

# **Patofyziologie poruch endokrinního systému II**

# Mezibuněčná komunikace

- Neurokrinní - neuroendokrinní
- Endokrinní (hormony)
- Parakrinní (cytokiny)
- Autokrinní (různé)

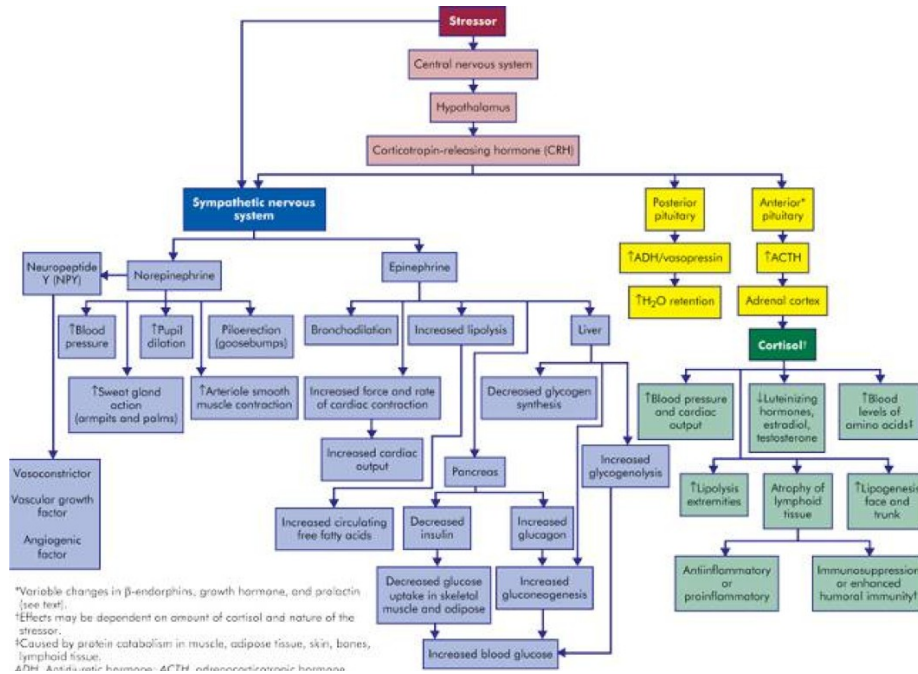
# Hormones

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

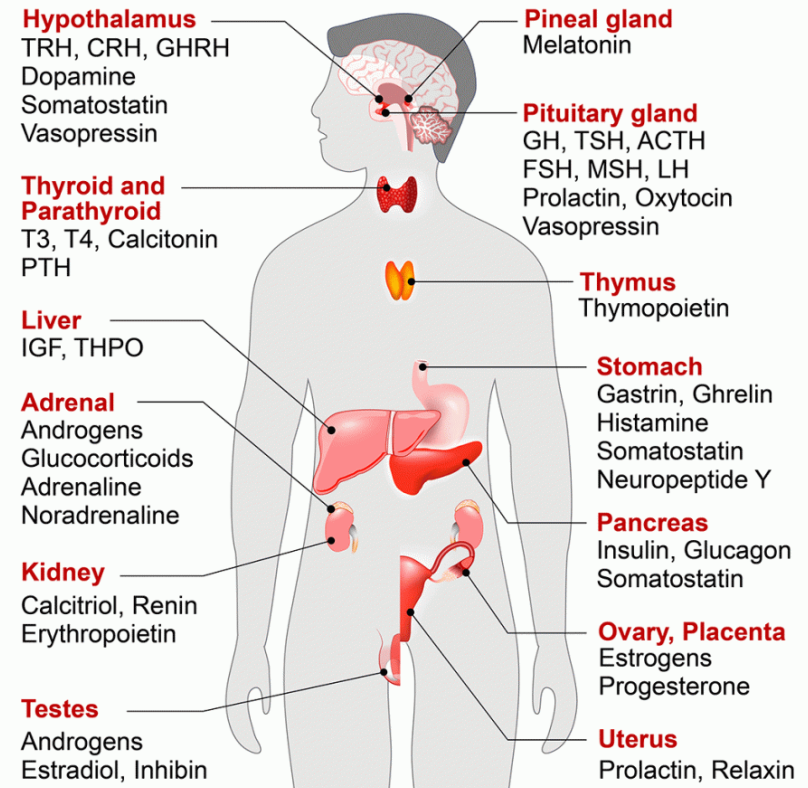
# Endocrine regulation

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

# Endokrinní systém

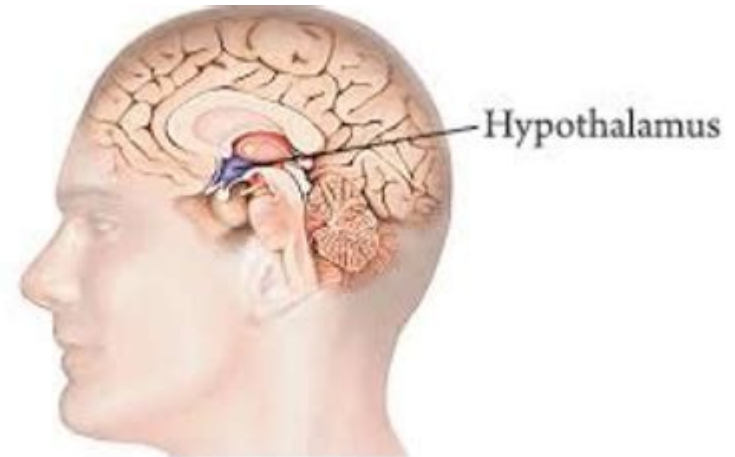


# HORMONES



# 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), Salsolinol (PRL)
- Statins
  - Somatostatin (GH), Dopamine (PRL)

# Endokrinní hypotalamus

## Uvolňovací faktory pro

Růstový hormon  
(GHRH)  
Štítnou žlázu (TRH)  
Kortikotropin (CRH)  
Pohlavní hormony  
(FSH RH, LH RH)

## Blokující faktory pro

Prolaktin (PIF)  
Růstový hormon

Pro přední lalok  
hypofýzy

## Hormony

Vasopresin (ADH)  
Oxytocin

Pro zadní lalok  
hypofýzy





# Hypothalamus - poruchy

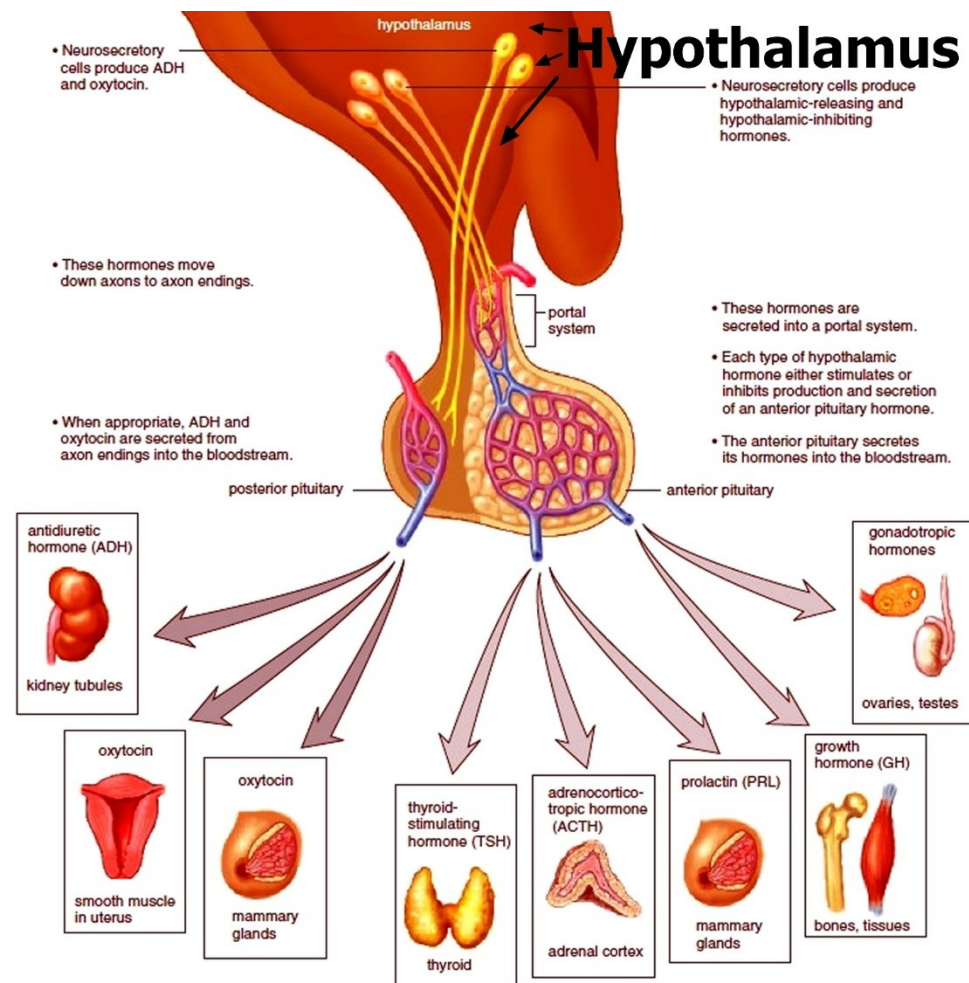
Příčiny: ↑ tu, ↓ trauma, kongenitální změny, poruchy prokrvení, autoimunita

Hypersekrece: jednotlivé hormony – typické příznaky

Hyposekrece:

hypotalamický panhypopituitarismus = snížení sekrece všech hormonů hypofýzy kromě prolaktinu

- porucha sexuálního vyžívání, spermatogeneze a menstruačního cyklu (FSH, LH)
- snížená odpověď na zátěž (stres) (CRH)
- hypotyreóza (TRH)
- poruchy růstu (GHRH)

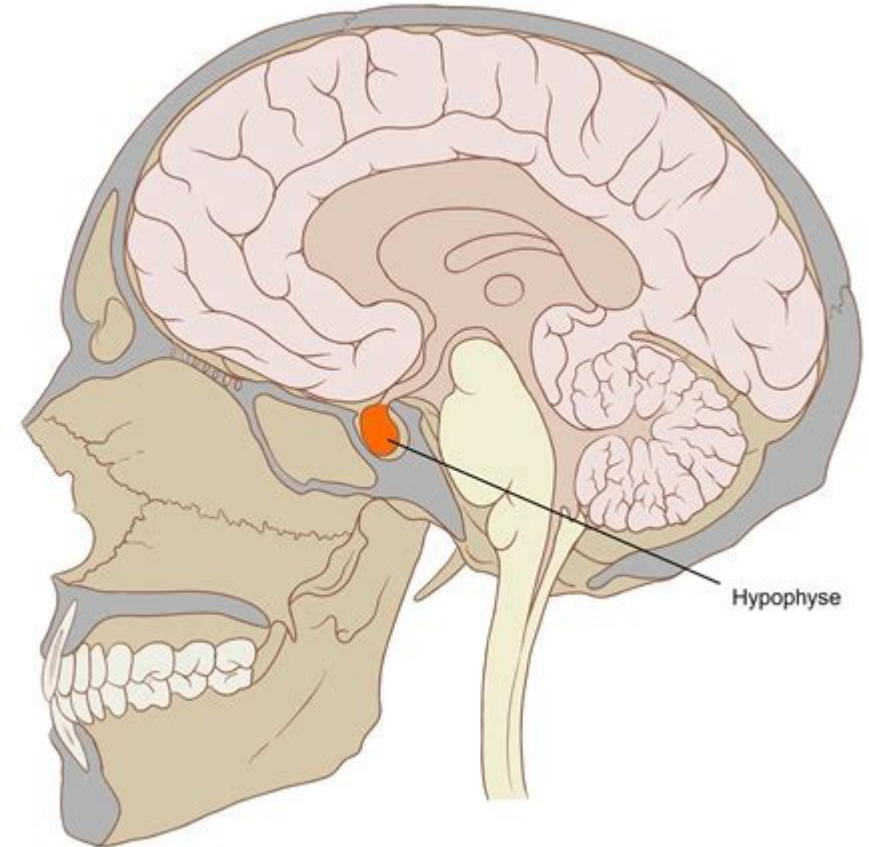


# Hypothalamus

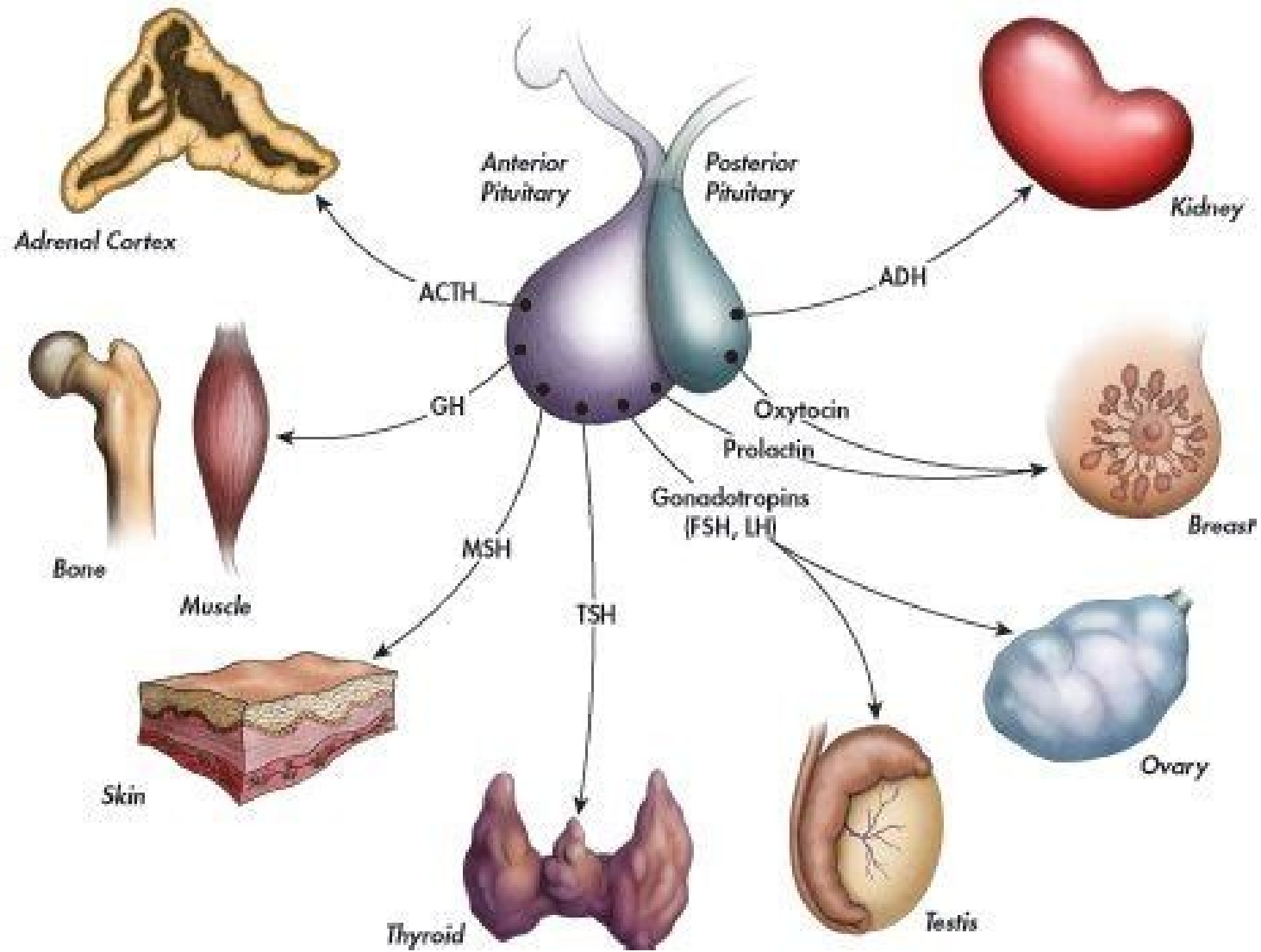
- Hypothalamic - pituitary axis
- Control of the production and release of pituitary hormones
- Pulsatile secretion
- Specific membrane receptors
- Second messenger
- Autoregulation

