

# Pathology of the thyroid gland - investigations

## local:

palpation  
ultrasonography  
cytology  
biopsy  
resection

## general:

aspection  
hormonal  
cardiac

# Pathology of the thyroid gland – clinical aspects

## hormonal production

hyperthyreosis vs thyreotoxicosis  
hypothyreosis

## local findings

goiter  
syndromes due to compression (s. VCS ...)

## associated autoimmune diseases of the thyroid and ...

type 1 DM  
chronic atrophic gastritis „A“

## metastases in carcinomas

neck lymphadenopathy  
lungs  
bones

# Pathology of the thyroid gland - hyperfunction

## thyreotoxicosis

### **hyperthyreosis positive**

- Graves-Basedow disease
- goiter colloid diffuse and nodular
- „toxic“ adenoma
- carcinoma (FTC)

### *secondary*

- hypophyseal adenoma (TSH+)

### **hyperthyreosis negative**

- thyroiditis
- exogenic administration of thyroxin

# Pathology of the thyroid gland - hypofunction

## hypothyroidism:

### **primary (insufficiency of the thyroid)**

- developmental / dysgenesis (TTF-2, PAX-8, TSH-R mutace)
- syndrome of thyroxin resistency (mutation TR $\beta$ )
  
- **postablative** (thyreoidectomy, radioiodine, radiotherapy)
- **autoimmune** thyreoiditis (Hashimoto)
- **lack of iodine in food**
- drugs (jodids, lithium)

### **secondary**

- hypophyseal

### **tertiary**

- hypothalamic

# Hypofunction - kretenism

# Diffuse and nodous goiter – non-toxic, follicular, koloid

**endemic**

**sporadic**

# Thyreoiditis

- Hashimoto thyreoiditis
- subacute lymphocytic thyreoiditis
- subacute granulomatous thyreoiditis
- Riedel goiter – IgG4 disease

*separate entity:*

**Graves / Basedow disease**  
**diffuse toxic goiter**

# Thyreoiditis

- Hashimoto thyreoiditis
- subacute lymphocytic thyreoiditis
- subacute granulomatous thyreoiditis
- Riedel goiter – IgG4 disease

*a separate entity:*

**Graves / Basedow disease**  
**diffuse toxic goiter**

*Robert James **Graves** (1797 – 1853)*

*Dublin 1821, described 1835*



# Thyreoiditis

- Hashimoto thyreoiditis
- subacute lymphocytic thyreoiditis
- subacute granulomatous thyreoiditis
- Riedel goiter – IgG4 disease

*a separate entity:*

**Graves / Basedow disease**  
**diffuse toxic goiter**

*Karl Adolf von **Basedow** (1799 – 1854)*

*Merseburg's trias 1840*

- *exophthalmus*
- *goiter*
- *palpitations*

# Neoplasms of the thyroid gland

## primary

### benign

**adenoma** – may appear as oncocytic variant  
**solid hyaline tumor**

### malignant

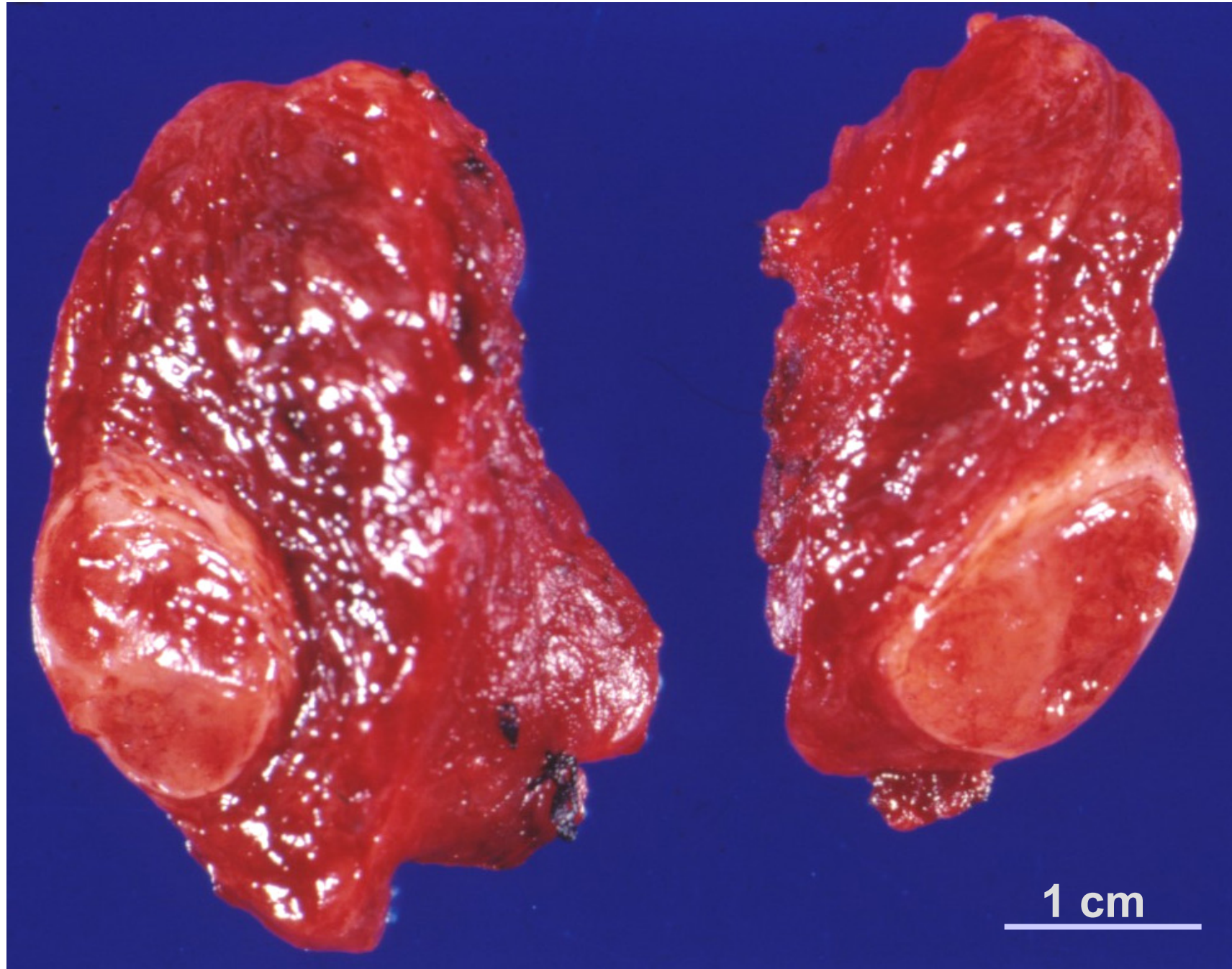
**carcinomas of the thyroid cells**  
may appear as oncocytic variant

