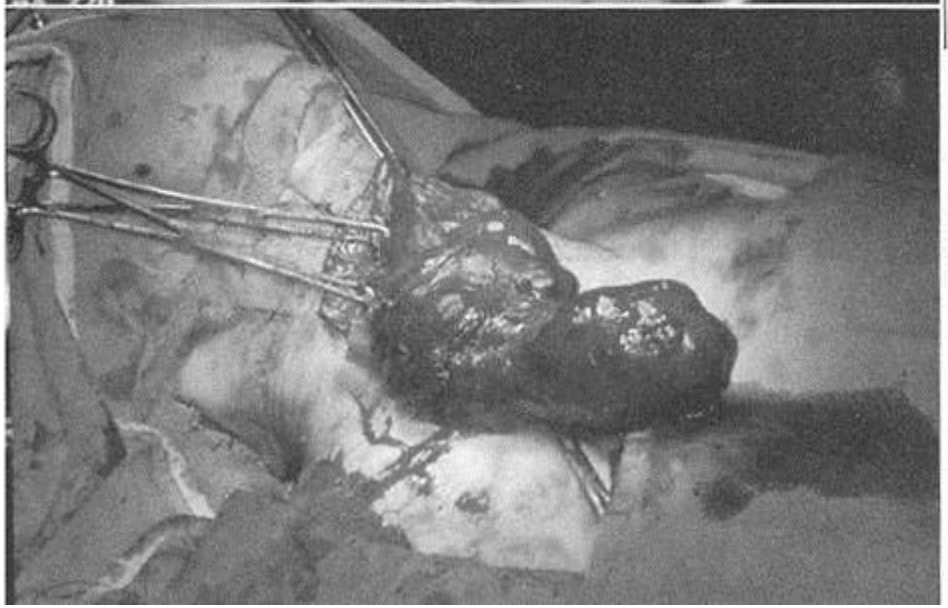
- Common Causes
  - *Graves
  - Adenoma
  - Multinodular Goiter
  - *Subacute Thyroiditis
  - *Hashimotoôs Thyroiditis
- Rare Causes
  - Thyrotoxicosis factitia, struma ovarii, thyroid metastasis, TSH-secreting tumor, hamburger

Goiter

- Endemic goiter
  - Caused by dietary deficiency of Iodide
  - Increased TSH stimulates gland growth
  - Also results in cretinism
- Goiter in developed countries
  - Hashimotoôs thryoiditis
  - Subacute thyroiditis
- Other causes
  - Excess Iodide (Amiodarone, Kelp, Lithium)
  - Adenoma, Malignancy
  - Genetic / Familial hormone synthesis defects