# Pituitary

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



# Hypofýza

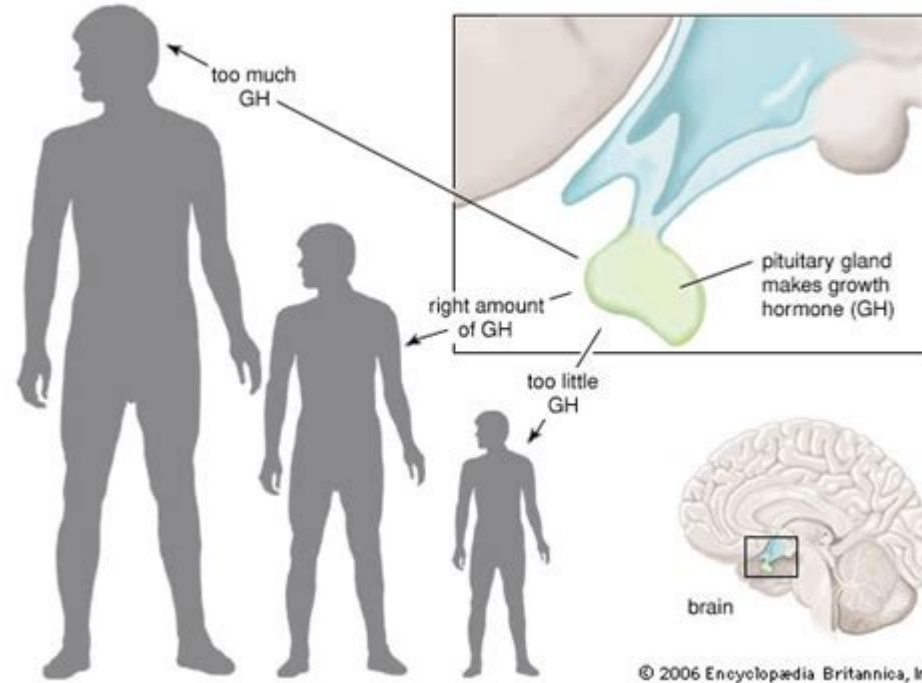


# Hypopituitarism

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

# Poruchy rústového hormonu

- GH overproduction
  - Gigantism
    - Before puberty
  - Acromegaly
    - After puberty



# Poruchy růstového hormonu - akromegalie



Age 9



Age 16



Age 33



Age 52



# Poruchy sekrece ADH

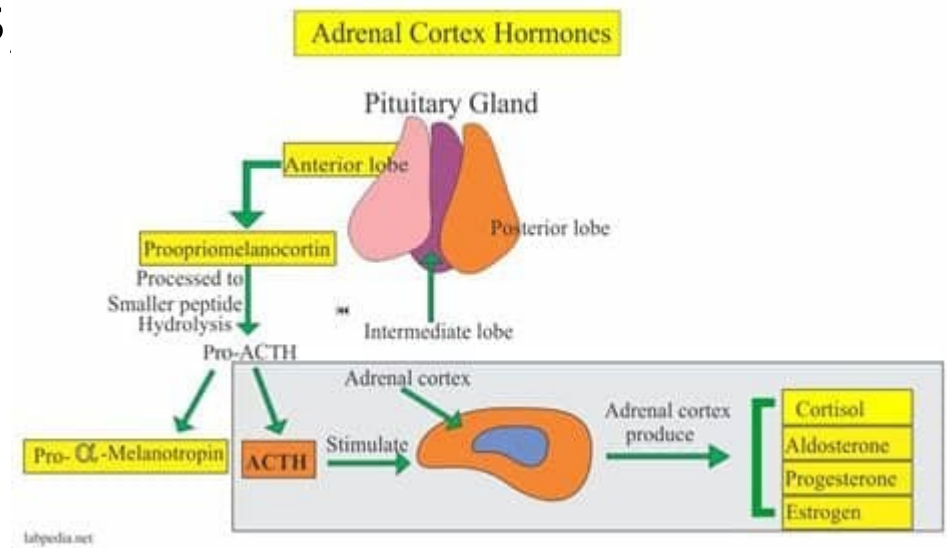
- ADH insufficiency
  - Diabetes insipidus
    - Polydipsia, polyuria
- Overproduction ADH
  - Syndrome of IADH
    - Hypoosmolarity of plasma, hyponatremia, oliguria

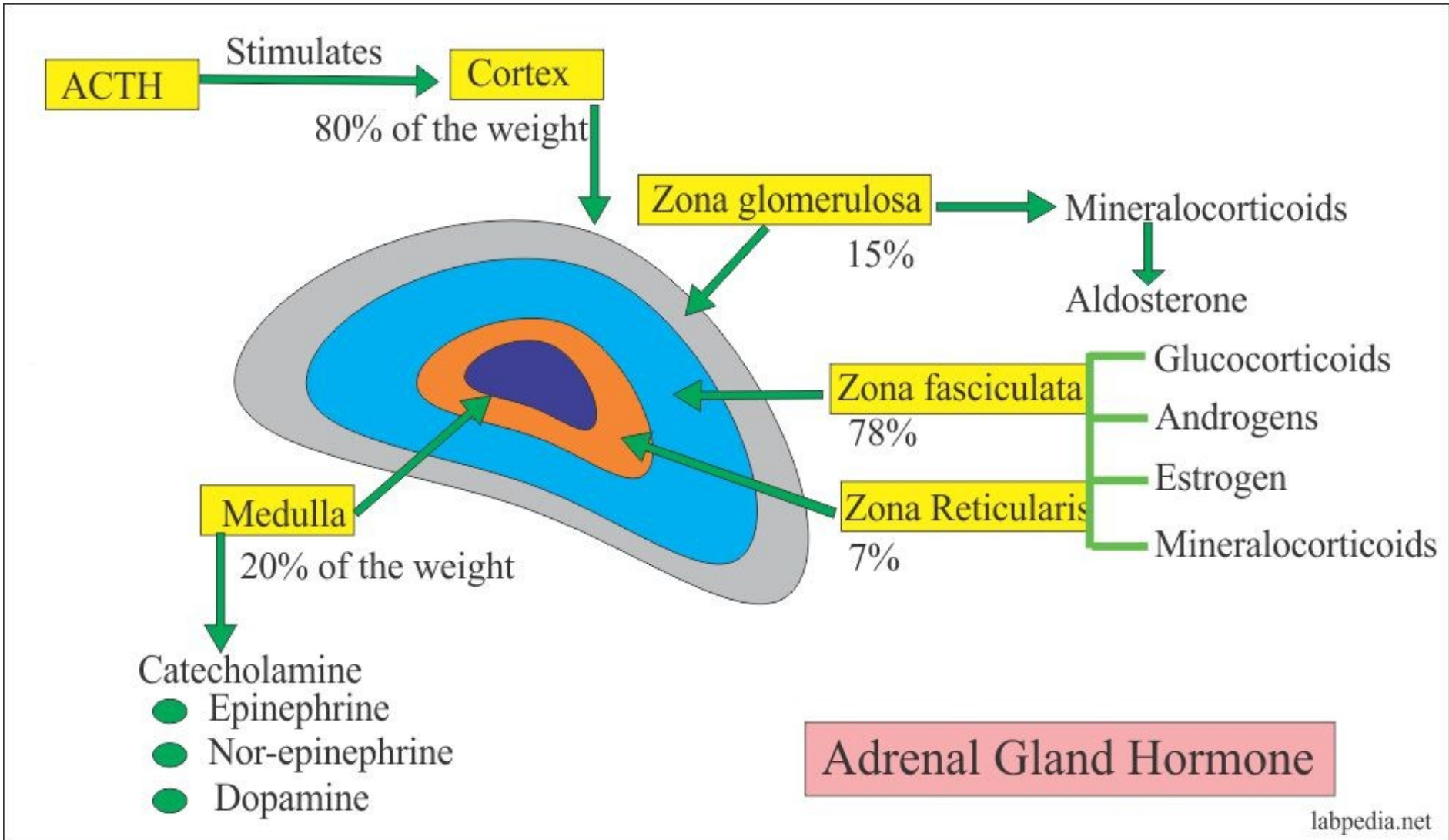


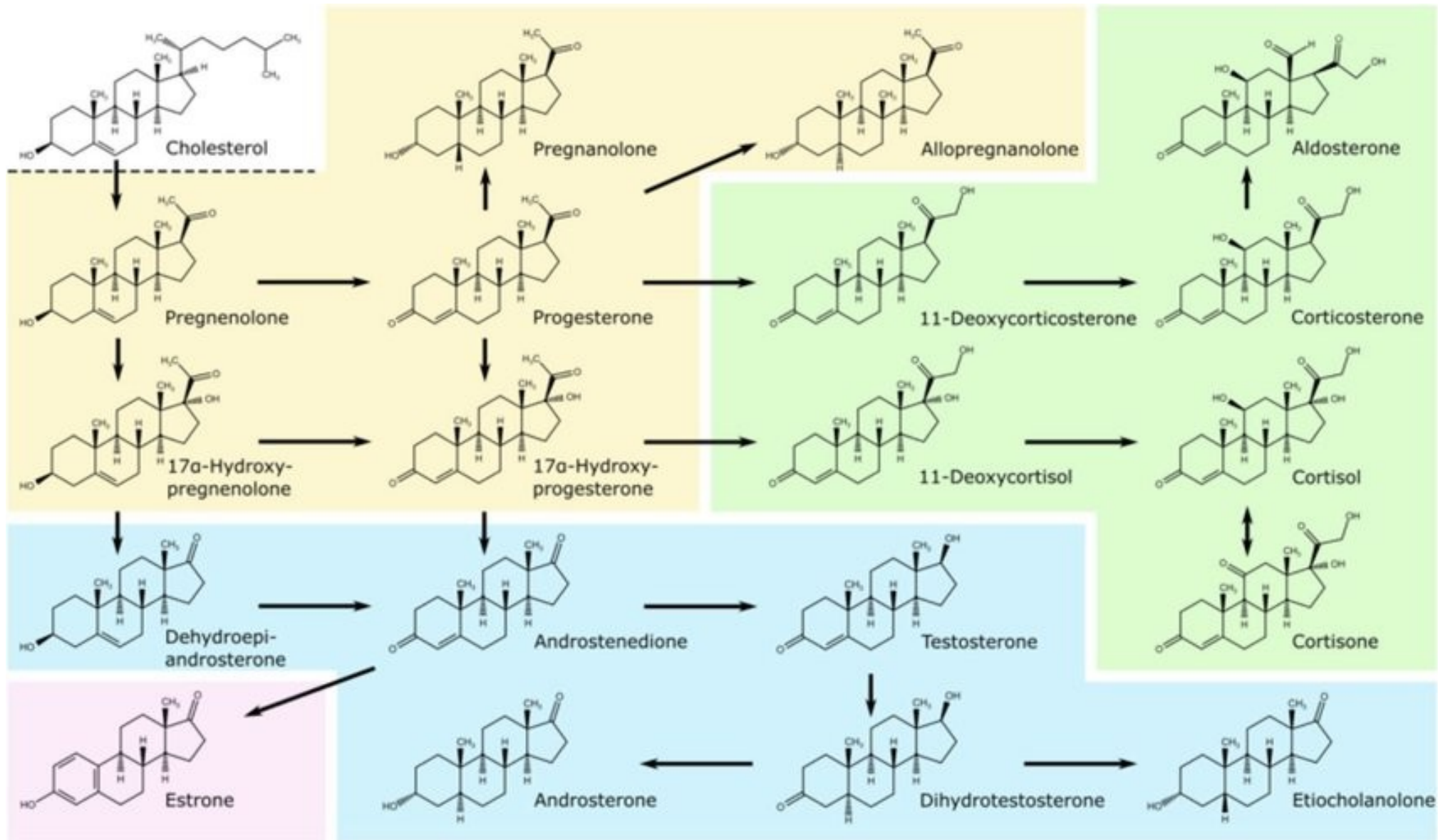
# Adrenal glands



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







# 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

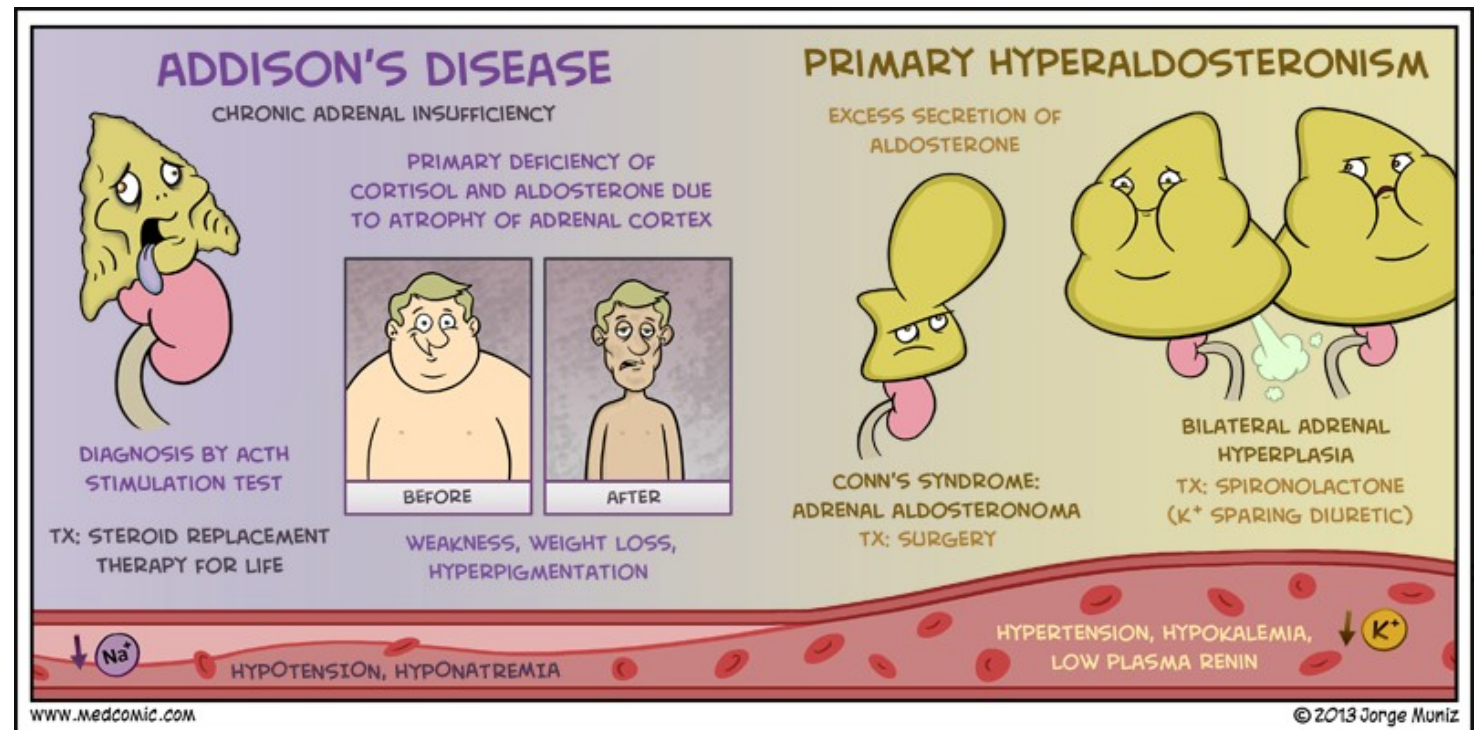
- Aldosterone insufficiency
  - Hypotension, hyponatremia, hyperkalemia
- Skin pigmentation
  - Pro-Opioid-Melanocyte-Stimulating-Hormone
- ACTH increased (differs from secondary adrenal insufficiency)



