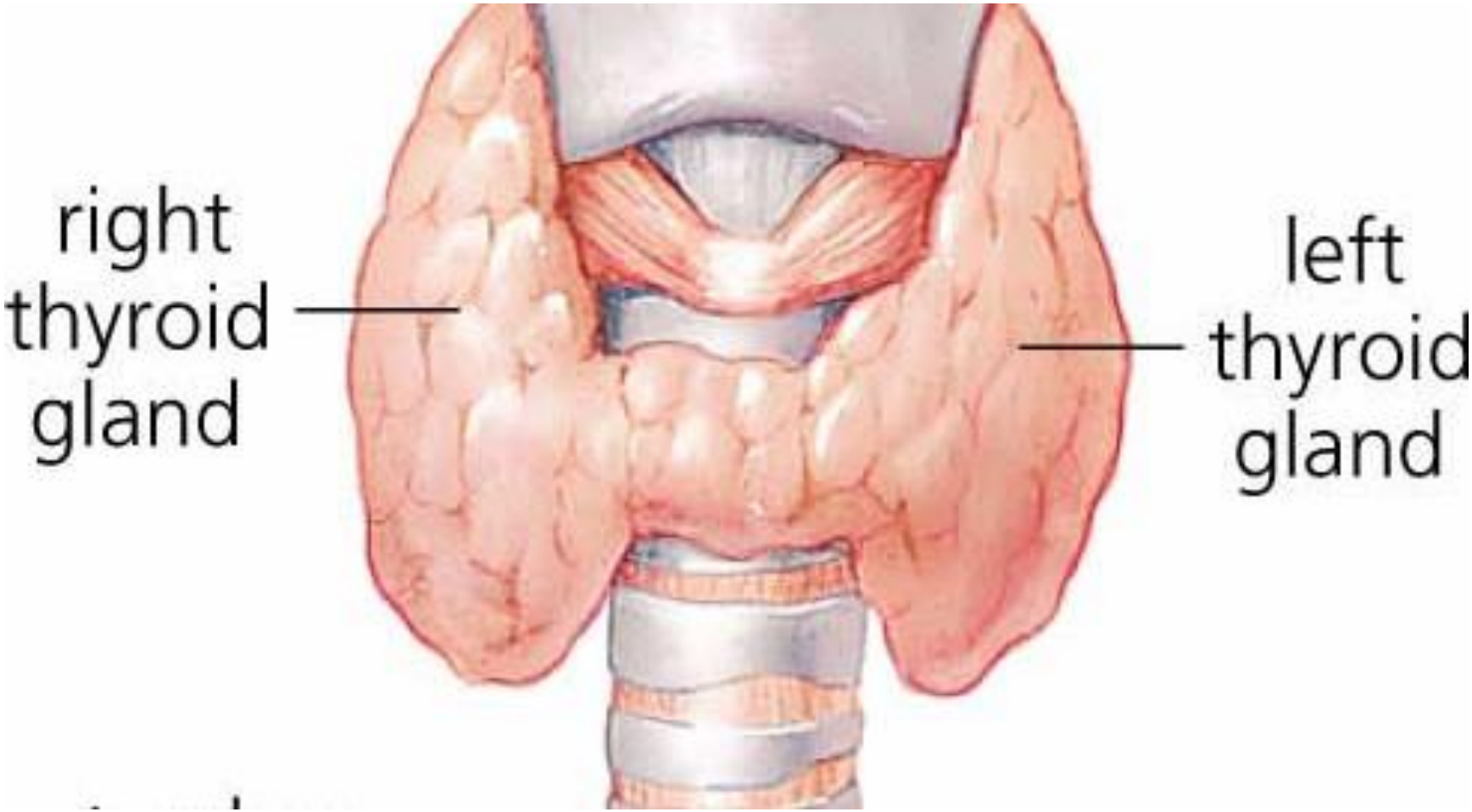
Endocrine system lectures 2&3
Thyroid gland

