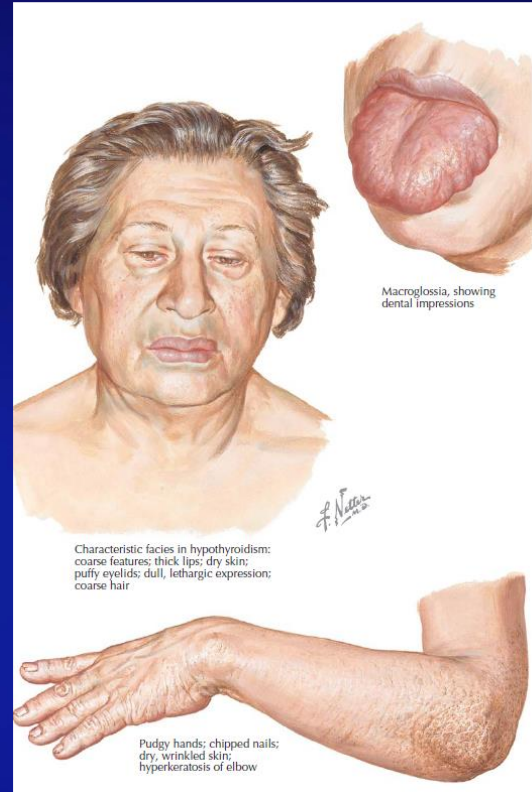


# Hypothyroidism



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- Etiology

## Primary hypothyroidism

- thyroiditis:
  - chronic autoimmune thyroiditis (Hashimoto thyroiditis) – **the most frequent cause of hypothyroidism in developed countries**
  - subacute; post-partum; painful
- congenital hypothyroidism

- Etiology

- iatrogenic hypothyroidism:

- thyroidectomy
- I131 therapy, anti-thyroid drugs, drugs blocking synthesis or release of T4 (amiodarone, lithium, iodide)
- iodine deficiency
- therapeutic irradiation for nonthyroidal malignancy