R


9580424
A
SOMATOM PLUS 4
VB20B
H-SP-CR
13-MAR-1997
07:35:45.30
IP -252.5
IMA 27
SEQ 27
R
kV 120



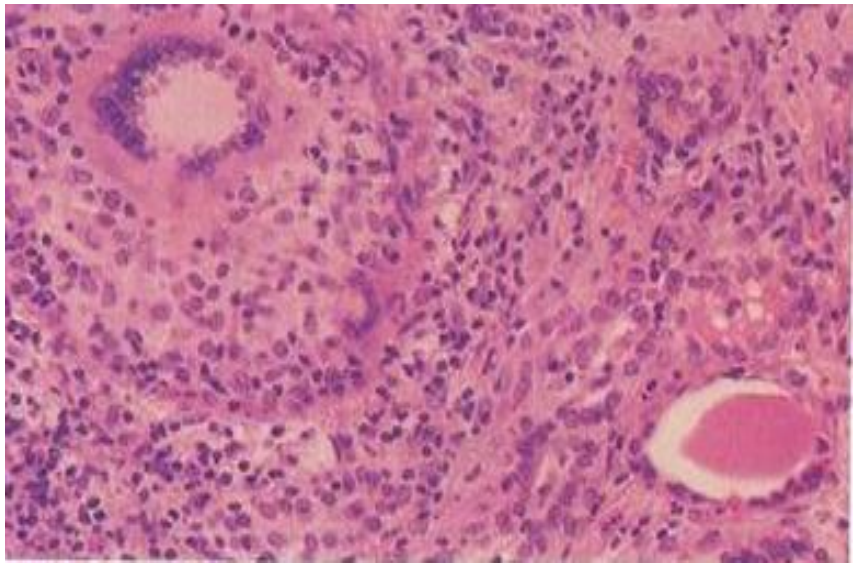
Graves

- Most common cause of hyperthyroidism
- Result of anti-TSH receptor antibodies
- Diagnosis
  - Symptoms of hyperthyroidism
  - Clinical exopthalmos and goiter
  - Low TSH, normal/high FT_4, anti-TSH Ab (Optional)
- If no clinical findings I^{123} may demonstrate increased uptake.
- Treatments
  - Medical – Propothyouracil, Methimazole, Propranolol
  - Surgical – Subtotal Thyroidectomy
  - Radiation – RAI ablation [I^{131}(mCi/g) x weight / %RAIU]

Subacute Thyroiditis

(DeQuervainôs, Granu

- Acute viral infection of thyroid gland
- Presents with viral prodrome, thyroid tenderness, and hyperthyroid symptoms
- Lab values
  - Variable TSH, T_4
  - High ESR
  - No antibodies
- Treatment
  - APAP, NSAID
  - Prednisone (?)
  - Levothyroxine (?)