Dr Heyam Awad

FRCPath

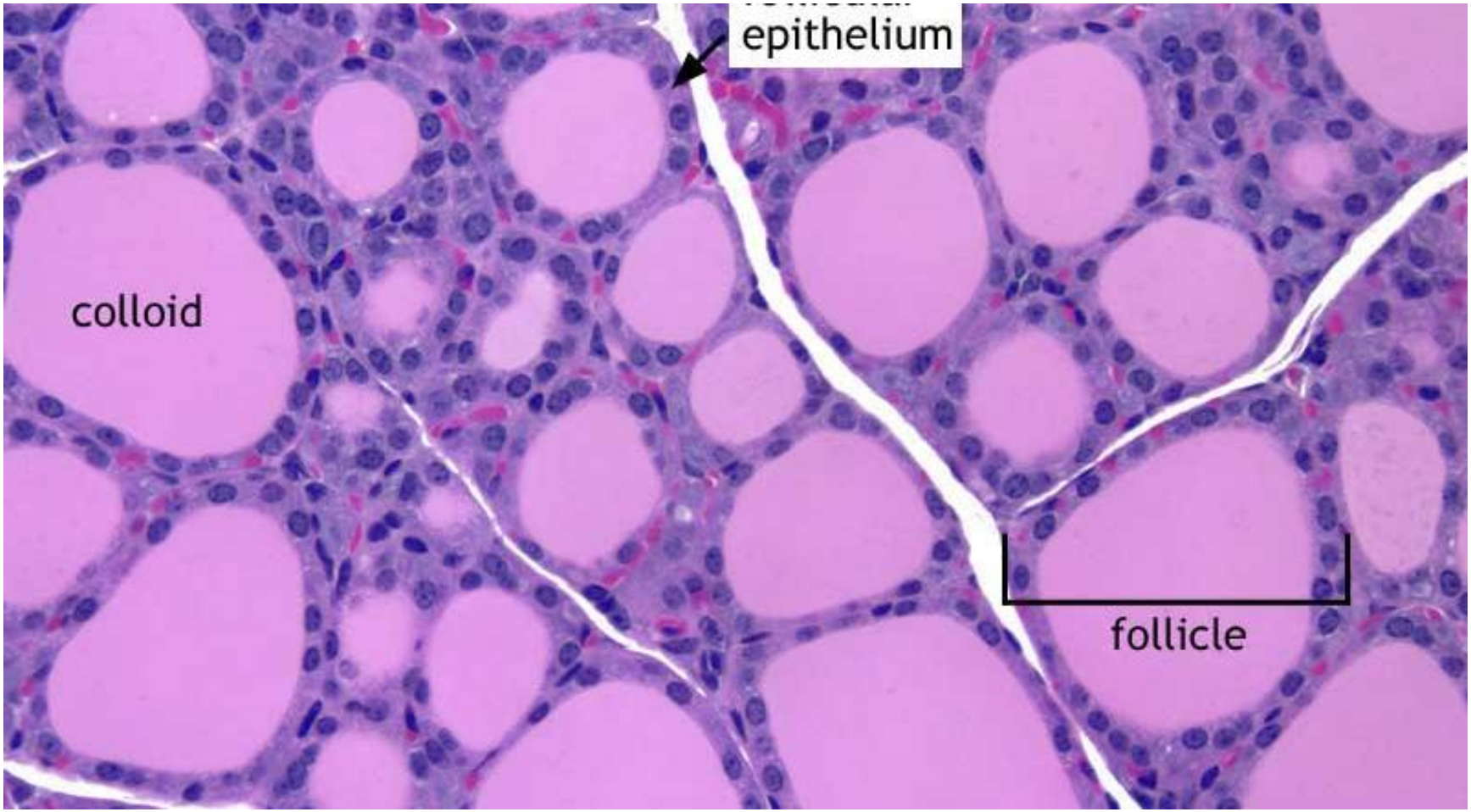
Thyroid gland: left and right lobes + isthmus



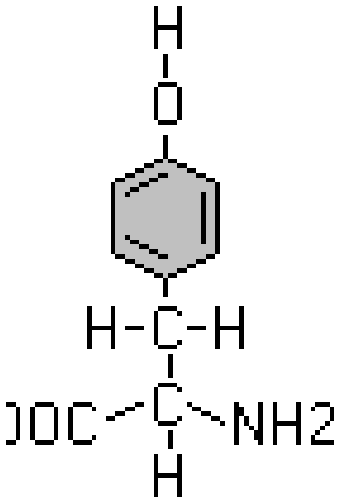
Thyroid gland histology

- Follicles lined by follicular epithelial cells which are cuboidal to low columnar
- The follicles contain colloid= thyroglobulin which is the iodinated precursor protein of thyroid hormones.