- rare causes

- thyroid agenesis or dysgenesis
- thyroid hormone resistance

- Etiology

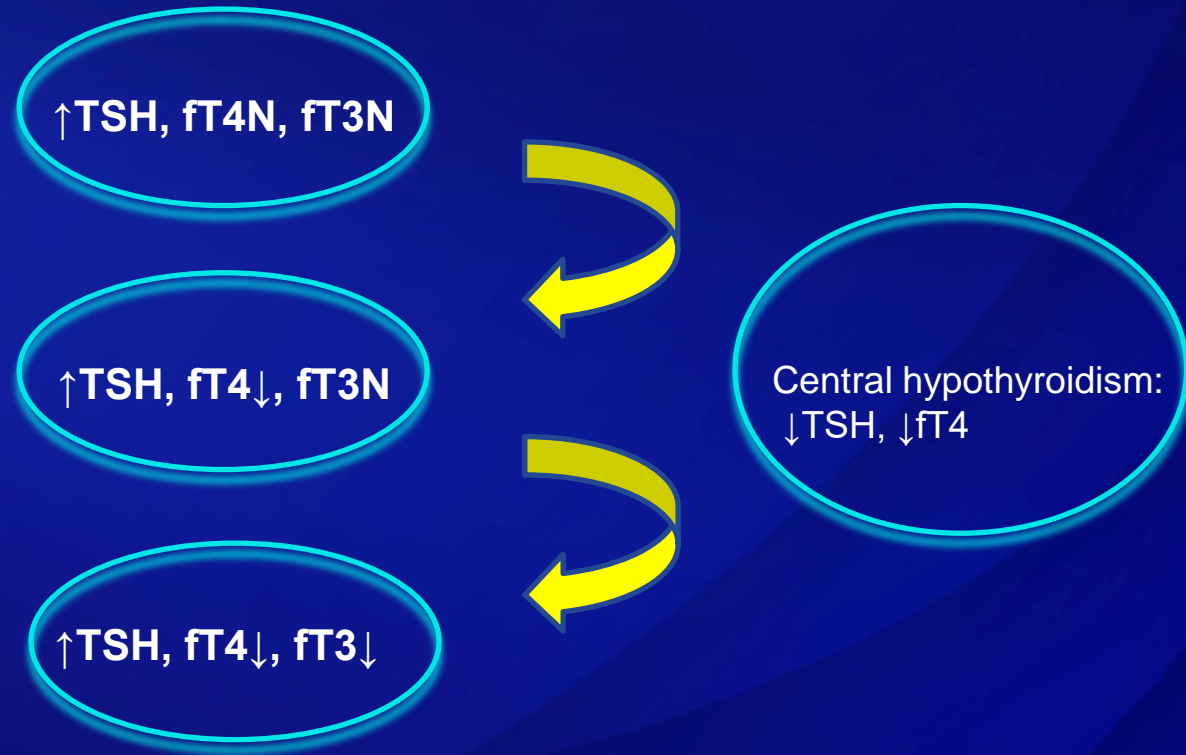
**central hypothyroidism**

- secondary: pituitary origin, tertiary: hypothalamic origin (tumors/inflammation, neurosurgery, irradiation)
- Sheehan's syndrome

- **Hormonal changes in course of hypothyroidism**

adults: 0.5-1% ♂, 5-7% ♀ (♀:♂ = 2-8 : 1)

↑ with age



- **Diagnostics**

- anamnesis and physical examination

- hormonal assessments

- primary hypothyroidism:  $\uparrow$ TSH,  $fT4\downarrow$

- central hypothyroidism:  $TSH\downarrow$  lub N,  $fT4\downarrow$

- subclinical (early) primary hypothyroidism:  $\uparrow$ TSH,  $fT4$  N,  $fT3$  N

- biochemistry

- $\uparrow$ total cholesterol,  $\uparrow$ LDL,  $\uparrow$ triglycerides

- anemia (iron or folate malabsorption, decreased erythropoietin, vit. B12 deficiency)

- $\downarrow$ Na

# Imaging

## thyroid ultrasound

- according to the final diagnosis:
- goiter
  - hypoechoogenic structure
  - changes after strumectomy
    - agenesis or dysgenesis of thyroid gland

## abdominal ultrasound

- ascites in severe hypothyroidism

## ecg

- sinus bradycardia
- low amplitude of the P wave and QRS complex
- alterations of the ST segment
  - flattened or inverted T waves

## chest x-ray

- pleural effusions in severe hypothyroidism
- myxedema heart disease (large heart)

- Treatment

- Levothyroxine (LT4): 7-day half-life, one dose a day

- ✓ initial dose – 25-50 ug/d

- ✓ **elderly, patients with cardiovascular diseases – lower initial dose!!!**

- ✓ the typical dose: 1.6-2 ug/kg body weight per day (elderly – 1 ug/kg body weight/d)

- ✓ **in case of suspicion of adrenal gland insufficiency – glucocorticoids must be supplemented first!!!**

Monitoring: TSH after 6-8 weeks (in case of central hypothyroidism – fT4), then every 3-6 months

- ✓ combined therapy (T4+T3): inconclusive results



- **Treatment of hypothyroidism in pregnant women**



- ✓ treatment is necessary not only in overt but also in subclinical, early hypothyroidism !!!
- ✓
- ✓ 30-50% LT4 dose increase
- ✓ full replacement dose: 2-2.4 ug/kg m.c./d

# Subclinical hypothyroidism

slightly elevated TSH with low-normal free thyroid hormones and discrete/absent symptoms

the decision to treat must depend on a careful consideration of the individual clinical situation and patient preference but usually is necessary when TSH > 10  $\mu$ IU/ml

# Subclinical hypothyroidism

- Causes of transient  $\uparrow$ TSH must be ruled out:
  - recovery after severe illness
  - laboratory issues
  - heterophilic antibodies or other interfering substances
  - pituitary adenoma (producing TSH)
  - thyroid hormone resistance
  - primary adrenal gland insufficiency (before the treatment with glucocorticoids)

**Subclinical hypothyroidism, TSH < 10 uIU/ml**

**Clinical  
assessment**

**High risk of CVD**

**Diastolic dysfunction of left ventricle  
hypertension  
Atherosclerosis risk factors  
dyslipidemia  
diabetes  
nicotinism**