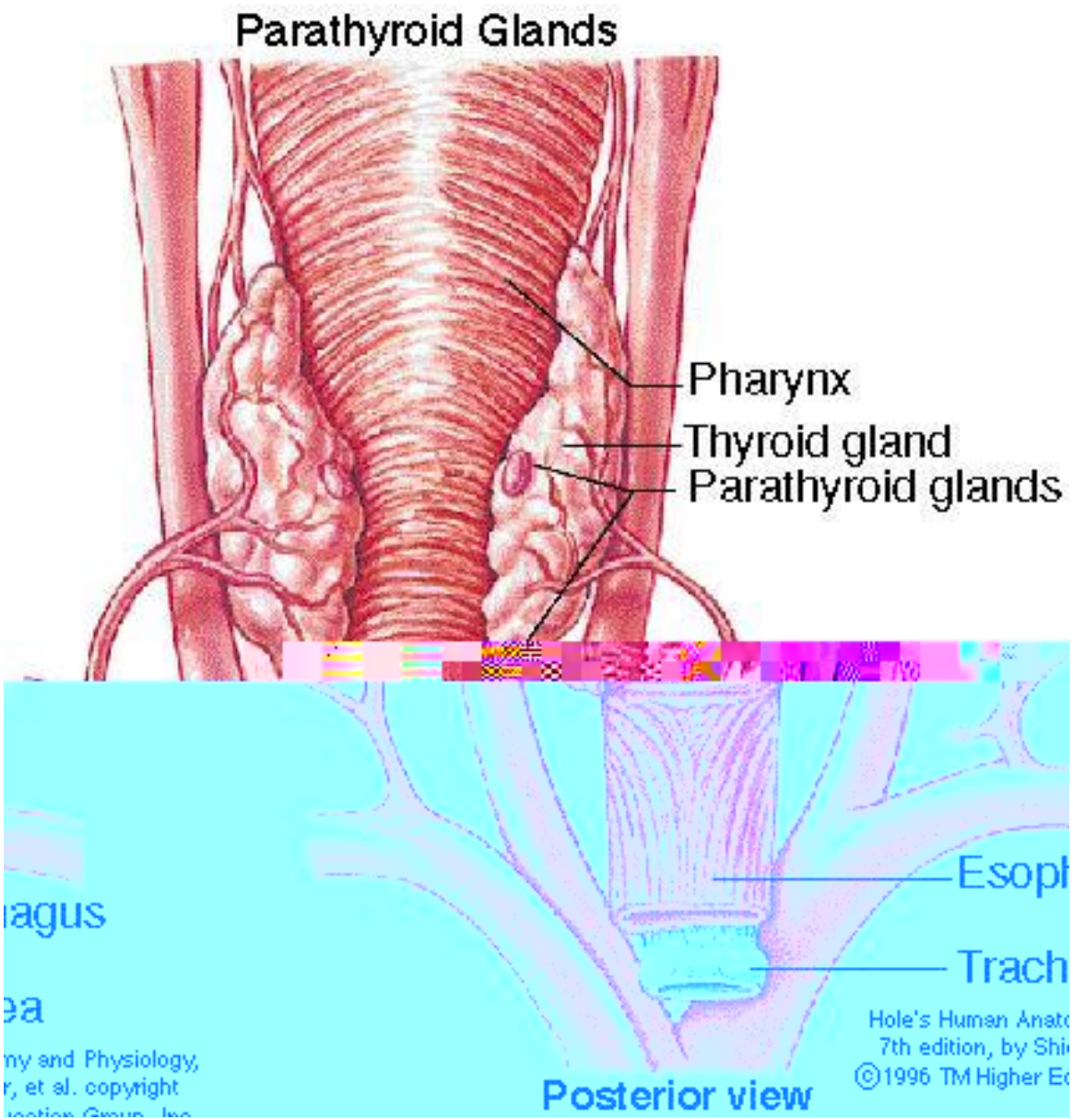


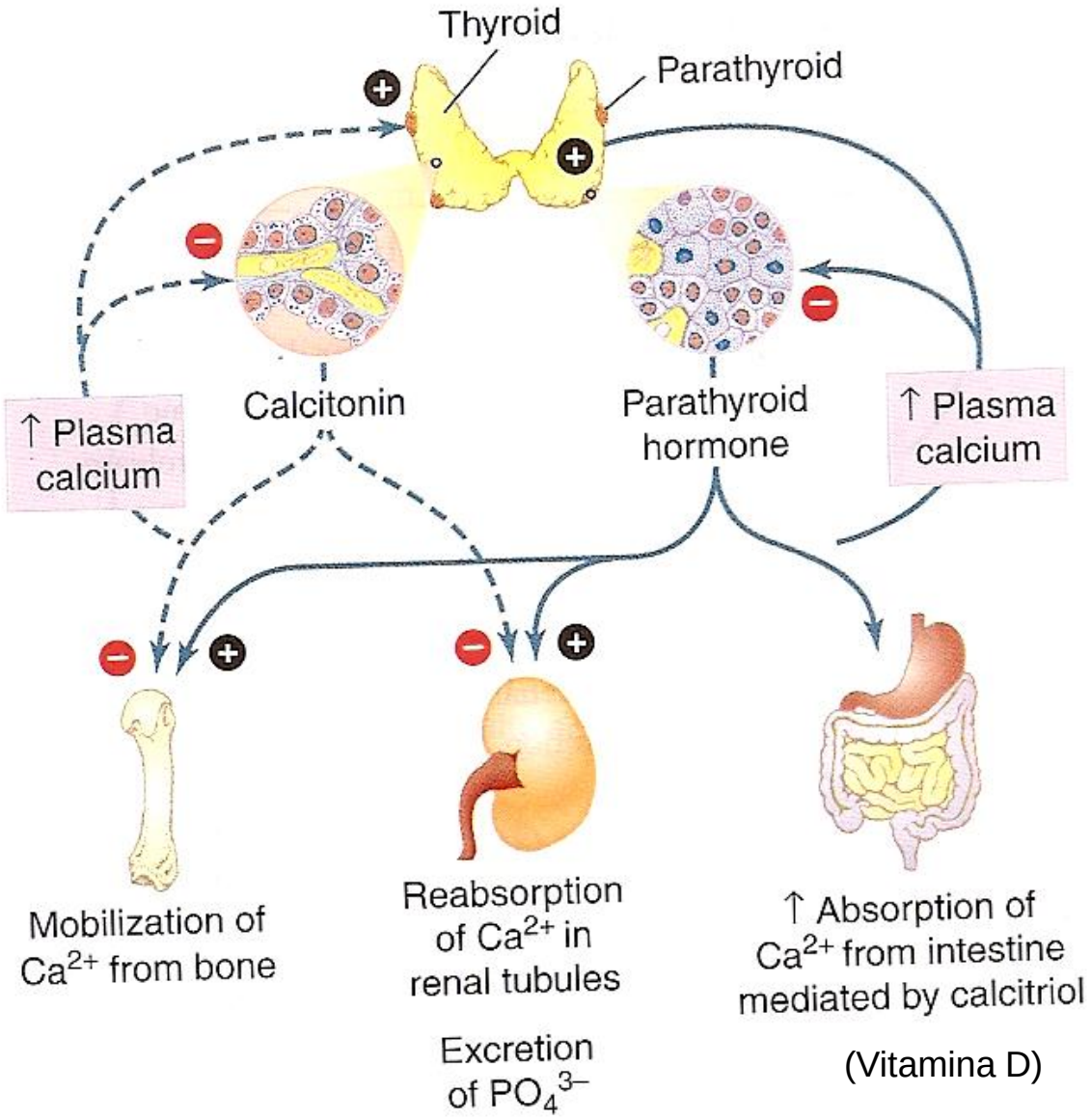
Calcium Regulation

Parathyroid

Parathyroid Gland

- This gland only secretes one hormone: Parathyroid Hormone (or PTH)
- PTH function
  - increases blood calcium (Ca^{2+}) levels and decreases blood phosphate (PO_4^{2-}) levels