# Conn's disease

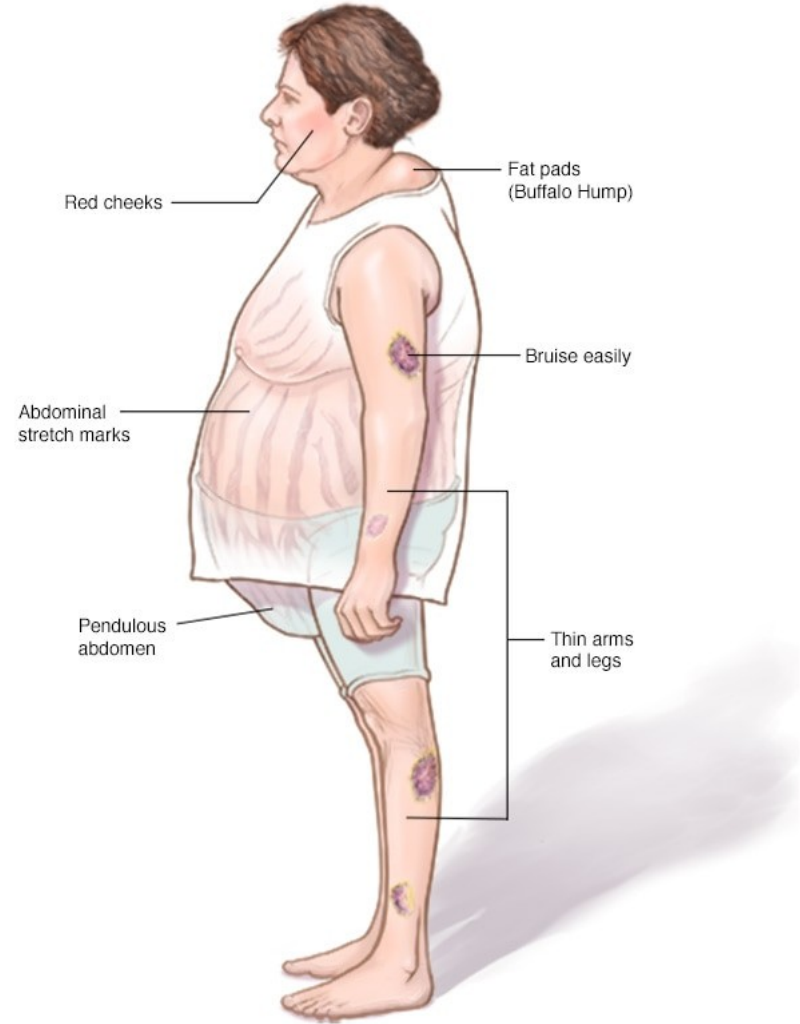
- Primary hyperaldosteronism
  - Mostly unilateral endocrine active tumor

- Hypertension
- Hyponatremia
- Hypokalemia



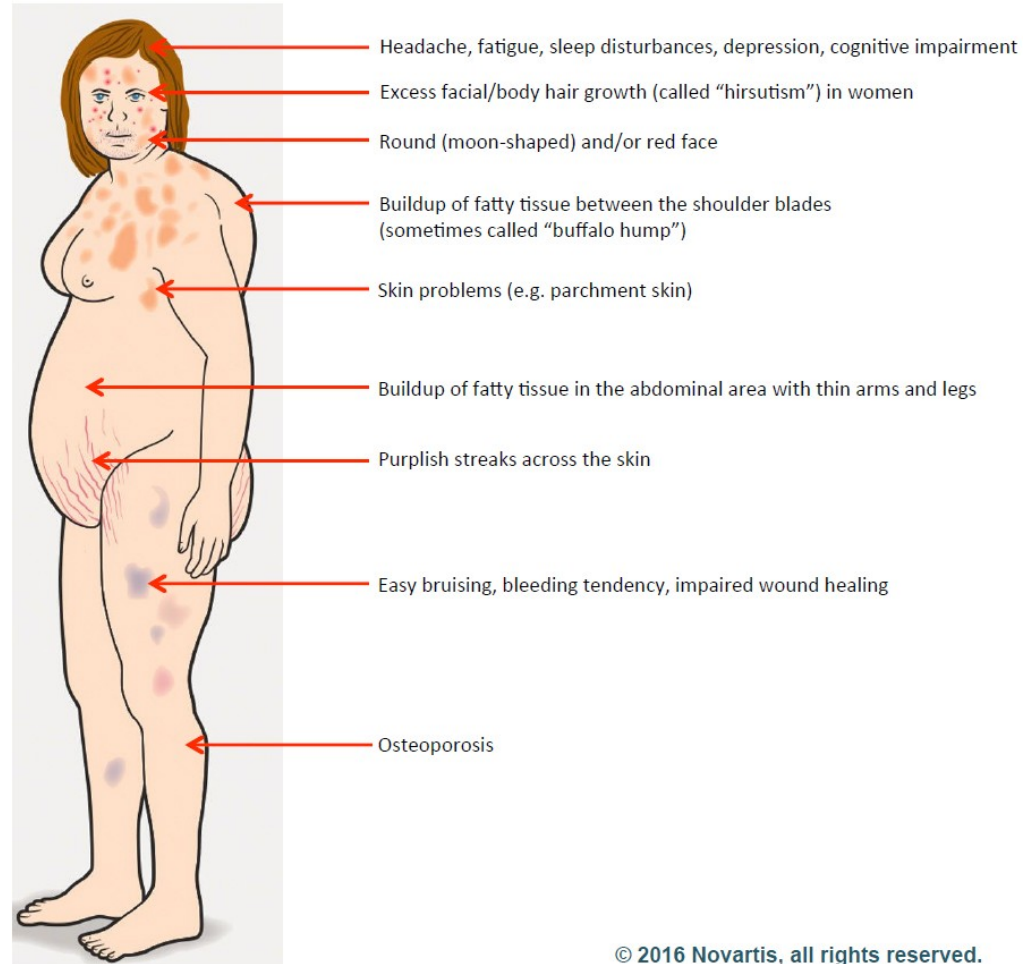
# Cushing's syndrome

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



# Cushing's syndrome

- Central obesity
- Hypertension
- Osteoporosis
- Reduced growth
- Mental changes



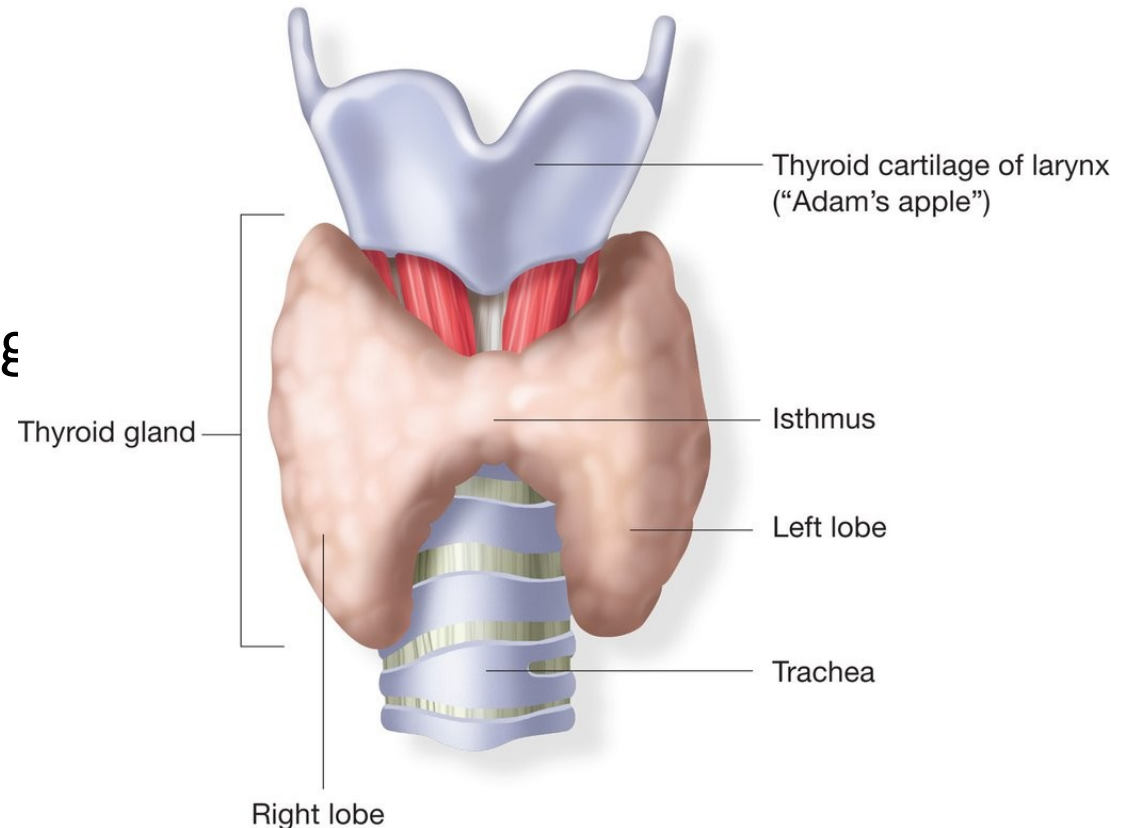
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- Hirsutism, acne, oligomenorrhea



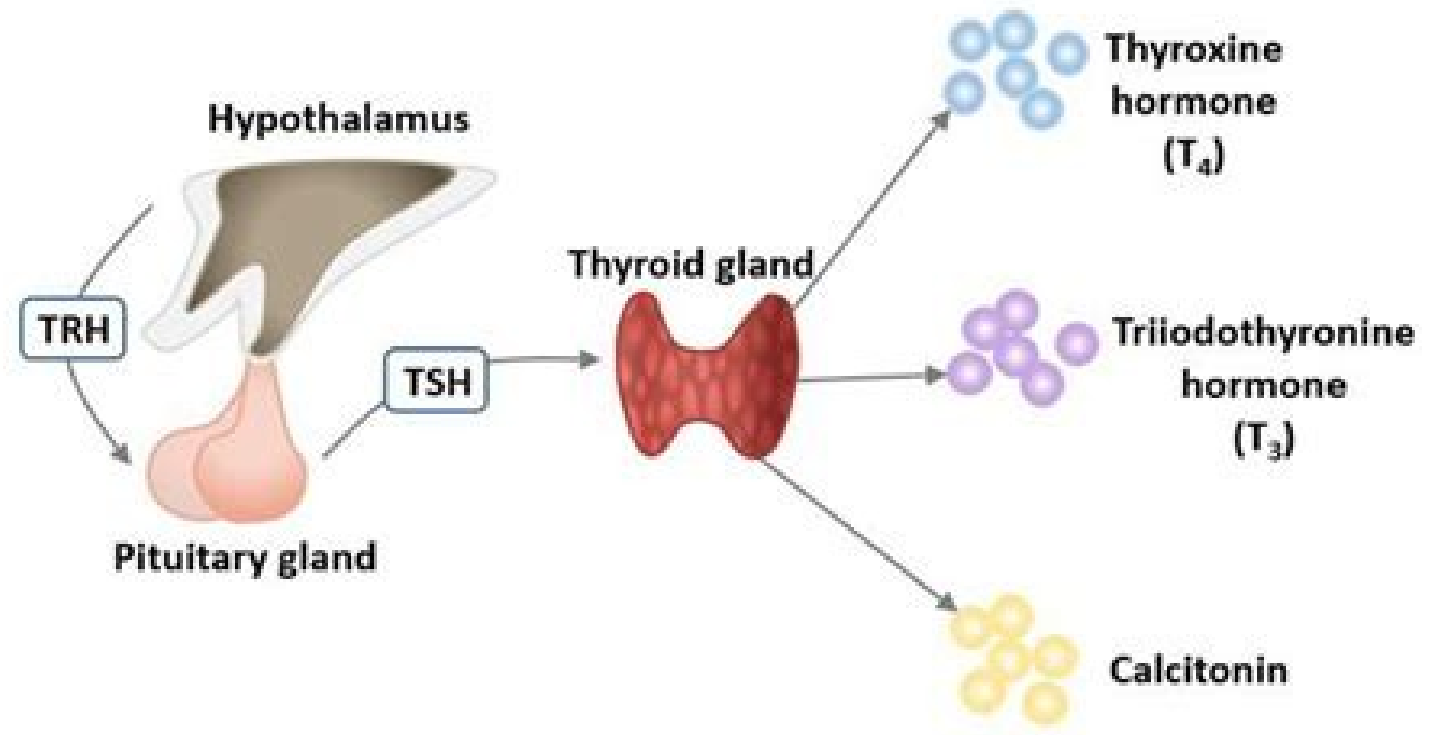
# Thyroid gland – physiology

- 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

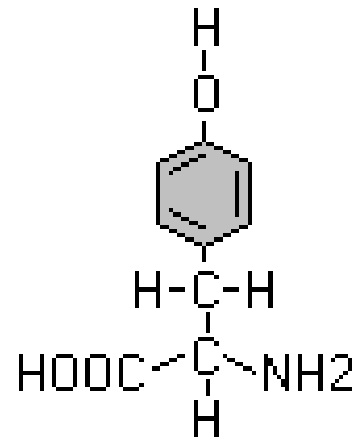


# Thyroid

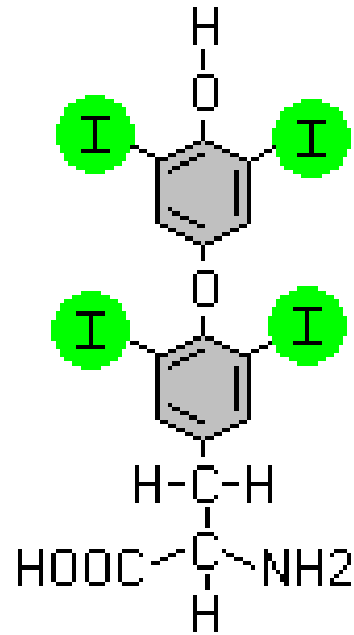
- Iodine is rare
- Ubiquitary receptors
- Highly potent action
- Very common disorders
  - 5% women
  - 0,5% men