**Iub**

**Symptoms and signs of  
hypothyroidism/goiter  
(+)anti-TPO  
Abnormal thyroid usg  
Pregnancy  
sterility**

**LT4 treatment is indicated**

**Low risk of CVD**

**Normal cardiac function  
Normal blood pressure  
Normal blood glucose/lipids levels**

**Iub**

**(-) symptoms/goiter  
(-) anti-TPO  
Normal thyroid gland in usg  
fertility  
Advanced age**

**No evidence in favor of LT4 treatment**

- Myxedema coma

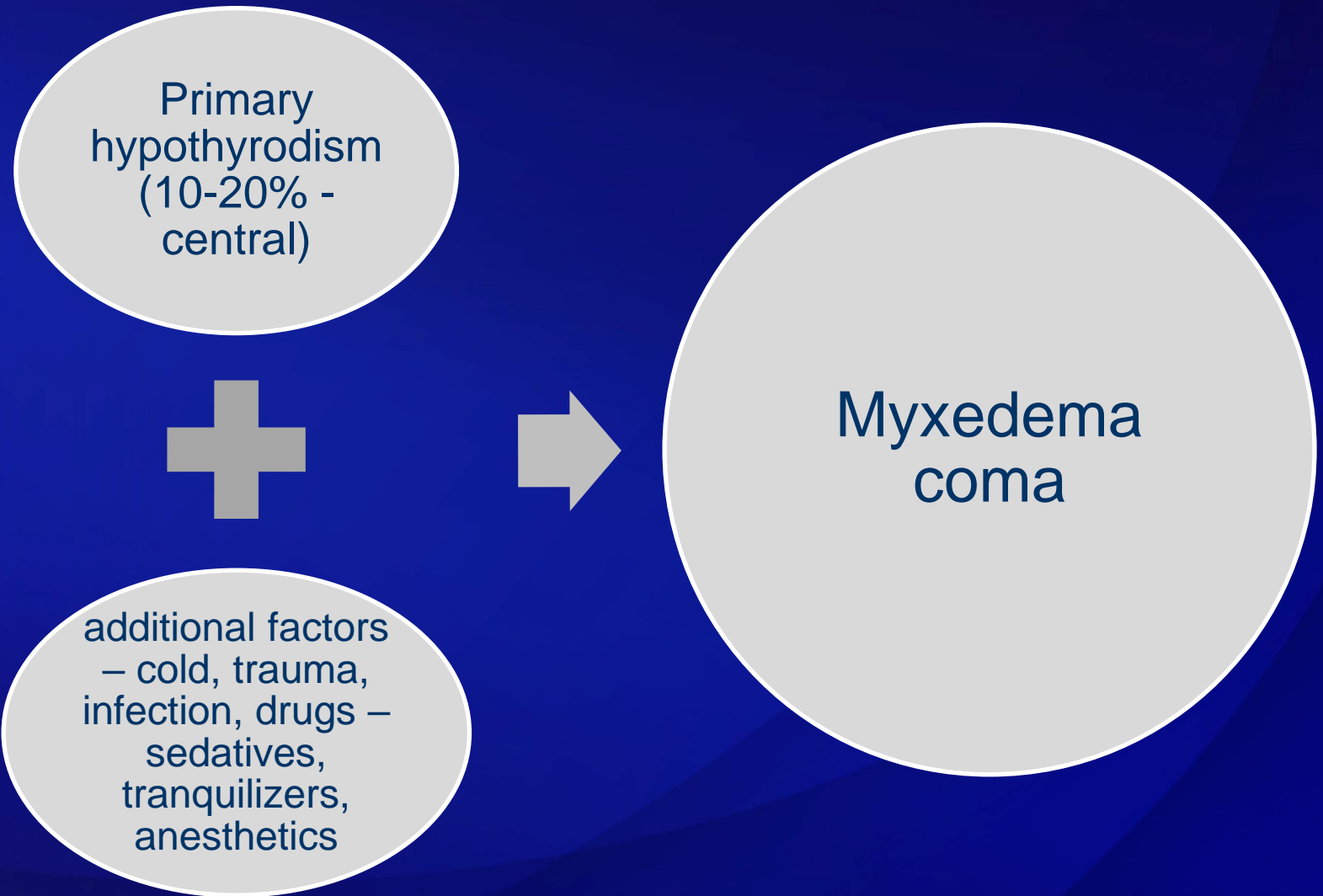
Ultimate stage of severe long-standing hypothyroidism, usually accompanied by a:

- coma,
- hypothermia,
- hypoventilation,
- hypoglycemia,
- dyselektrolitemia

- rare
- usually old women (60-70 yrs.)
- high mortality



# Etiology



- Signs and symptoms

- weakness → stupor → coma
- hypothermia (<30 degrees)
- pale, yellowish skin, swelling of the face
- hypoventilation
- bradycardia, hypotension
- ↓muscle tension, seizures
- delay in deep tendon reflexes
- ↓peristalsis, bowel obstruction
- bladder atony

- **Diagnostics**

- physical examination, anamnesis

- laboratory assays

- $\uparrow$ TSH,  $\downarrow$ fT4,  $\downarrow$ fT3 (in central hypothyroidism -  $\downarrow$ TSH,  $\downarrow$ fT4,  $\downarrow$ fT3)
- exclusion of concomittant adrenal gland insufficiency
- hypoxemia, hypercapnia, acidosis
- hypoglycemia,  $\downarrow$ Na,  $\uparrow$  CPK,  $\uparrow$  GOT,  $\uparrow$  LDH, hypercholesterolemia, anemia



- Diagnostics

- imaging

- ECG: sinus bradycardia, low voltage of P waves, prolonged PR and QT intervals, inverted T waves, atrio-ventricular bloc
- chest x-ray – enlarged heart silhouette, pleural effusions
- abdominal usg - ascites
- **Head CT – necessary to exclude other causes of disturbances of consciousness!**

# • Treatment

- ✓ Intensive Care Unit
- ✓ **immediately a full dose of LT4!**
- ✓ LT4 i.v. 500-800 ug, followed by 50-100 ug 1x/d thereafter
- ✓ **carefully in patients with CVD !!!**
- ✓ alternatively – LT4 + LT3
- ✓ oral administration is less effective than intravenous because of malabsorption

- ✓ hydrocortisone 100 mg i.v. initially and 50-100 mg i.v. every 6-8 h for 7-10 days
- ✓ treatment with hydrocortisone needn't be started if initial serum cortisol level is  $\geq 30$  ug/dl
- ✓ Intubation, assisted ventilation
- ✓ **external warming should be avoided because it may lead to vascular collapse due to peripheral vasodilatation**
- ✓ hypertonic saline and glucose
- ✓ intensive treatment of concomittant diseases
  
- mortality 30-60%
- worse prognosis – elderly with CVD and disturbances of consciousness

# Thyroiditis



# Thyroiditis

Acute		Subacute	Chronic
<u>Suppurative</u> <ul style="list-style-type: none"><li>• Infectious thyroiditis</li></ul>	<u>Non-suppurative</u> <ul style="list-style-type: none"><li>• Postirradiation thyroiditis</li><li>• Drug-induced thyroiditis</li><li>• Thyroiditis after excessive palpation</li></ul>	<ul style="list-style-type: none"><li>• de Quervaine's thyroiditis</li><li>• Silent thyroiditis</li><li>• Transient thyroiditis</li><li>• Post-partum thyroiditis</li></ul>	<ul style="list-style-type: none"><li>• Hashimoto thyroiditis</li><li>• Riedel thyroiditis</li><li>• Bacterial thyroiditis (syphilis, tuberculosis)</li><li>• Fungal thyroiditis</li></ul>

# Acute thyroiditis

## Acute infectious (suppurative) thyroiditis

- Etiology: any bacterium (aerobic and anaerobic), fungi
- risk factors:
  - trauma of the neck
  - suppurative infection of the surrounding tissues
  - disturbances of the immune system
  - previous pathology of thyroid gland (nodular goiter, cysts, thyroid carcinoma)
  - persistence of thyroglossal duct

# Acute infectious thyroiditis

- risk factors:
  - previously performed surgery (parathyroidectomy)
  - septic embolism (bacterial endocarditis)
- a patient with a completely normal thyroid gland may develop bacterial thyroiditis
- **frequency** – acute infectious thyroiditis is extremely rare

- **Signs and symptoms**

- fever (38-40 degrees)
- local pain and tenderness in the affected lobe or entire thyroid gland
- painful and difficult swallowing, sore throat
- erythema of overlying skin (skin is also warmer)
- thyroid swelling or abscess formation
- ↑ cervical lymph nodes
- usually - euthyrosis

- **complications**

- fistula (tracheal, esophageal)
- necrotic mediastinitis, pericarditis



- **Diagnostics**

- anamnesis + physical examination

- laboratory assays:

- leukocytosis + ↑ ESR
- TSH, fT4 – usually N

- **Diagnostics**
- imaging
  - usg: thyroid abscess (hypoechoogenic nodule)
  - **thyroid scintigraphy: cold nodule**
  - **fine needle biopsy + culture of the aspirate**
  - neck CT or MRI – in case of recurrent acute infectious thyroiditis in children (piriform sinus fistula)

- **Treatment**

- ✓ hospitalisation

- ✓ antibiotics – cloxacillin, nafcillin + cephalosporine III gen.  
or gentamicin, clindamicin

- ✓ surgical drainage

# Acute non-suppurative thyroiditis



- **Postirradiation thyroiditis**
  - I131 treatment
  - external irradiation
- 2 weeks after irradiation, disappears after 2-4 weeks
- symptoms: tenderness of entire thyroid gland, pain in the anterior neck radiating to ear, jaw or chest
- diagnostics: hormonal assays – sometimes transient thyrotoxicosis, usually hypothyreosis
- treatment: painkillers, non-steroidal anti-inflammatory drugs, prednisone, propranolol in case of transient thyrotoxicosis

# Subacute thyroiditis

- de Quervain's thyroiditis
  - spontaneous remission in 90% of patients
  - lasts 6 weeks – 6 months
  - can relapse only in 2% of patients
  - permanent hypothyroidism in 10% of patients

- **Etiology**

- usually after viral infection of upper respiratory tract (coxsackie, mumps, measles, adenovirus and other)

- genetic predisposition (HLA Bw35)

- after immunomodulation (IL-2 + TNF $\alpha$  lub IFN- $\gamma$ , immunosupresion)

- 5 cases/100 000/year

- ♀ : ♂ = 4 : 1

- **Signs and symptoms**

- thyroid enlargement
- pain and tenderness of thyroid gland, radiating to ears, jaw and chest
- **overlying skin is normal!**
- **cervical lymphnodes are not enlarged**
- malaise, painful muscles and joints
- fever (38-40 degrees)
- very rarely – painless

## ➤ **typical 4 phases**

I phase – acute inflammation – 1-2 weeks

II phase – transient thyreotoxicosis - 4-6 weeks

III phase - hypothyrosis – transient, 10% - permanent

IV phase - euthyrosis



# Diagnosics

- anamnesis + physical examination
- laboratory assays
  - moderate leukocytosis + ↑ ESR (even > 100/1h), ↑CRP
  - thyrotoxicosis: ↓TSH, ↑fT4
  - hypothyroidism: ↑TSH, ↓fT4
  - usually ↓ anti-TPO, anti-TG

# Diagnostics

## ➤ imaging

- usg – enlarged thyroid gland, hypoechogenic structure, vascularisation – N Iub ↓
- iodine uptake < 5%
- FNB: granulomas, plasmocytes, granulocytes

- **Treatment**

- ✓ glucocorticoides (prednisone - 4-6 weeks) – severe cases, very effective – fast improvement (almost „diagnostic”)
- ✓ painkillers, NSAIDs, aspirin
- ✓ beta-blockers (propranolol) – in case of transient thyrotoxicosis
- ✓ LT4 – in case of hypothyroidism

# Chronic autoimmune thyroiditis /Hashimoto disease/



The logo of the association consists of the portrait of Dr. Hashimoto who described the chronic thyroiditis for the first time in 1912. Since then, this new clinical entity has been internationally coined as “Hashimoto disease” or “Hashimoto thyroiditis”. The members of the association would like to pass on his pioneering spirit.



- **Hashimoto disease**

- the most common type of thyroiditis

- the most frequent cause of hypothyroidism

- leads to permanent hypothyroidism

- 2% of population, ♀:♂ = 5:1, 5-10% women after delivery

- **Hashimoto disease**

➤ may coexist with:

- Turner syndrome (50%), Down syndrome (16-28%)
- autoimmune polyglandular syndromes
- Sjögren's syndrome

- **Etiology and pathogenesis**

- autoimmune disease

- genetic predisposition

- risk factors:

- ❖ nicotine

- ❖ stress

- ❖ high iodine intake

- ❖ pollution

- ❖ selenium deficiency

- ❖ chronic viral hepatitis C

- ❖ drugs (INF $\alpha$ )