Thyroid
Parathyroid
Calcitonin
Parathyroid hormone
↑ Plasma calcium
↑ Plasma calcium
Mobilization of Ca^{2+} from bone
Reabsorption of Ca^{2+} in renal tubules
Excretion of PO_4^{3-}
↑ Absorption of Ca^{2+} from intestine mediated by calcitriol
(Vitamina D)

PTH function *(continued)*

- How does PTH work?
  - PTH causes Ca^{2+} & PO_4^{2-} to be released from bone into blood (by increasing osteoclast activity)
  - PTH causes the kidneys to remove PO_4^{2-} ions from the urine
  - PTH increases vitamin D production, so that you absorb more Ca^{2+} during digestion
- PTH is regulated by blood calcium levels-- not by other glands!

Parathyroid Hormone

- Produced by Parathyroid Chief cells
- Secreted in response to low iCa^{++}
- Stimulates renal conversion of 25-$(OH)D_3$ to 1,25-$(OH)_2D$ which increases intestinal Ca^{++} absorption
- Directly stimulates renal Ca^{++} absorption and PO_4^{3-} excretion
- Stimulates osteoclastic resorption of bone

Hypocalcemia

- Decreased PTH
  - Surgery
  - Hypomagnesemia
  - Idiopathic
- Resistance to PTH
  - Genetic disorders
  - Bisphosphonates
- Vitamin D abnormalities
  - Vitamin D deficiency
  - Rickets (VDR or Renal hyroxylase abnormalities)
- Binding of Calcium
  - Hyperphosphate states (Crush injury, Tumor lysis, etc.)
  - Blood Transfusion (Citrate)

Hypercalcemia

- Hyperparathyroidism
  - Primary, Secondary, Tertiary
  - MEN Syndromes
- Malignancy
  - Humoral Hypercalcemia
  - PTHrP (Lung Cancer)
  - Osteoclastic activity (Myeloma, Lymphoma)
- Granulomatous Diseases
  - Overproduction of 1,25 $(OH)_2D$
- Drug-Induced
  - Thiazides
  - Lithium
  - Milk-Alkali
  - Vitamin A, D
- Renal failure

Hypercalcemia

- Signs & Symptoms
  - Bones (Osteitis fibrosa cystica, osteoporosis, rickets)
  - Stones (Renal stones)
  - Groans (Constipation, peptic ulcer)
  - Moans (Lethargy, depression, confusion)
- Medical Treatment
  - SERMôs (Evista)
  - Bisphosphonates (Pamidronate)
  - Calcitonin (for severe cases)
  - Saline diuresis
  - Glucocorticoids (for malignant/granulomatous diseases)
  - Avoid thiazide diuretics
- Surgical Treatment
  - Single vs. Double adenoma simple excision
  - Multiple Gland hyperplasia total parathyroid with autotransplant vs. 3½ gland excision

Primary Hyperparathyroidism

- Diagnosis
  - Signs & Symptoms
  - Elevated serum calcium
  - Elevated PTH
- Etiology
  - Solitary Adenoma (80-85%)
  - Double Adenomas (2-4%)
  - Muliple Gland Hyperplasia (10-30%)
  - Parathyroid Carcinoma (0.5%)
  - MEN syndromes (10% of MGH have MEN 1)