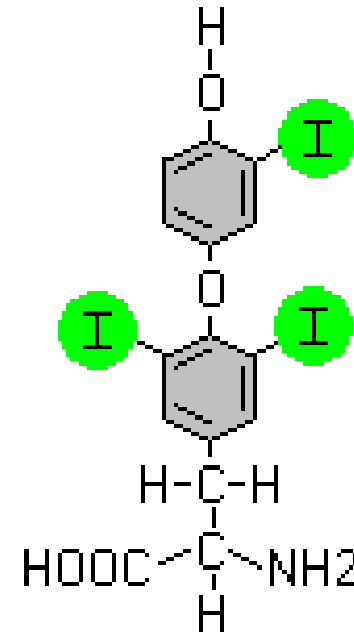
# Thyroid hormones



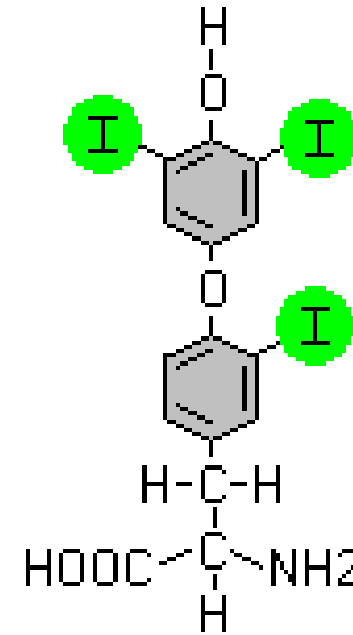
**Tyrosine**



**Thyroxine (T4)**

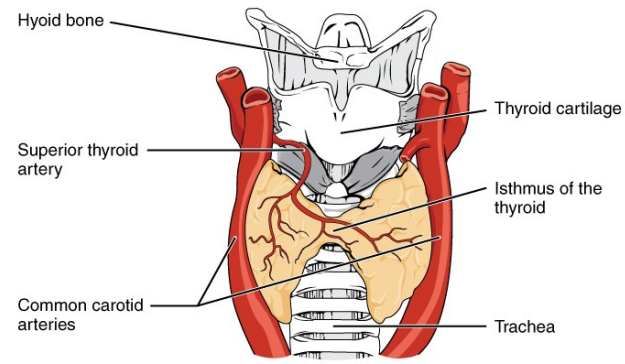


**Triiodothyronine (T3)**

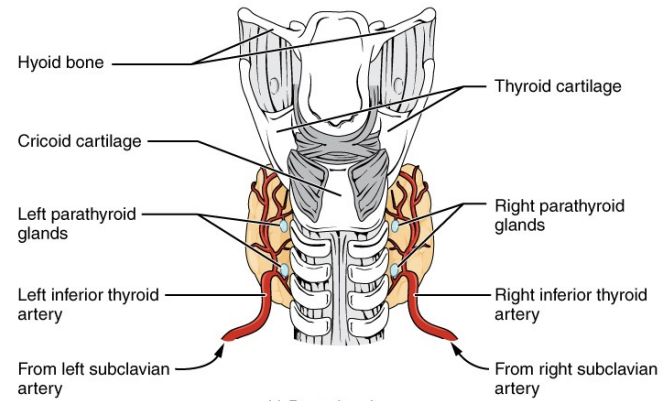


**"Reverse T3"  
(inactive)**

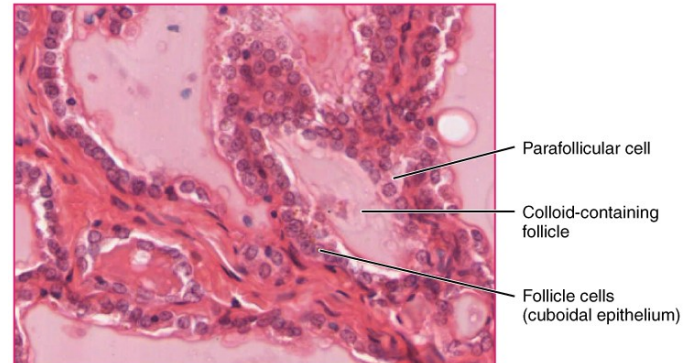
# Thyroid gland



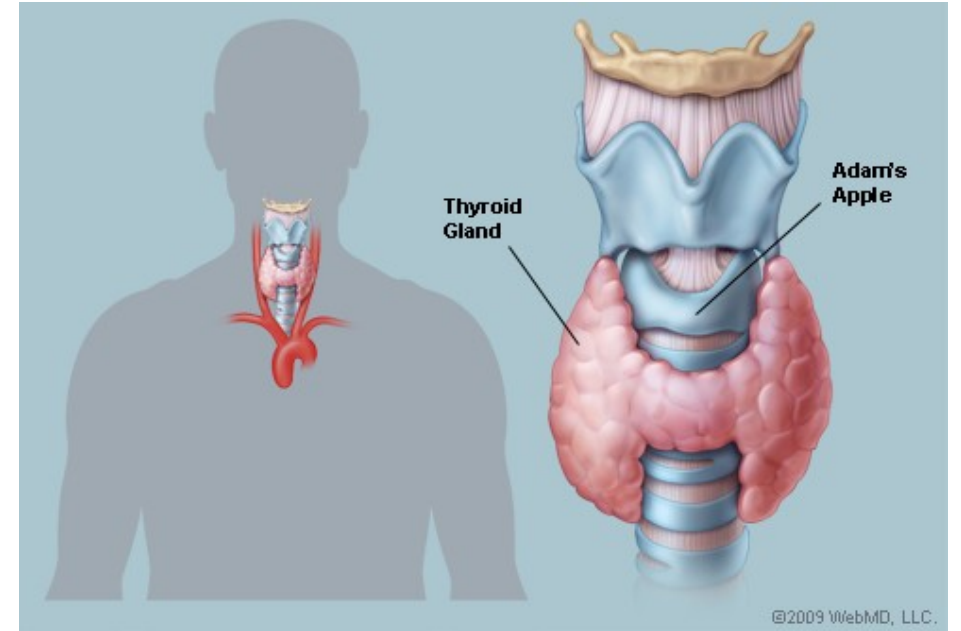
a) Anterior view



b) Posterior view

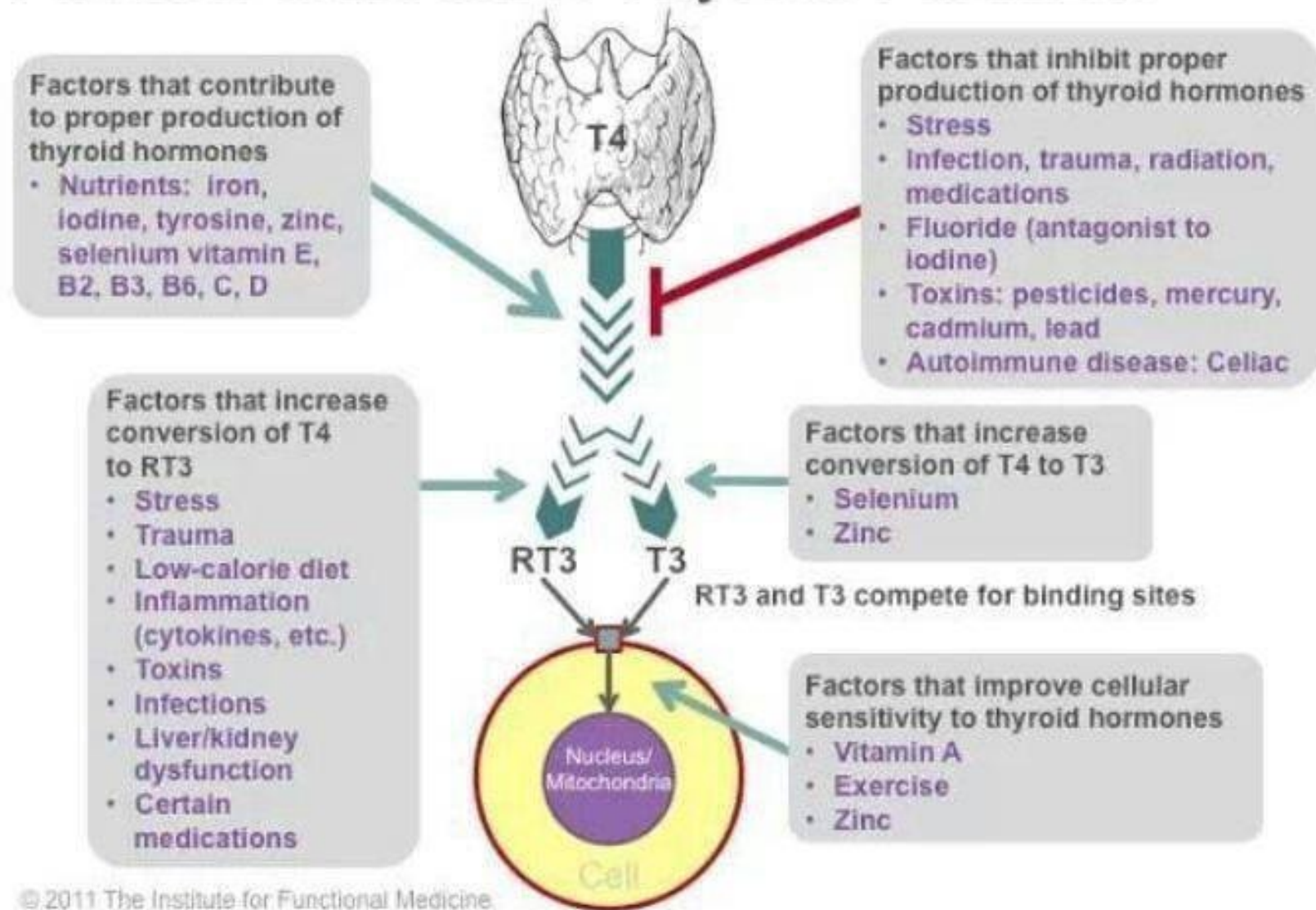


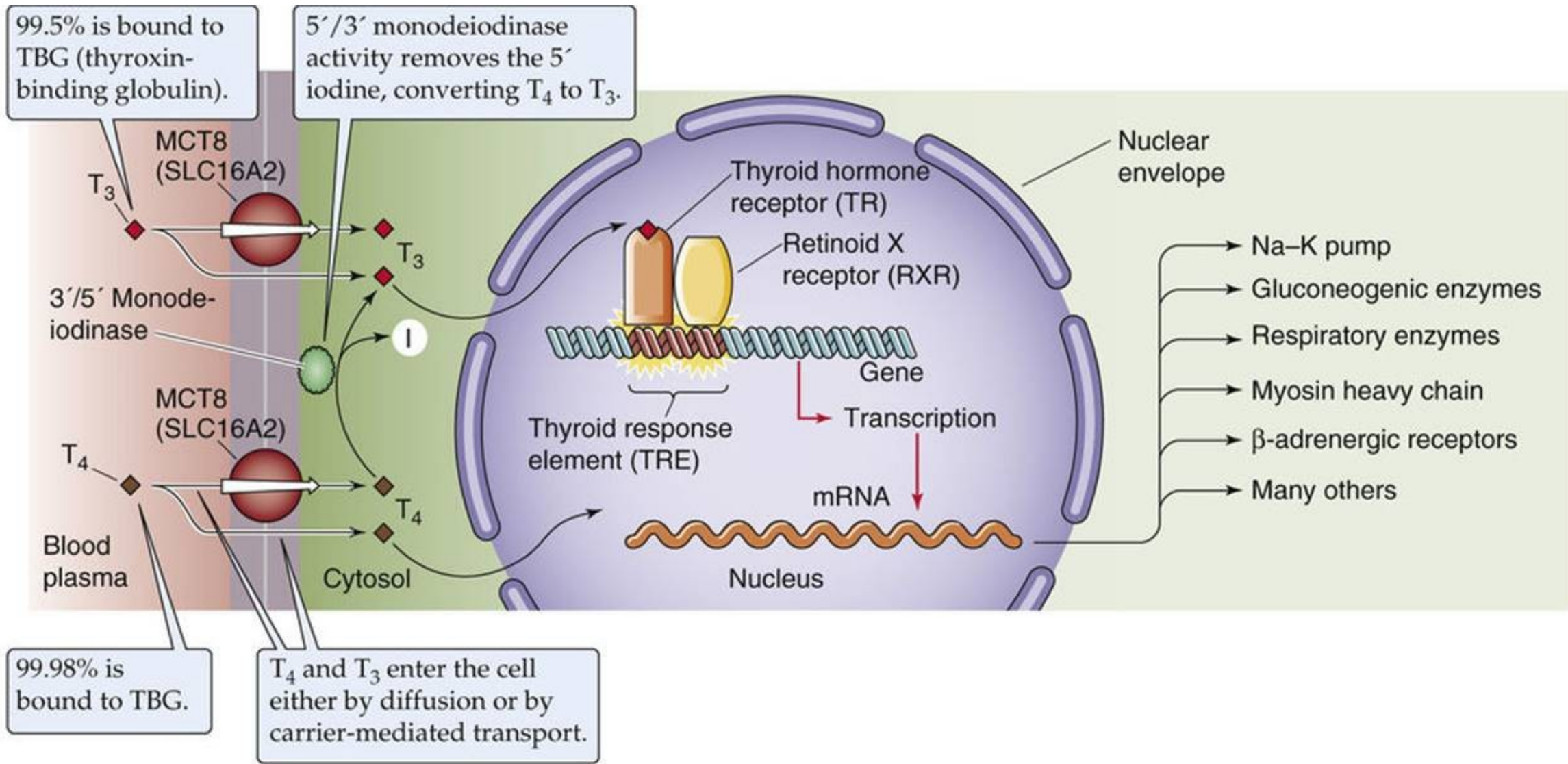
c) Thyroid follicle cells

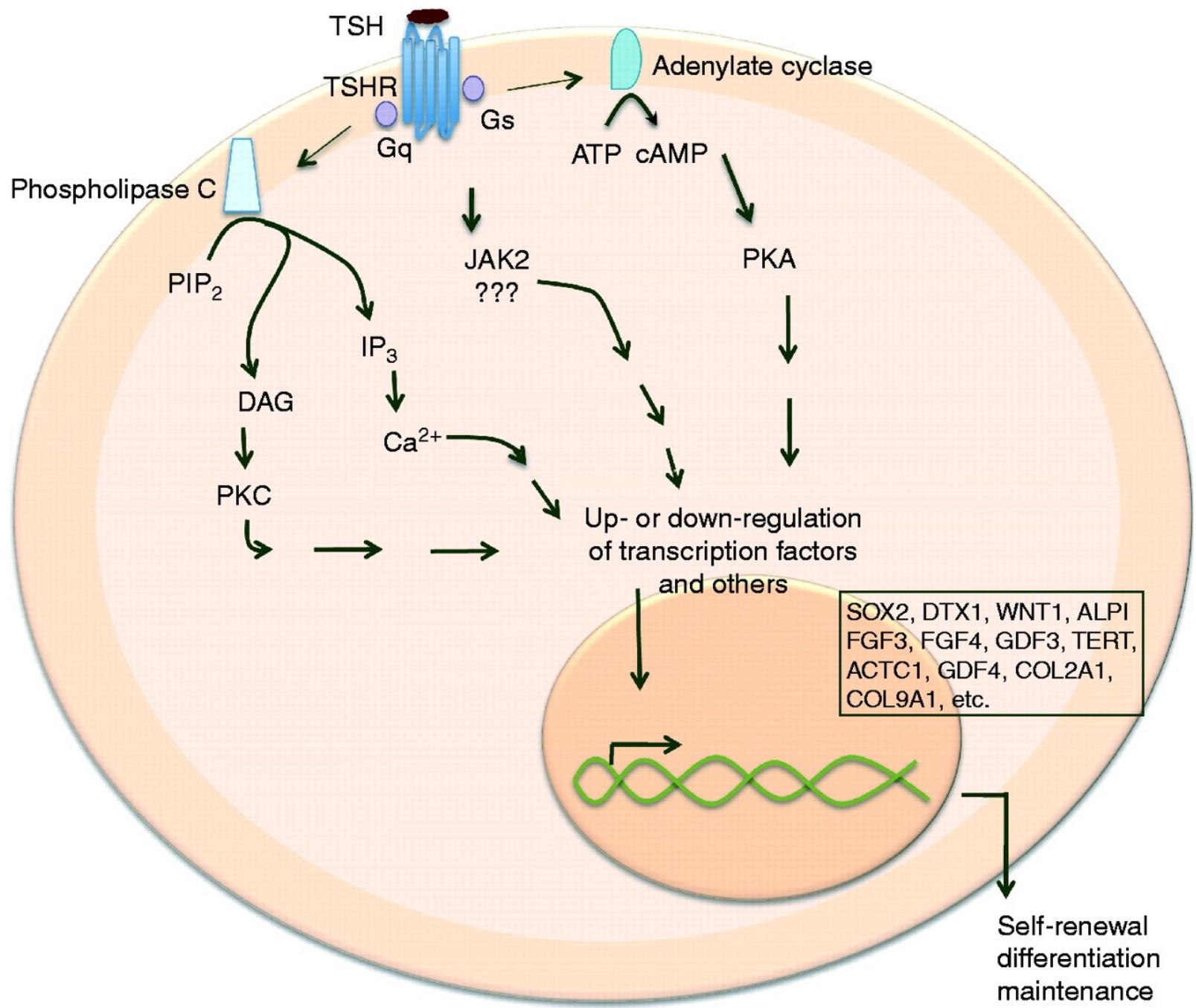


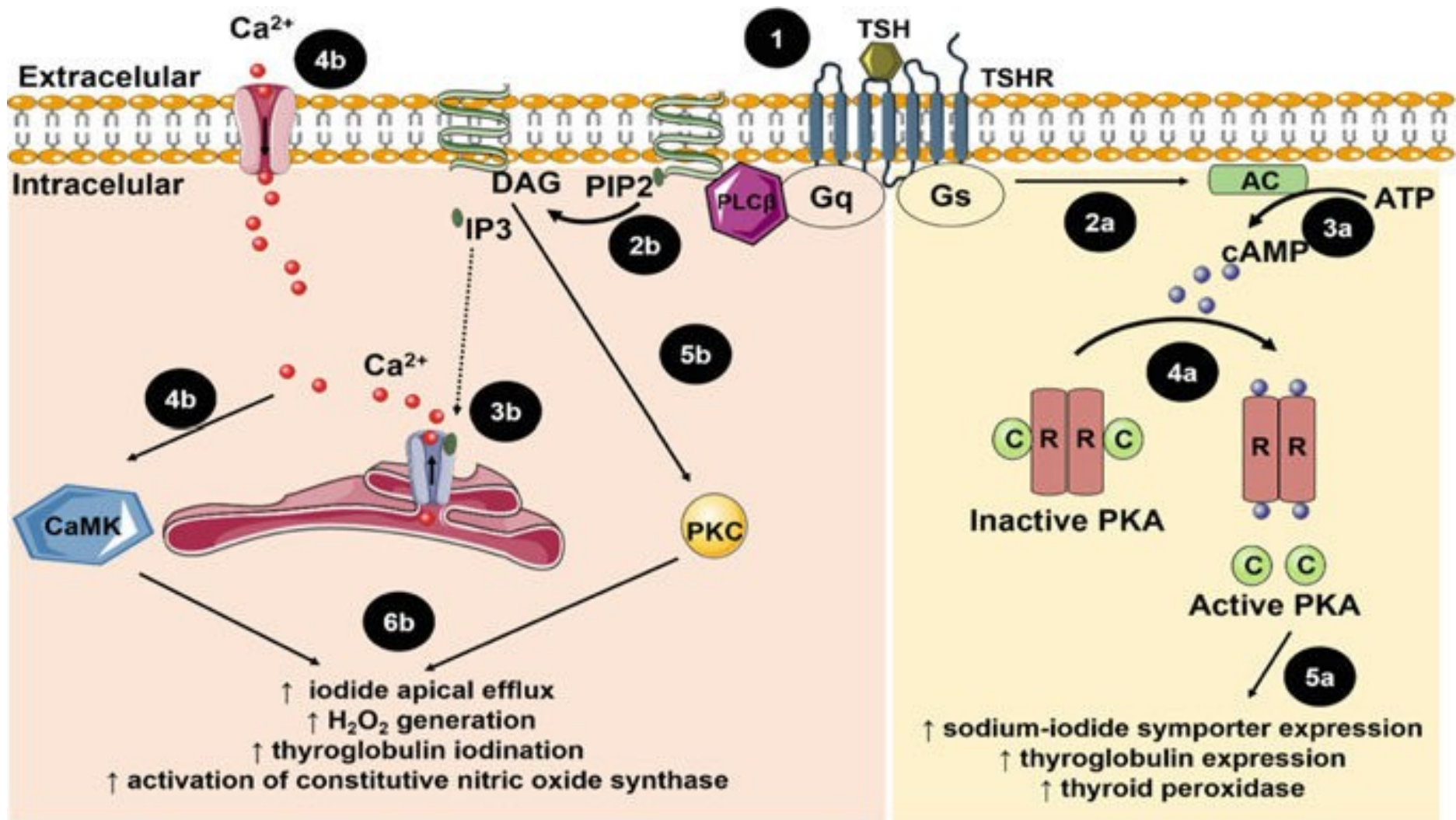
©2009 WebMD, LLC.