- ❖ monoclonal antibodies anti-CD52

- **Signs and symptoms**

- goiter or thyroid atrophy

- signs of hypothyroidism

- rarely – Hashitoxicosis – (+) TRAB (anti-TSHR antibodies) or thyroid destruction, transeint thyrotoxicosis

- sometimes – subclinical hypothyroidism (progression to permanent hypothyroidism - 3-5% patients/year)



- **Diagnostics**

- anamnesis + physical examination

- hormonal results:

- ↑TSH, fT4 N or ↓
- ↑ anti-TPO, anti-TG (90%)

- imaging

- thyroid gland usg: ↓ echogenicity
- FNA (rarely necessary) – limfocytes, plasmocytes (higher risk of thyroid lymphoma)



- **Treatment**

- ✓ goiter oppressing the trachea or abnormal FNA result → thyroidectomy
- ✓ hypothyroidism → LT4

- **Post-partum thyroiditis**

- 10% ♀ during the first year after delivery or abortion



- more frequently in:

- ♀ with (+) anti-TPO during the first trimester of pregnancy
- ♀ with:
- autoimmune thyroid disease in family
- patients with diabetes type 1 – 25%
- ♀ after previous post-partum thyroiditis – 70%

- **Post-partum thyroiditis**

- **symptoms**

- 30% of patients – tri-phasic course:

- I phase – transient thyrotoxicosis

- II phase – transient hypothyroidism, permanent when  
↑↑TSH

- III phase – euthyroidism

- **Diagnostics**

- ↑ anti-TPO, anti-TG
- absence of TRAB (anti-TSHR)
- ESR, blood count N
- Scintigraphy with technetium (contraindicated during lactation) – ↓ uptake
- Iodine uptake (contraindicated during lactation) < 5%

- **Treatment**

- transient thyrotoxicosis – beta-blocker
- hypothyroidism – LT4 – it is possible to try withdraw LT4 after 6-9 months
- 30-40% of patients – permanent hypothyroidism

- Painless (silent) thyroiditis

- 3-times more frequent than post-partum thyroiditis
- similar to subacute thyroiditis but without pain or tenderness
- usually spontaneous resolution, rarely – permanent hypothyroidism

# Riedel thyroiditis (chronic sclerosing thyroiditis)

- etiology – unknown – autoimmune?
- patophysiology – extensive fibrosis, not only of thyroid gland but also surrounding organs
- leads to compression of trachea, esophagus and other adjacent structures
- frequency – rare, ♀:♂ = 3:1, usually between 30 and 60 years of age
- 1/3 of patients – fibrosis of at least 1 area (excluding the neck)





# Signs and symptoms

- extremely hard goiter
- dyspnea, stridor
- hoarseness (uni- or bilateral laryngeal nerve palsy)
- dysphagia
- tetany in case of fibrosis of parathyroid glands
- in 30% of patients - hypothyroidism

# Diagnostics

- anamnesis + physical examination – small extremely hard goiter („like a stone”)
- laboratory results
  - TSH N, fT4 N
  - in 30% of patients - ↑TSH, ↓fT4
  - in 40-70% of patients - (+) anti-TPO and anti-TG
- imaging
  - CT or MRI of orbits, mediastinum, abdomen
  - FNA extremely hard to perform, usually non-diagnostic, sometimes – surgical biopsy

# Treatment

- ✓ glucocorticoids: prednisone - 4-6 months
- ✓ tamoxifen - has been successful in many of patients and is thought to suppress transforming growth factor beta (TGF $\beta$ )
- ✓ surgery may be required to preserve tracheal and esophageal function
- ✓ treatment with LT4 in case of
- ✓ tetany – calcium and vitamin D  
Denie tężyczki – wapń i witamina D

# Drug-induced thyroiditis

- amiodarone
- lithium
- interferone  $\alpha$  (+ ribavirin, + IL-2)

- **Amiodarone-induced thyroiditis**

- 20% - hypothyroidism – treatment: LT4, treatment with amiodarone may be continued

- 23% - thyreotoxicosis: 2 types

- type I: previous thyroid pathology, excessive production of thyroid hormones; treatment – anti-thyroid drugs + kalium perchlorate
- type II: destructive inflammation of previously normal thyroid gland; treatment – glucocorticoids, beta-blockers, NSAIDs
- frequently – mixed forms of inflammation; treatment – anti-thyroid drugs + glucocorticoids