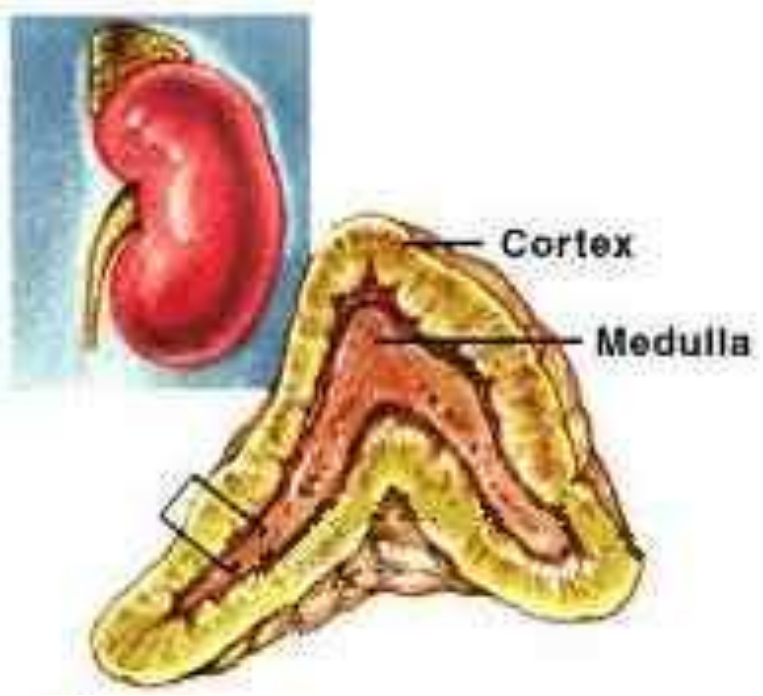
Parathyroidectomy

- 1990 NIH Guidelines
  - Serum Ca++ > 12 mg/dl
  - Hypercalciuria > 400 mg/day
  - Classic symptoms
    - Nephrolithiasis
    - Osteitis fibrosa cystica
    - Neuromuscular disease
  - Cortical bone loss with DEXA Z score < -2
  - Reduced creatinine clearance
  - Age < 50
- Other considerations
  - Vertebral osteopenia
  - Vitamin D deficency
  - Perimenopause

Adrenal Glands

An adrenal gland is found on top of each kidney. Each adrenal gland has two regions that carry out **separate** functions!

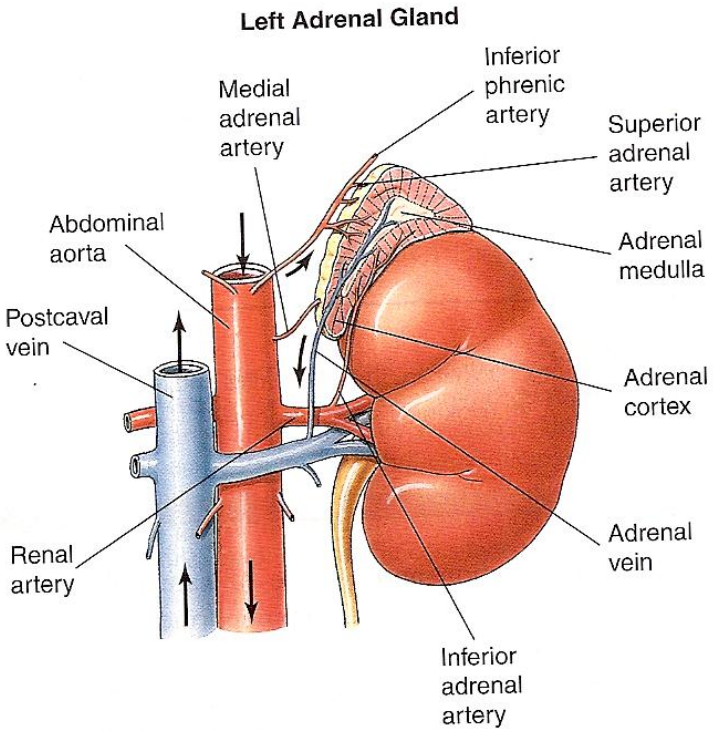
- The adrenal medulla
- The adrenal cortex



Glándulas Adrenales

Sobre los riñones.

- Médula adrenal.
- Corteza adrenal



Glándulas Adrenales

Médula adrenal

- Estimulada por SNA simpático
- Secreción de catecolaminas

- **Adrenalina:** respuesta de lucha-huida
  - Incrementa actividad cardíaca y PA.
  - Incrementa ventilación pulmonar.
  - Incrementa la TMB.
  - Incrementa catabolismo de HC (glucogenólisos y glucolisis) y de lípidos
- **Noradrenalina**
  - Sólo un 20%