# Factors that Affect Thyroid Function





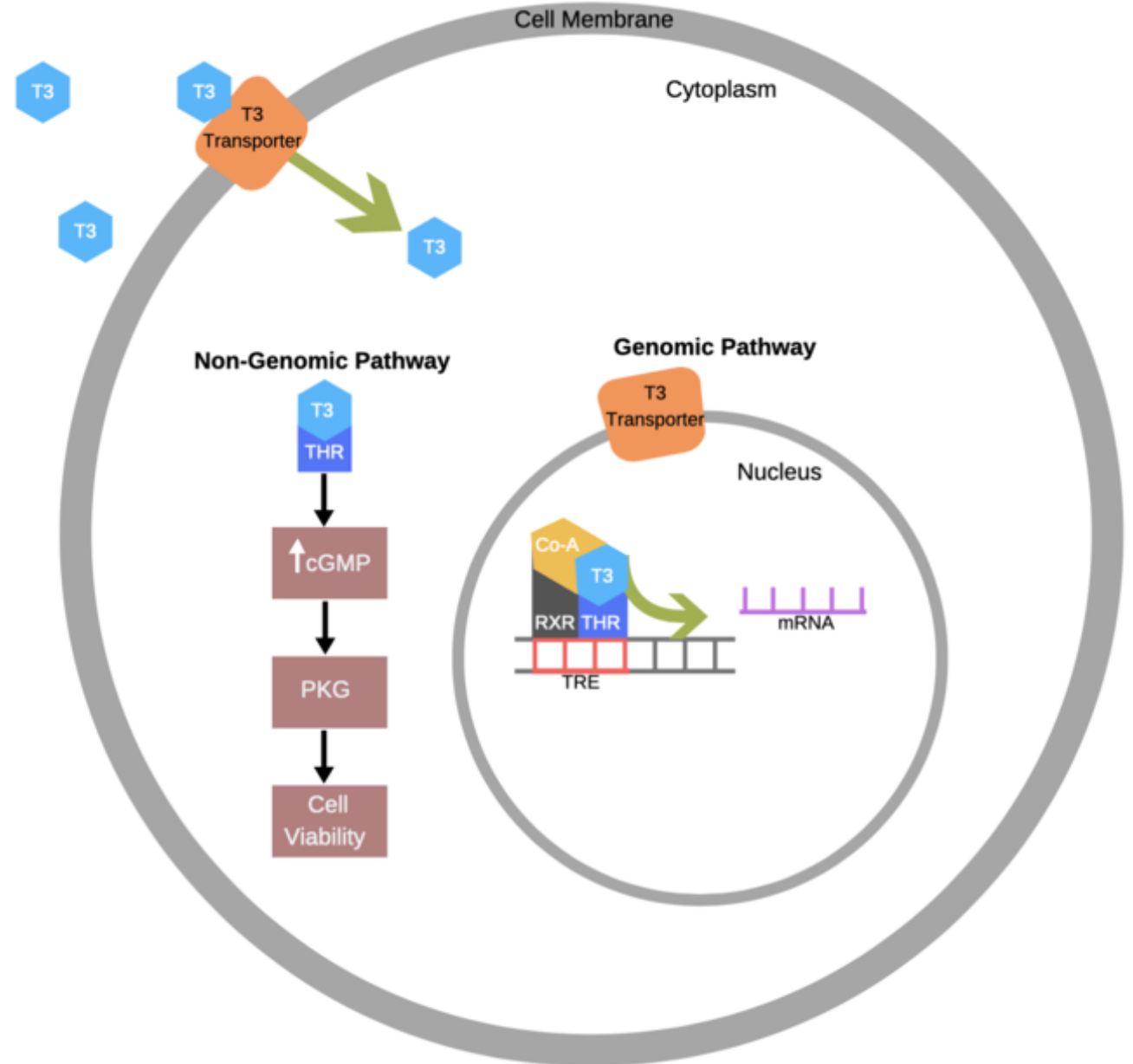






# Repression of TR

- Depression
- Loss of vision
- Heart problems
- Weight gain
- Fatigue
- Hearing loss
- Sensitivity to cold
- Weakness
- Issues with digestion
- Cognitive impairment



# Hyperthyroidism vs hypothyroidism

## **Hypothyroidism**      **Hyperthyroidism**

### Symptoms:

Extreme Tiredness/Lethargy/  
Lack of Stamina/Motivation  
Memory Loss/'Brain Fog'  
Depression/  
Mood Swings  
Hearing Loss

Weight  
Gain

3pm  
crash

Broken  
Sleep

Brittle/  
Ridged  
Nails

Joint/  
Muscle  
Pain

Hair  
Loss

Constipation

Prmenstrual Tension

Intolerance to Cold/Heat/  
Sweating/Low Body Temperature

Tingling & Numbness in Extremities

### Signs:

Sparse Eyebrows  
Especially outer ends

Swelling of the Face  
Especially around Eyes  
(Oedema)

Changes at the back of  
the Eye (at Fundus Oculi)

Wasting of Tongue

Listless, dull to look Eyes  
Hoarseness

Rapid Heart  
Rate with  
weak force  
of contraction

Slow Thinking

Slow Pulse  
Rate

Non pitting oedema of ankles

Cold/dry/sore/scaly skin/brittle nails

Low basal activity level temperature

Dry/course/brittle hair or hair loss

Unexplained Weight Gain

Pounding Heart Beat

Nervousness

Sluggish  
Movement

### Symptoms:

Protusion of one or both  
eyeballs (exophthalmos)

Breathlessness

Nervousness

Difficulty  
Sleeping/  
Insomnia

Fatigue

Itching  
-overall

Heartbeat  
Sensations

Palpitations

Weakness

Diarrhoea

Increased Bowel Movements

Heat Intolerance

Light or Absent  
Menstruel Periods

Design mouseman info 2012

### Signs:

Protruding Eyes  
(exophthalmos)

Hair Loss

Staring Gaze

Nausea & Vomiting

Warm Moist Skin

Goitre

Fast  
Heart  
Rate

Trembling  
Hands

Skin Blushing/ Flushing

Blood Pressure- high

Pulse- Pounding

Weight Loss

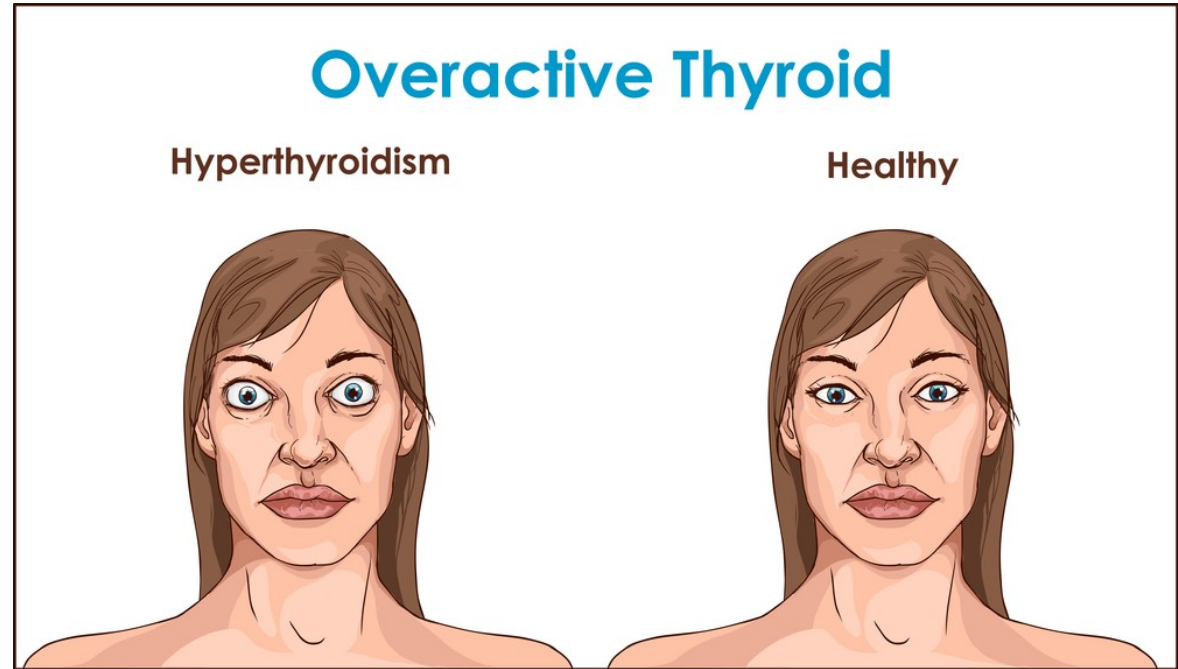
Muscle Weakness

Breast Development in Men

Design mouseman info 2012

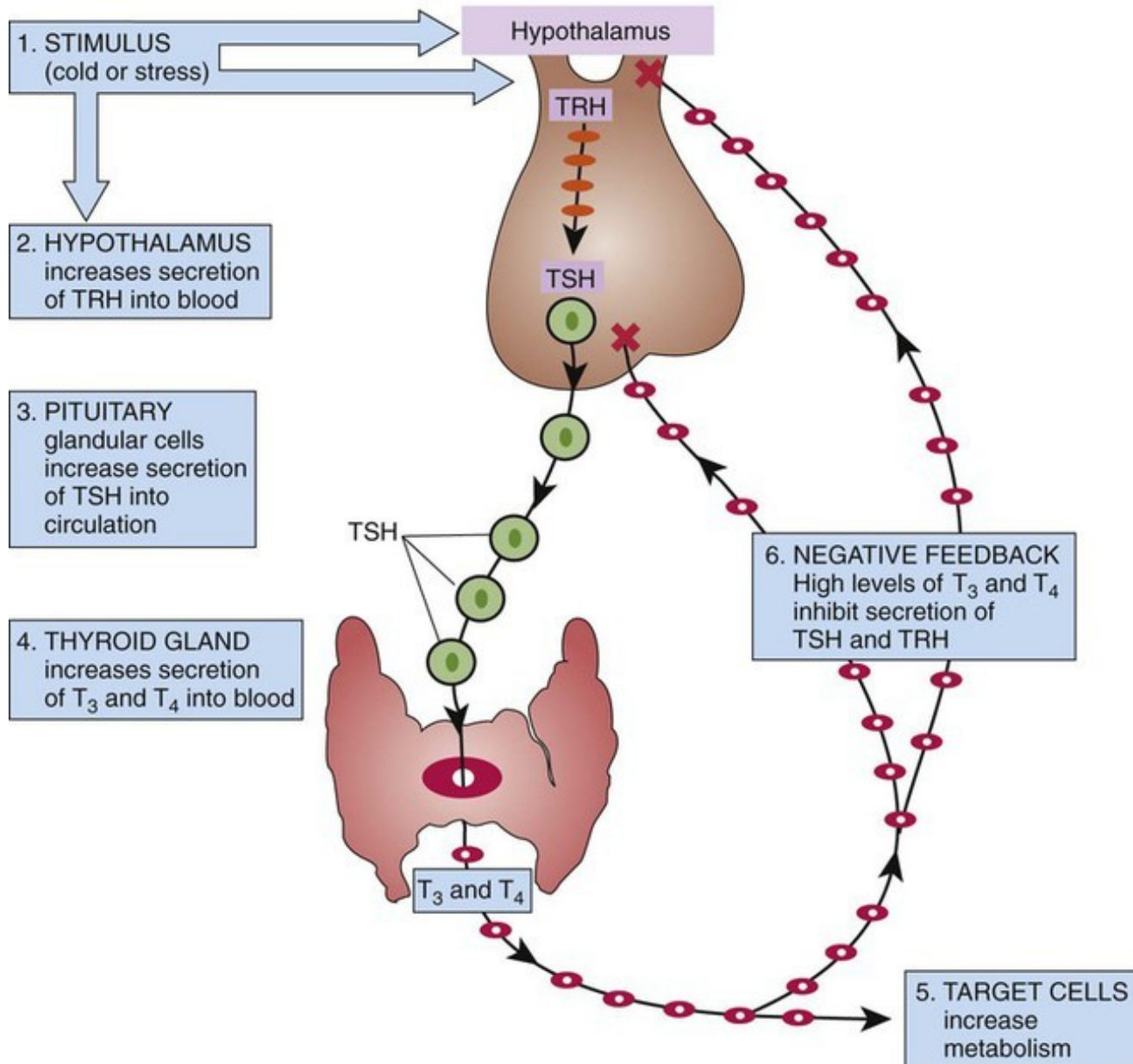
# Hyperthyroidism

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



# Causes of hyperthyroidism

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



# Hyperthyroidism DiffDg

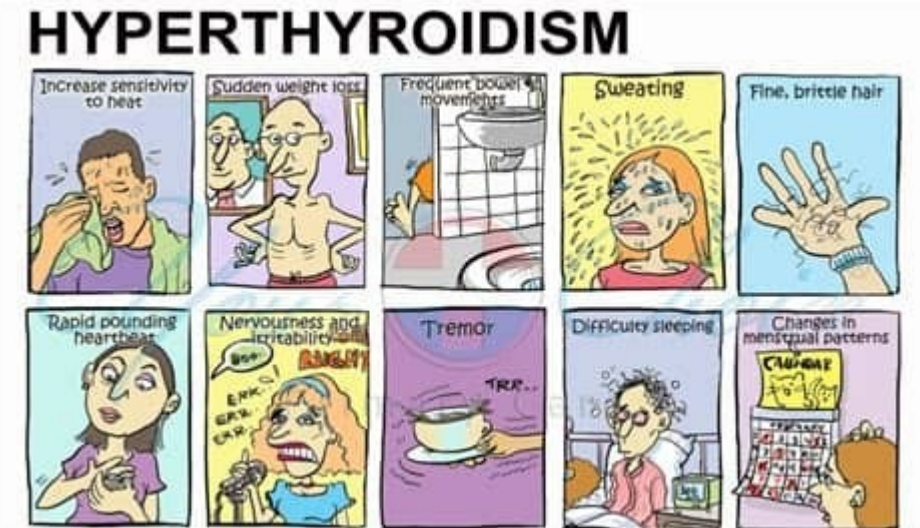
- Graves' Disease
- Toxic Multinodular Goiter
- Toxic Adenoma
- Thyroiditis
  - silent (Hashimoto's) – painless, often post partum
  - subacute (de Quervain's) – painful, post viral
  - drug-induced – amiodarone, lithium, interferon
- Thyrotoxicosis factitia
  - ingestion