**carcinoma of calcitonin producing C cells**

## secondary - rare

metastatic – renal cell carcinoma

# Adenoma



# Solid hyaline tumor

# Papillary thyroid carcinoma (PTC)

**75 – 85% of thyroid carcinomas**

# Papillary thyroid carcinoma (PTC)

## mutations

***BRAF***                      **45 – 80%**

***RET***                              **5 – 25%**

***RAS***

***TERT promotor***

**rearrangement RET/PTC (10q11.2) – *Rearranged during Transfection***  
**tyrosin kinase receptor**

**expressed in cells of neural plate, not in thyroid cells**

→ constitutive expression, RET gives promotor and dimerisation function  
expressed in about 50% PTC

# Papillary thyroid carcinoma (PTC)

**RET - PTC1** inv(10) *gen not well identified, locus only D10S170*  
**spontaneous PTC (20%)**

**RET - PTC2** t(10;17) *gen coding a regulatory subunit of  $\alpha$  cAMP dependent protein kinase A*  
**microcarcinomas (10%)**

**RET - PTC3** inv(10)  
**agressive PTC, rapidly growing**  
70% of patients with PTC, who were <10 years  
at the time of Czernobyl 1986

RET - PTC4 delší variantou RET/PTC3

RET - PTC5 invt(10) RFG5 RET fused gene 5 / také Černobyl  
RET - PTC6 t(7;10) HTIF1 human transcription intermediary factor 1  
RET - PTC7 t(1;10) transkripční koaktivátor pro jaderné receptory 6 a 7  
RET - PTC8 t(10;14) kinetin

# Papillary thyroid carcinoma (PTC)

## morphological variants

papillary

follicular

encapsulated

**papillary microcarcinoma**



# Follicular thyroid carcinoma (FTC)

**10 – 20% carcinomas**

# Follicular thyroid carcinoma (FTC)

## RAS

*protein p21 (GTP binding protein)*

**point mutations up to 50%**

may appear even in some adenomas = early oncogenic event

**PAX8 - PPAR $\gamma$**       t(2;3)

- **paired box homeotic gene 8** – specifický transkripční faktor gl th váže se na promotor a enhancer genu pro thyroxin, peroxidázu
- **peroxisomálními proliferátory aktivovaný receptor gama** (jaderný) tumor supresorový gen působící v gl th inhibuje růst, podporuje apopt.

gene fusion is specific in FTC, it is not present in adenomas (dif dg help)

# Anaplastic thyroid carcinoma (ATC)

**< 5% carcinomas**

# Anaplastic thyroid carcinoma (ATC)

***TP53*** mutated

late oncogenic event

**Rare thyroid cell carcinomas**

**Poorly differentiated carcinoma**

**Squamous cell carcinoma**

# Medullary carcinoma of the thyroid (MCT)

**5% carcinomas**

# Medullary thyroid carcinoma (MTC)

proto-oncogene **RET** 10q11.2 / 21 exons

point mutations – affecting the extracellular domain of the protein  
– constitutive RET protein activation through dimerization

- **sporadic**

**MTC** 75% (mutation exon 16 in 50%)

- **familial**

**FMTC** 25% (mutations exons 10, 11, 13 - 15)

- **familial**

as syndromes

**MEN**

**MEN2A** (mutation exon 10 and 11)

parathyroid adenoma – hyperparath  
feochromocytoma

**MEN2B** (mutation exon 16)

feochromocytoma  
marfanoid habitus, giant lips  
ganglioneuromatosis

**Hyperplasia of C cells in familial MTC, children, young adults**