# 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



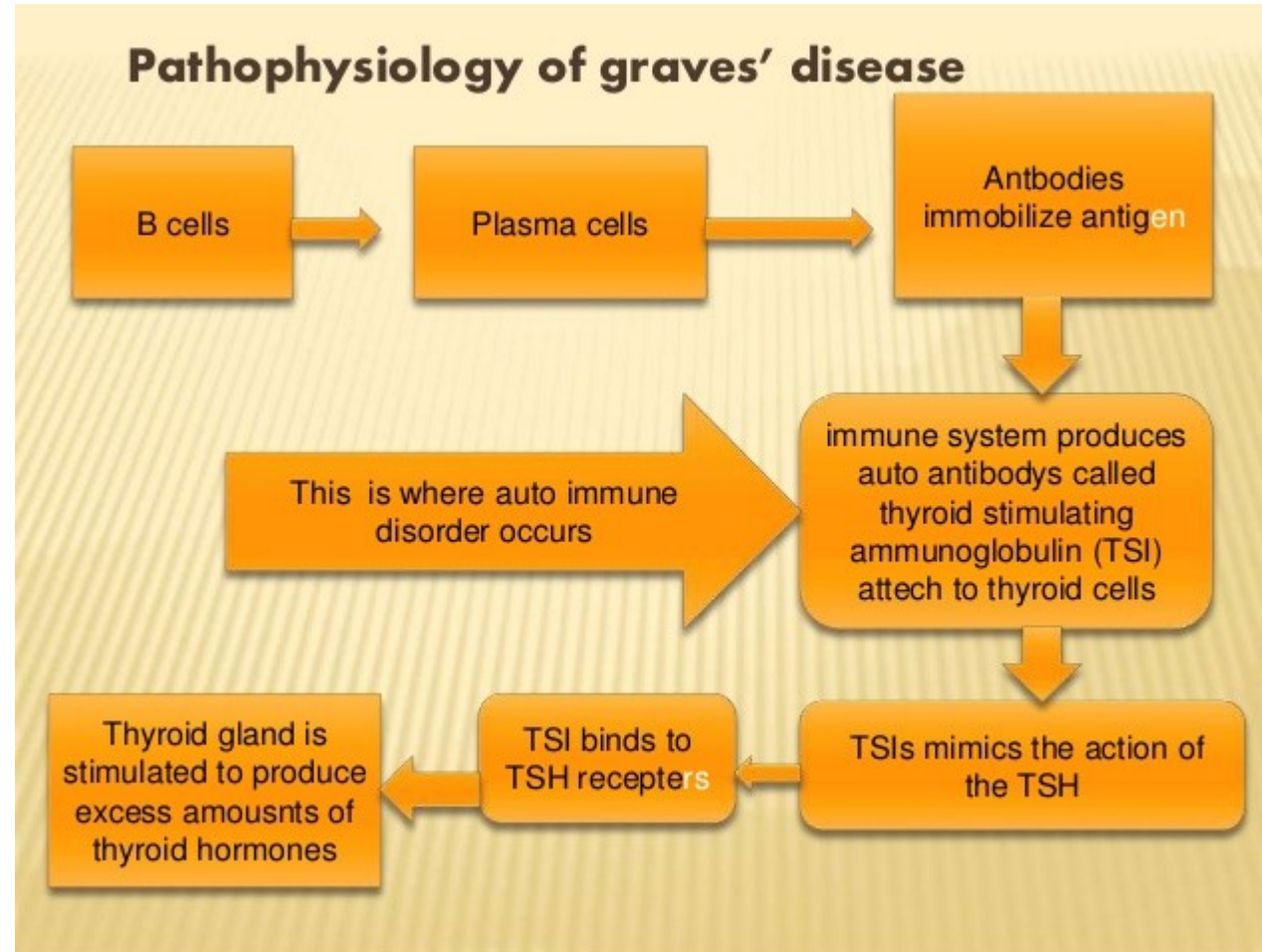


# Grave's disease

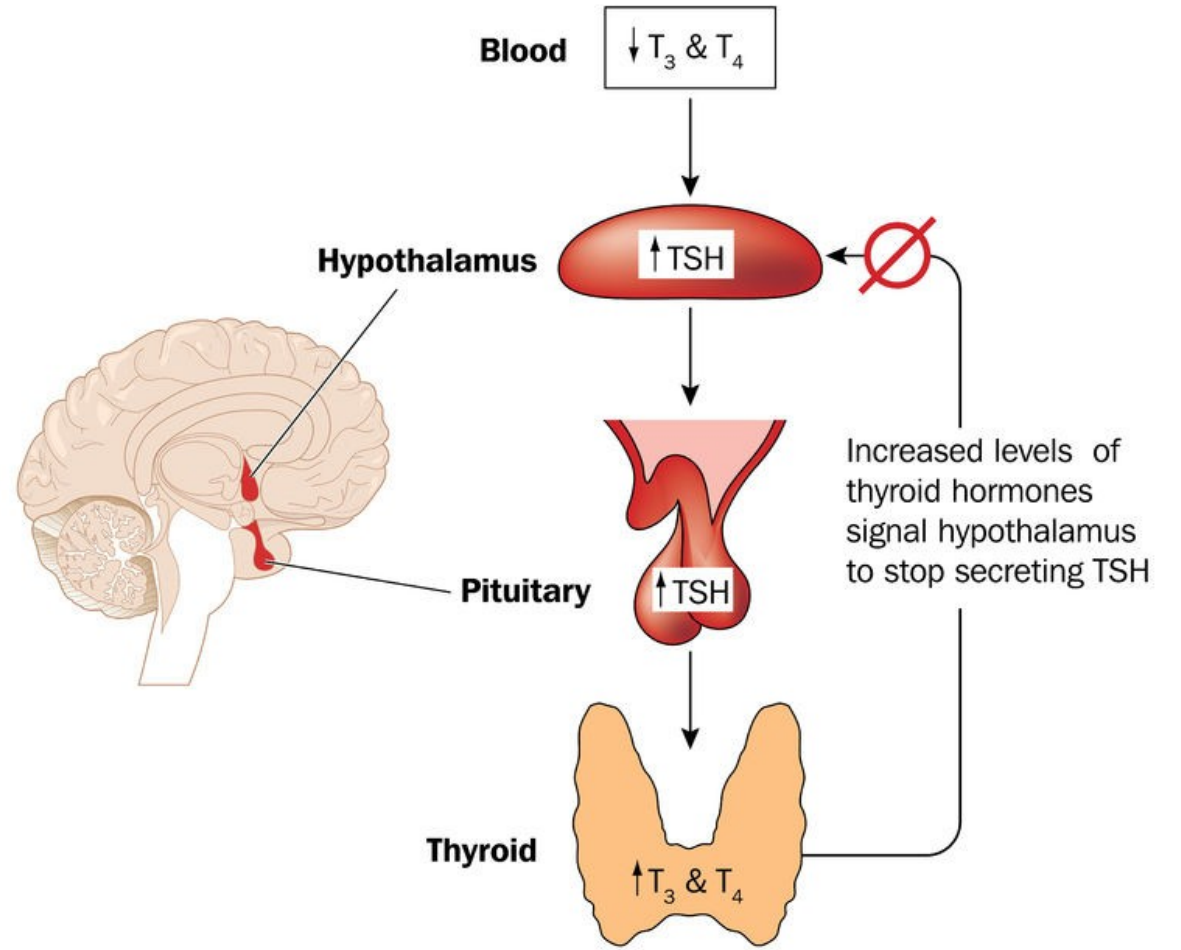
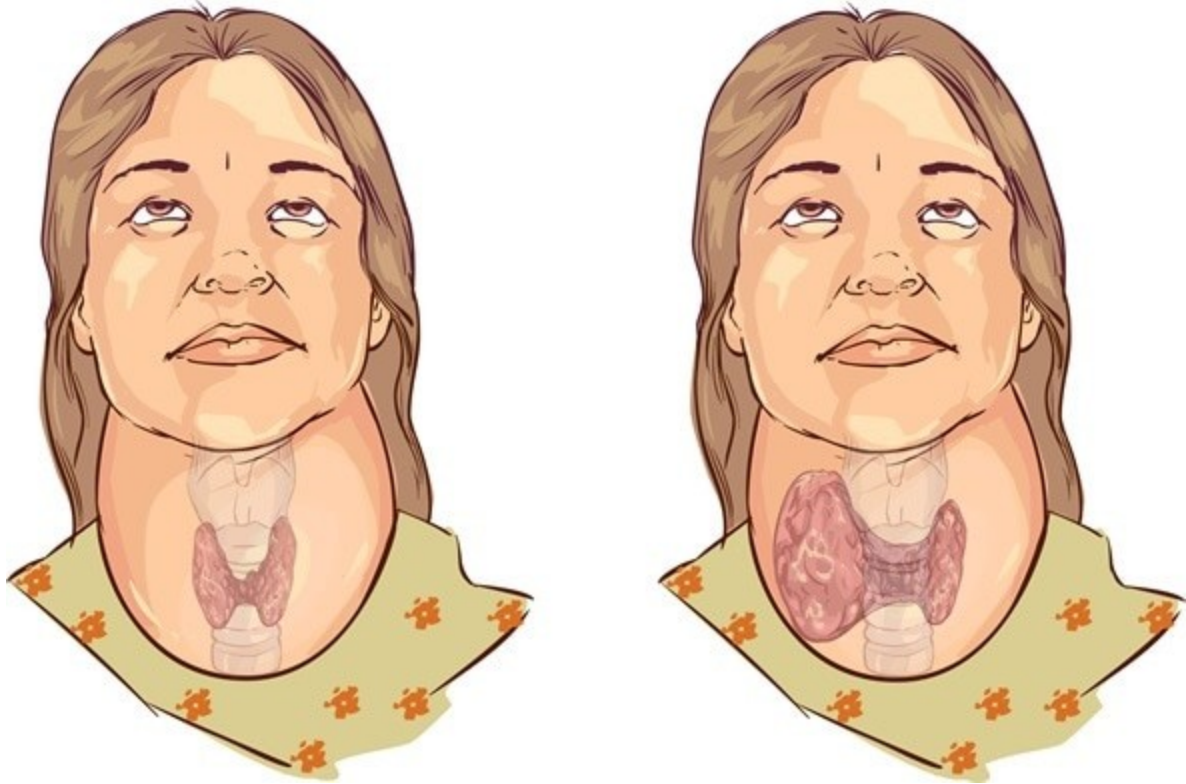
SIGNS	SYMPTOMS
<ul style="list-style-type: none"><li>• Resting tremor</li><li>• Hyperreflexia</li><li>• Atrial tachyarrhythmias (including atrial fibrillation)</li><li>• Enlarged painless thyroid with thrill and bruit</li><li>• Warm, moist, and smooth skin</li><li>• Hair loss</li><li>• Onycholysis (Plummer's nails)</li><li>• Gynecomastia</li><li>• Localized dermatopathy (pretibial myxedema)</li><li>• Thyroid acropachy (clubbing)</li><li>• Stare, eyelid lag, proptosis</li></ul>	<ul style="list-style-type: none"><li>• Irritability</li><li>• Tremor</li><li>• Proximal-muscle weakness</li><li>• Difficulty sleeping</li><li>• Palpitations</li><li>• Heat intolerance</li><li>• Weight loss</li><li>• Increased appetite</li><li>• Increased frequency and loose stools</li><li>• Menstrual irregularity (oligomenorrhea, amenorrhea)</li><li>• Decreased libido and erectile dysfunction</li><li>• Photophobia, gritty eye sensation, xerophthalmia, blurry vision, diplopia</li></ul>



# Pathophysiology of Graves diseases



# Goiter



# Hypothyroidism

## Hypothyroidism: Clinical Symptoms and Signs

### Endocrine

- Infertility and subfertility
- Menstrual disturbances
- Galactorrhea
- Goiter
- Glucose metabolism dysregulation
- Sexual dysfunction
- Increased prolactin
- Pituitary hyperplasia

### Skeletal

- Muscle weakness
- Muscle cramps
- Arthralgia
- Creatine phosphokinase elevation
- Ruffian's syndrome (hypothyroid myopathy)
- Osteoporosis (rare due to over treatment)

### Electrolytes and kidney function

- Deterioration of kidney function
- Decreased estimated glomerular filtration rate
- Hyponatremia

### Skin and Hair

- Dry skin
- Hair loss
- Coarse skin
- Loss of lateral eyelashes (rare)
- Yellow palms of the hand
- Alopecia areata

### General Metabolism

- Weight gain (increased BMI)
- Cold intolerance / Hypothermia
- Fatigue
- Low metabolic rate
- Myxedema



Chaker L et al., Lancet 2017

### Neurological

- Impaired memory
- Parosmia
- Mood impairment
- Impaired cognitive function
- Delayed relaxation of tendon reflexes
- Depression
- Dementia
- Hoarseness of voice, decreased taste, vision, or hearing
- Ataxia
- Carpal tunnel syndrome and other nerve entrapment syndromes
- Myxedema coma

### Cardiovascular

- Fatigue or exertion shortness of breath
- Dyslipidemia
- Bradycardia
- Hypertension
- endothelial dysfunction or increased intima-media thickness
- Diastolic dysfunction
- Pericardial effusion
- Hyperhomocysteinemia
- ECG changes

### GI/hepatic

- Constipation
- Reduced esophageal motility, non-alcoholic fatty liver disease
- Acute liver rare

### Haematological

- Bleeding
- Fatigue
- Mild anemia
- Acquired von Willebrand disease
- Decreased protein C and S
- Increased red cell distribution width
- Increased mean platelet volume

# Hyposekrece T3, T4 v dětství

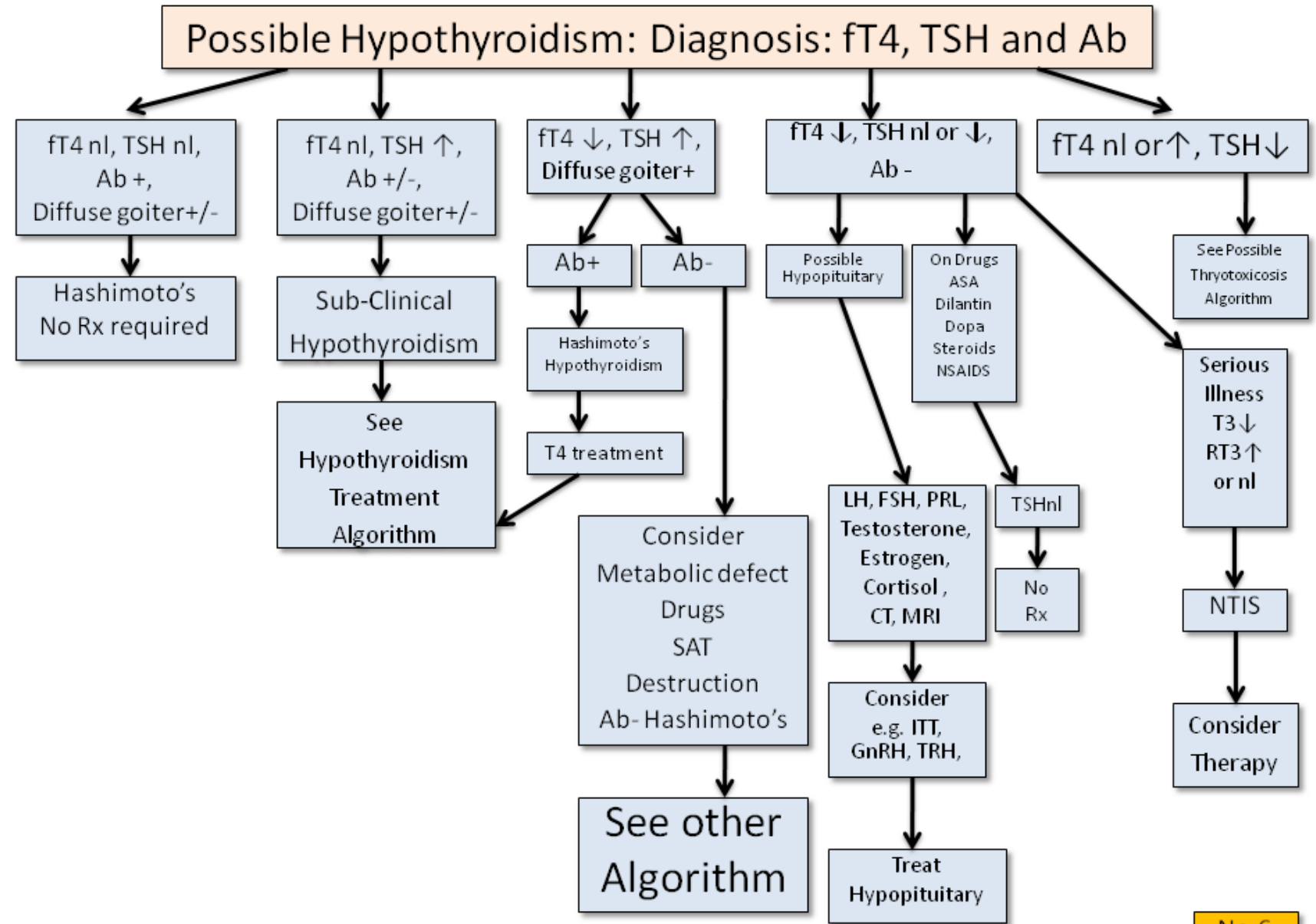
## Kretenismus

nedostatek T3 a T4 již intrauterinně,  
porucha vývoje žlázy nebo endemický  
nedostatek jodu

- poruchy růstu, kratší končetiny
- poruchy intelektu, spavost
- únava, svalová slabost
- zácpa, velké břicho



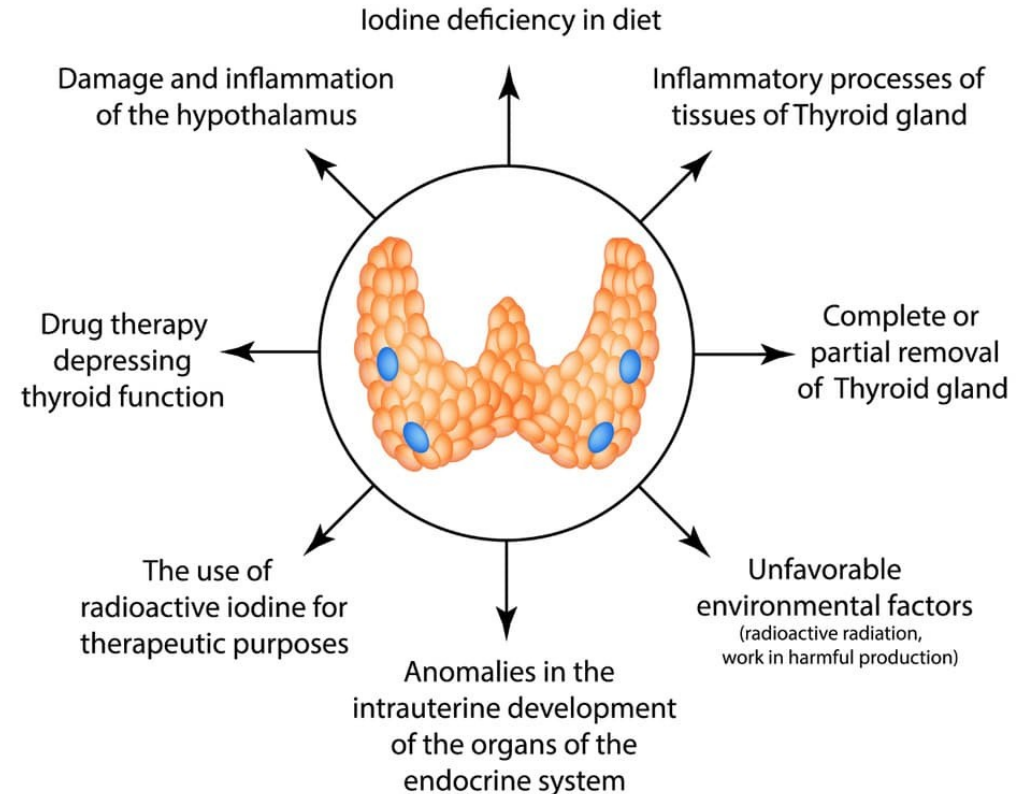
# Hypothyroidism



# Hypothyroidism

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

## CAUSES OF HYPOTHYROIDISM

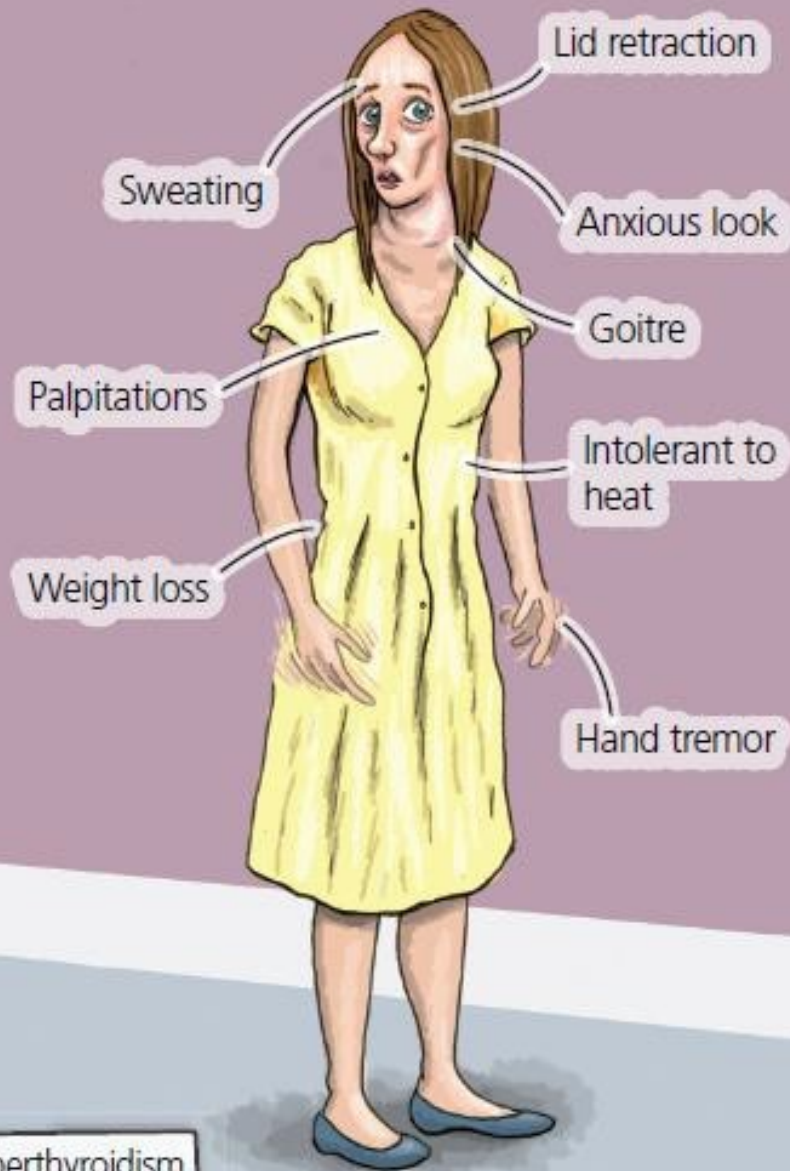


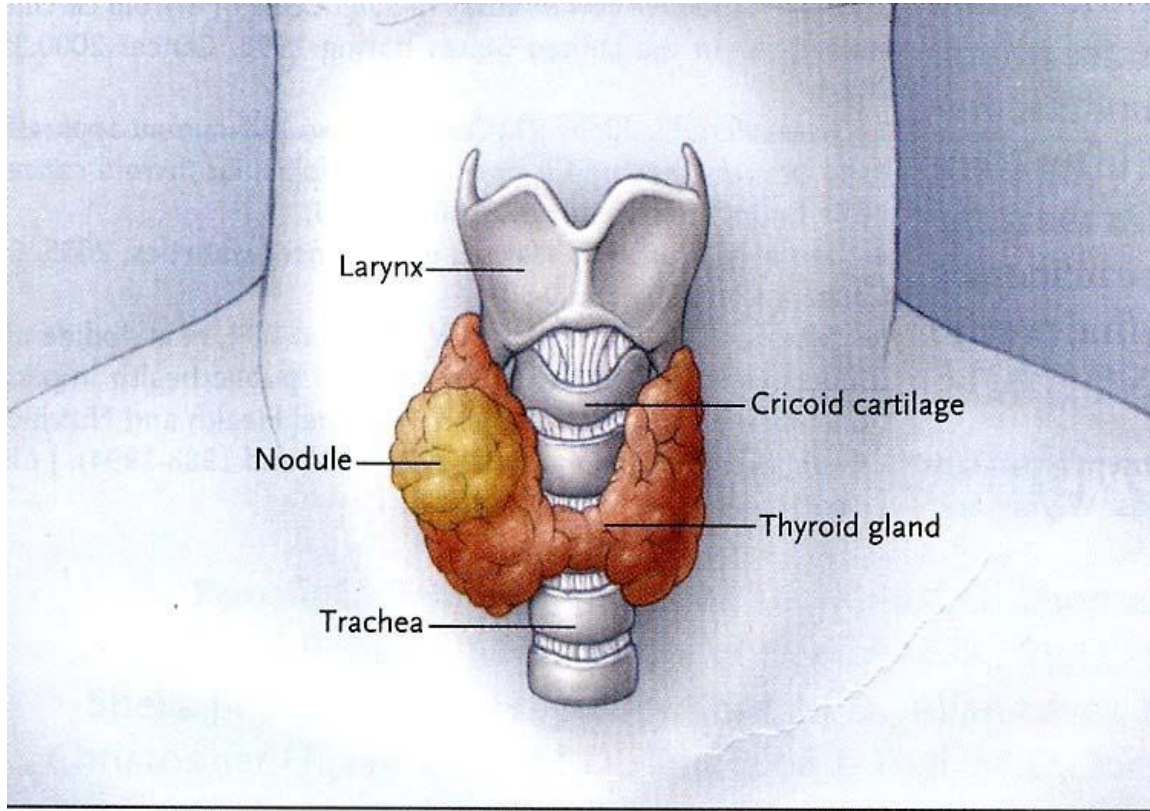
# Hypothyroidism

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



## Features of hypothyroidism and hyperthyroidism





### Benign Nodules (95%)

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

### Carcinomas (5%)

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

### Common Varieties of Thyroid Nodules.

# HASHIMOTO'S DISEASE

**Normal Thyroid** ✓

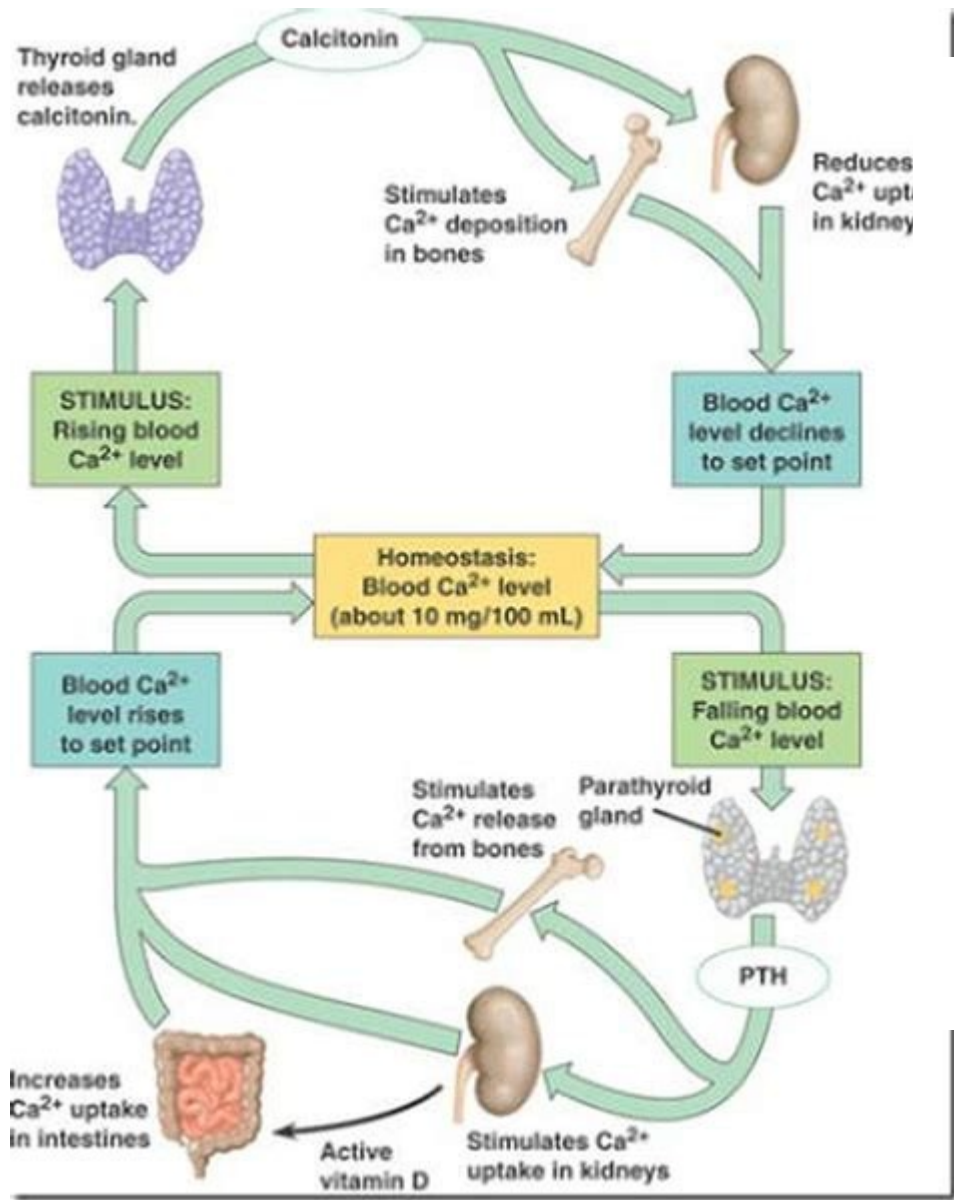
**Hashimoto's Disease** ✗

**Enlarged and Inflamed Underactive Thyroid (Goiter)**

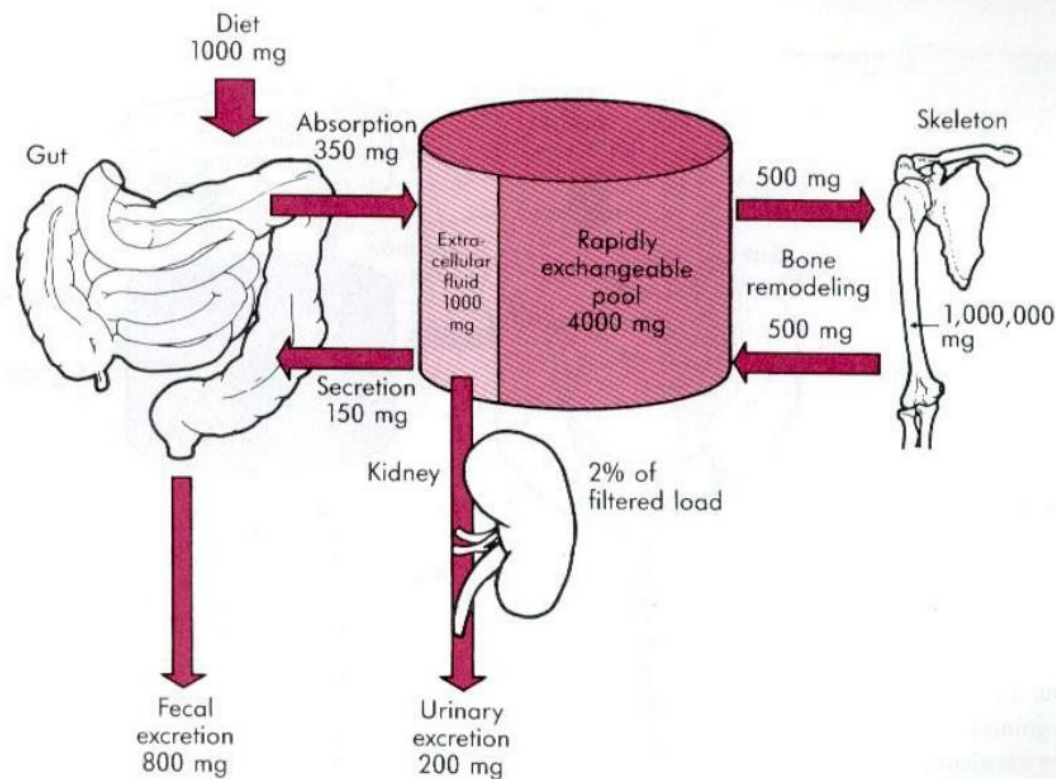
Hashimoto's Disease, is an Autoimmune Disease in Which the Thyroid Gland is Gradually Destroyed

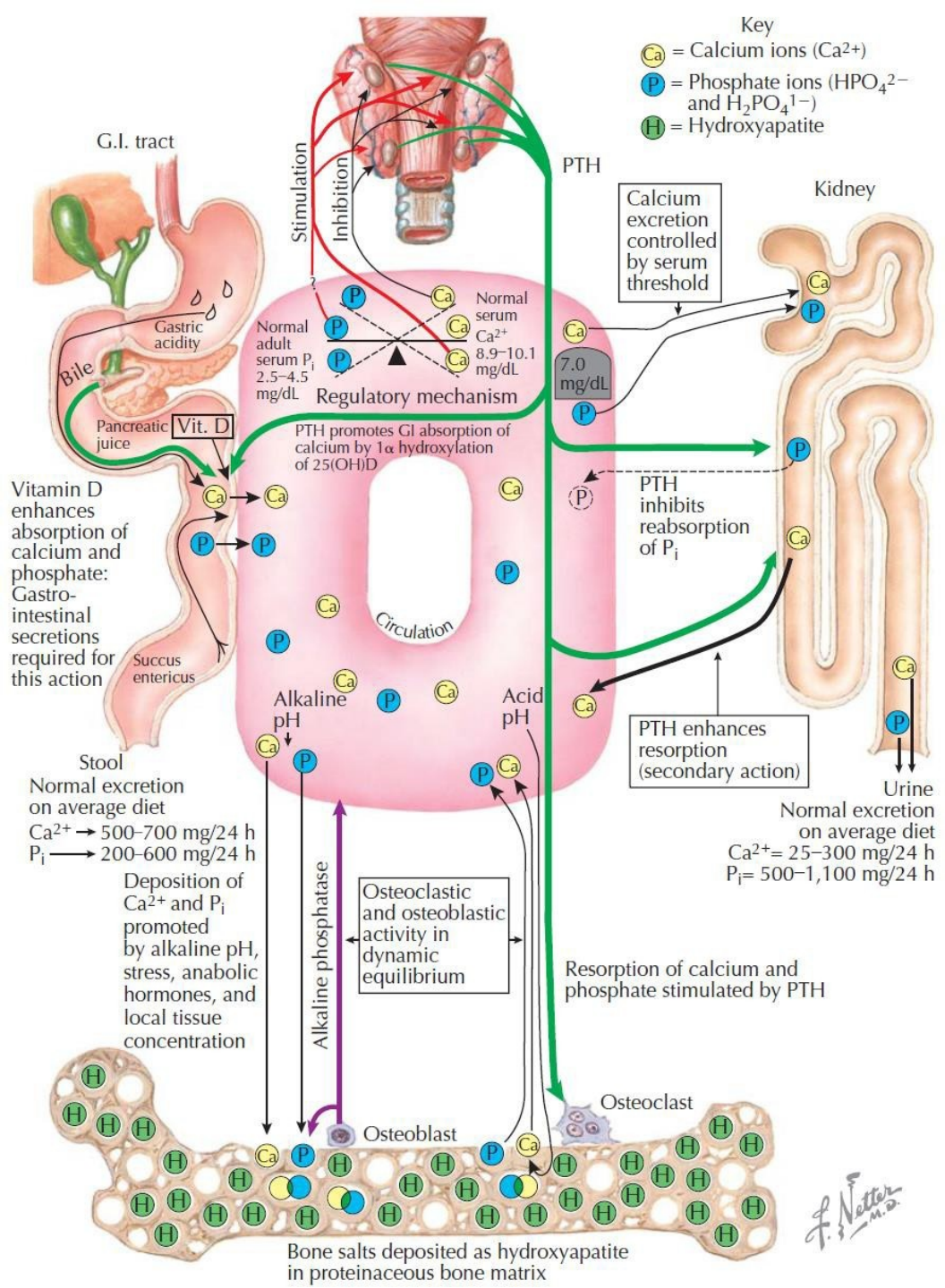
**Symptoms:**

- Enlargement of the Tongue
- Memory Lapses Depression
- Goiter A puffy Face Brittle Nails Hair Loss
- Pale, Dry Skin
- Excessive or Prolonged Menstrual Bleeding
- Joint Pain and Stiffness
- Muscle Aches, Weakness, Tenderness and Stiffness
- Constipation
- Fatigue and Sluggishness
- Increased Sensitivity to Cold
- Unexplained Weight Gain



# Calcium Turnover





# 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

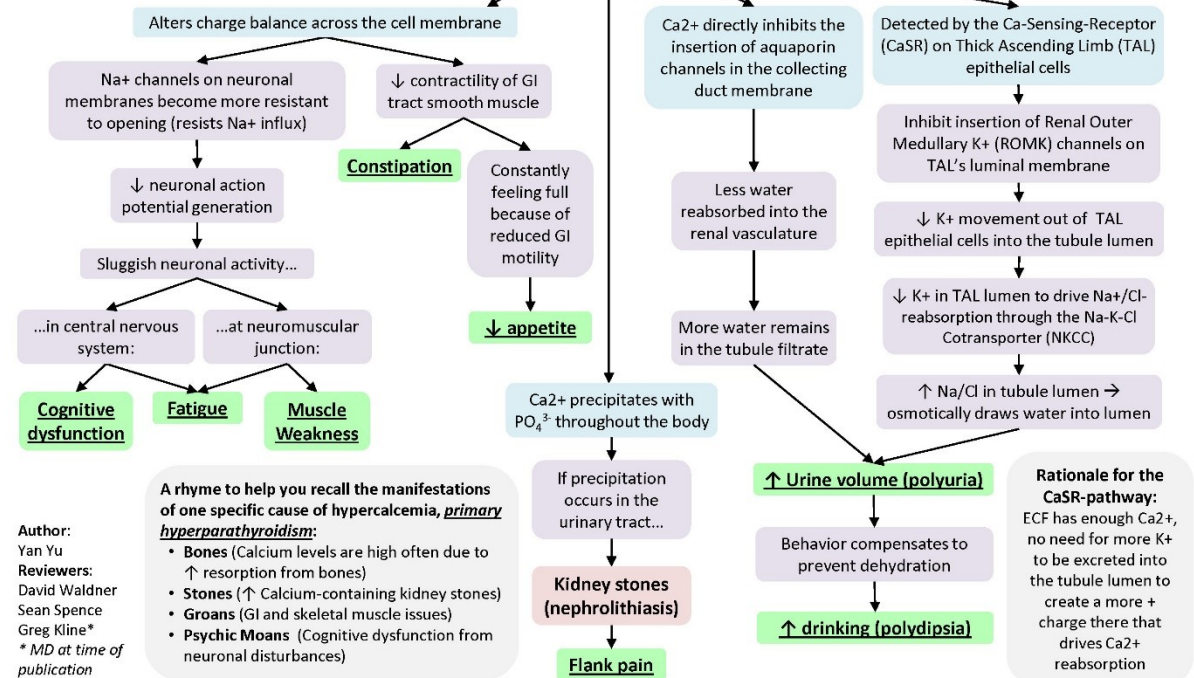
- Diuretics
- Bisphosphonates
- Calcitonin

### Hypercalcemia: Clinical Findings

**Note:** "Total Ca<sup>2+</sup>" in the blood is either "free", or bound to albumin. The lab value measures the "Total Ca<sup>2+</sup>", but it is the "free Ca<sup>2+</sup>" that carries out Ca<sup>2+</sup>'s functions and determines if someone is hyper- or hypo-calcemic.

**Hypercalcemia**  
(serum [Ca<sup>2+</sup>] > 2.5mmol/L)

**Note:** sick/ICU patients have ↓ serum albumin, due to ↓ synthesis from a sick liver. Their lab Ca<sup>2+</sup> values can be "normal", but they may be truly hypercalcemic (more "free Ca<sup>2+</sup>", less "albumin-bound Ca<sup>2+</sup>").  
Correct this by adding 0.2mmol/L to the lab Ca<sup>2+</sup> value for every 10g/L drop of albumin below 40g/L



Author: Yan Yu  
Reviewers: David Waldner, Sean Spence, Greg Kline\*  
\* MD at time of publication

Legend: Pathophysiology Mechanism Sign/Symptom/Lab Finding Complications Published May 7, 2013 on www.thecalgaryguide.com

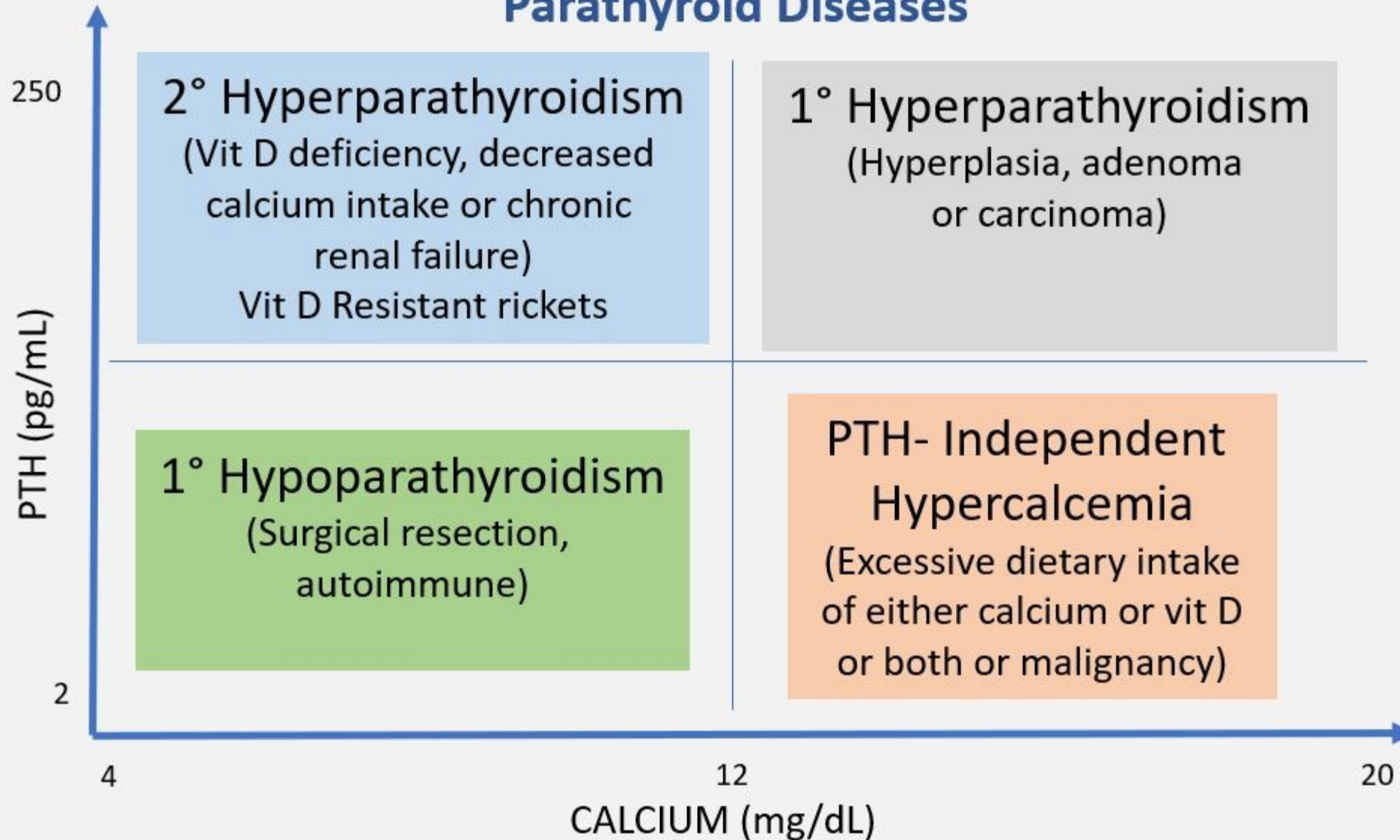


# Hypocalcemia

**Table 1.** Causes of hypocalcemia.

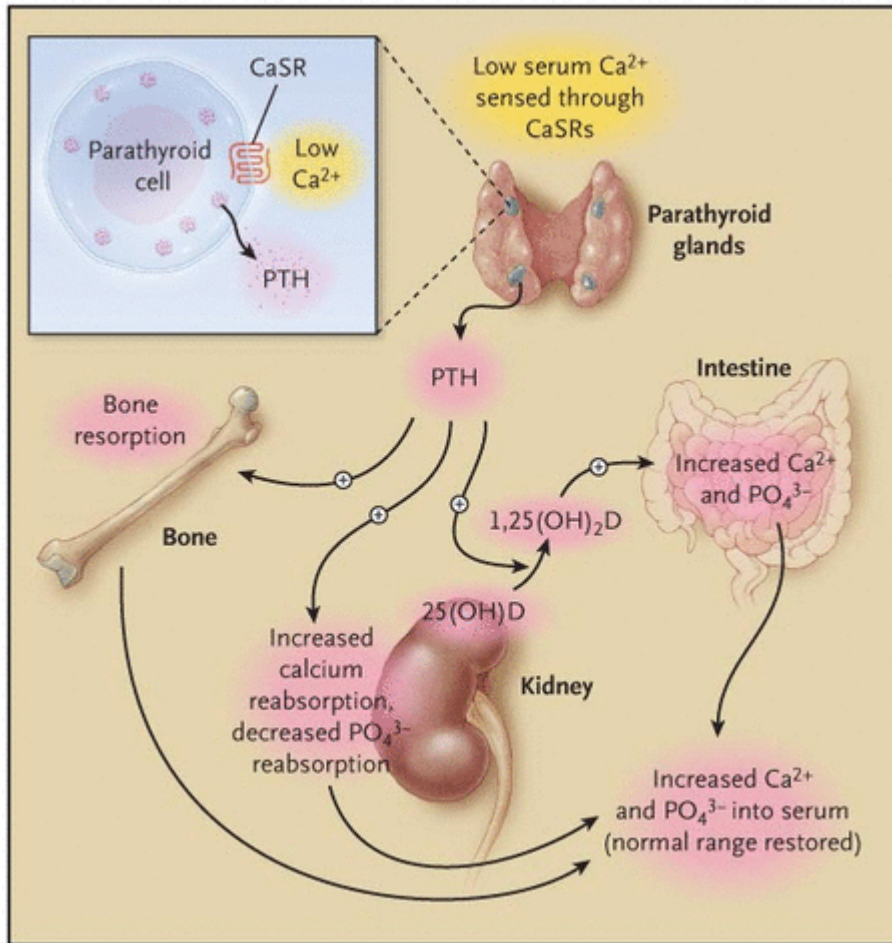
Low PTH levels (hypoparathyroidism)	High PTH levels (secondary hyperparathyroidism)
<p><i>Parathyroid Destruction</i></p> <ul style="list-style-type: none"> <li>Surgery</li> <li>Auto-immune (isolated or polyglandular)</li> <li>Cervical irradiation</li> <li>Infiltration by metastasis or systemic diseases (Sarcoidosis, amyloidosis, hemochromatosis, Wilson's disease, thalassemia)</li> </ul> <p><i>Reduced parathyroid function</i></p> <ul style="list-style-type: none"> <li>Hypomagnesemia</li> <li>PTH gene defects</li> <li>Calcium sensing receptor mutations</li> </ul> <p><i>Parathyroid agenesis</i></p> <ul style="list-style-type: none"> <li>DiGeorge Syndrome</li> <li>Isolated x-linked hypoparathyroidism</li> <li>Kenny-Caffey syndrome</li> <li>Mitochondrial neuropathies</li> </ul>	<p><i>PTH resistance</i></p> <ul style="list-style-type: none"> <li>Pseudohypoparathyroidism</li> <li>Hypomagnesemia</li> </ul> <p><i>Vitamin D deficiency</i></p> <ul style="list-style-type: none"> <li>Nutritional</li> <li>Lack of sunlight</li> <li>Malabsorption</li> <li>Vitamin D dependent rickets               <ul style="list-style-type: none"> <li>type I (lack of activity of 1<math>\alpha</math>-hydroxylase)</li> <li>type II (Vitamin D receptor resistance)</li> </ul> </li> <li>Chronic renal disease</li> </ul> <p><i>Drugs</i></p> <ul style="list-style-type: none"> <li>Bisphosphonates, cisplatin, ketoconazole, gallium nitrate, anticonvulsants</li> </ul> <p><i>Hyperphosphatemia</i></p> <ul style="list-style-type: none"> <li>Renal insufficiency</li> <li>Massive tumor lysis</li> <li>Acute rhabdomyolysis</li> </ul> <p><i>Acute pancreatitis</i></p> <p><i>Hungry bone</i></p> <p><i>Toxic shock syndrome</i></p> <p><i>Acute severe illness</i></p> <p><i>Calcium chelators (citrate blood transfusions, phosphate)</i></p>

## Parathyroid Diseases





# Hypoparathyroidism



Mechanism	Risk Factor/Comorbidity	Etiology
Destruction or Removal	Surgery	Removal or damage to blood supply
	Disorder Dependent	Autoimmune
	Radiation therapy	Destruction of gland--Rare
	Cancer	Metastatic infiltration
	Transfusion dependent thalassemia	Iron Infiltration
	Wilson's Disease	Copper infiltration
	Amyloidosis	Amyloid deposition
Impaired PTH secretion or action	Malnutrition, Malabsorption, Alcoholism, Drugs, RTA	Severe Magnesium Deficiency
	Chronic Renal Failure, IV magnesium administration	Hypermagnesemia
Genetic Disorders of PTH synthesis or parathyroid gland development	Family History of hypocalcemia or hypoparathyroidism	Multiple and varied

**Děkuji za pozornost**