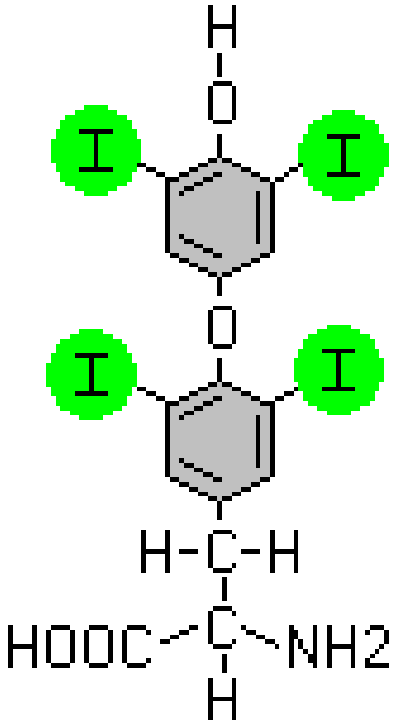
histology



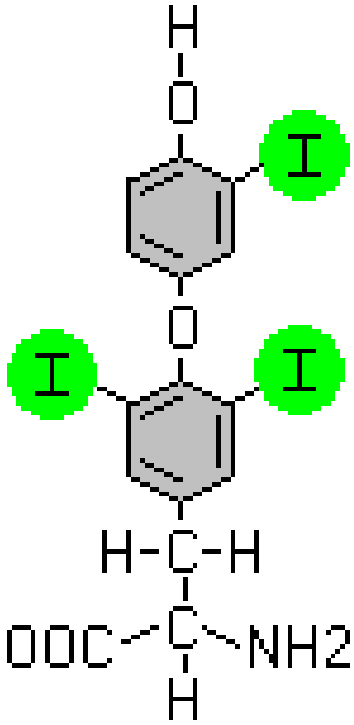
Thyroid hormones



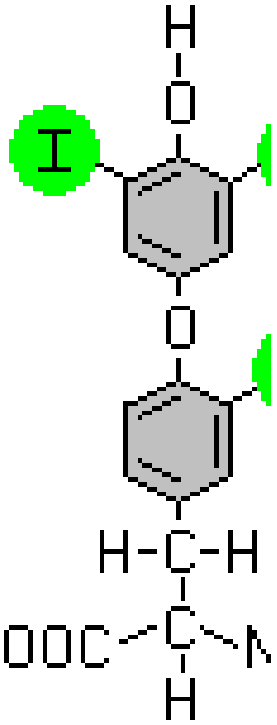
Tyrosine



Thyroxine (T4)



Triiodothyronine (T3)



"Reverse T
(inactive

Diseases of thyroid gland

Same general rule of all endocrine glands!

- Mass effect
- Hyperthyroidism (thyrotoxicosis)
- Hypothyroidism

- Again, there is no relation between mass effect and level of hormonal production

Thyroid diseases

Mass effect:

- Thyroiditis: inflammation that causes enlargement of the gland.
- Graves disease
- Diffuse nontoxic goiter and multinodular goiter
- neoplasms

increased thyroid hormone= thyrotoxicosis

*Thyrotoxicosis means: increased thyroid hormone, regardless of the cause of the increase.

*Hyperthyroidism is the most common cause of thyrotoxicosis and it means there is actual increase in thyroid hormone production from the thyroid gland.

NOTE: 1. actual increase excludes relative increase in cases of thyroiditis where there is destruction of the gland causing increased release (not production) of thyroid hormones… so there is **a relative** net increase in T3 & T4.. Here we have thyrotoxicosis but no hyperthyroidism

2. from the thyroid gland: this excludes **ectopic** production of thyroid hormones

HOWEVER, this is philosophical!! In clinical practice most people use the two terms to mean the same thing!!!!

1.Thyrotoxicosis Associated with hyperthyroidism (Thyroid hyperfunction):

1. ***Primary***

a. Diffuse toxic hyperplasia (Graves disease)
b. Hyperfunctioning (Toxic) multinodular goiter)
c. Hyperfunctioning (toxic) adenoma

2. Secondary -- TSH-secreting pituitary adenoma (rare)

2. Thyrotoxicosis not associated with hyperthyroidism : less common

- Excessive release of pre-formed hormone in thyroiditis (just increased release with no increased overall production)
- Ectopic secretion of thyroid hormones.. So thyroid function is normal.

Clinical manifestations of thyrotoxicosis

- Thyroid hormones increase basal metabolic rate, increase appetite, increase breakdown of fat and glucose
- Also increase heart rate, cause hypertension
- Increase body temperature

- SO if these hormones are increased you expect to see a wide range of symptoms

Clinical manifestations of thyrotoxicosis

a. Constitutional symptoms : warm flushed skin, heat intolerance and excessive sweating ,weight loss despite increased appetite.

b. Malabsorption, and diarrhea (because of increased intestinal motility)

c. Tachycardia and elderly patients may develop heart failure due to aggravation of pre-existing heart disease

d. Nervousness, tremor, and irritability.

e. A wide, staring gaze and lid lag because of sympathetic overstimulation of the levator palpebrae superioris

f. 50% develop proximal muscle weakness (thyroid myopathy).

g. Thyroid storm .. See next

Thyroid storm

- Abrupt onset of severe hyperthyroidism, and this condition occurs most commonly in individuals with Graves disease and it is a medical emergency because significant numbers of untreated patients die of cardiac arrhythmias
- Usually occurs in untreated or undertreated people

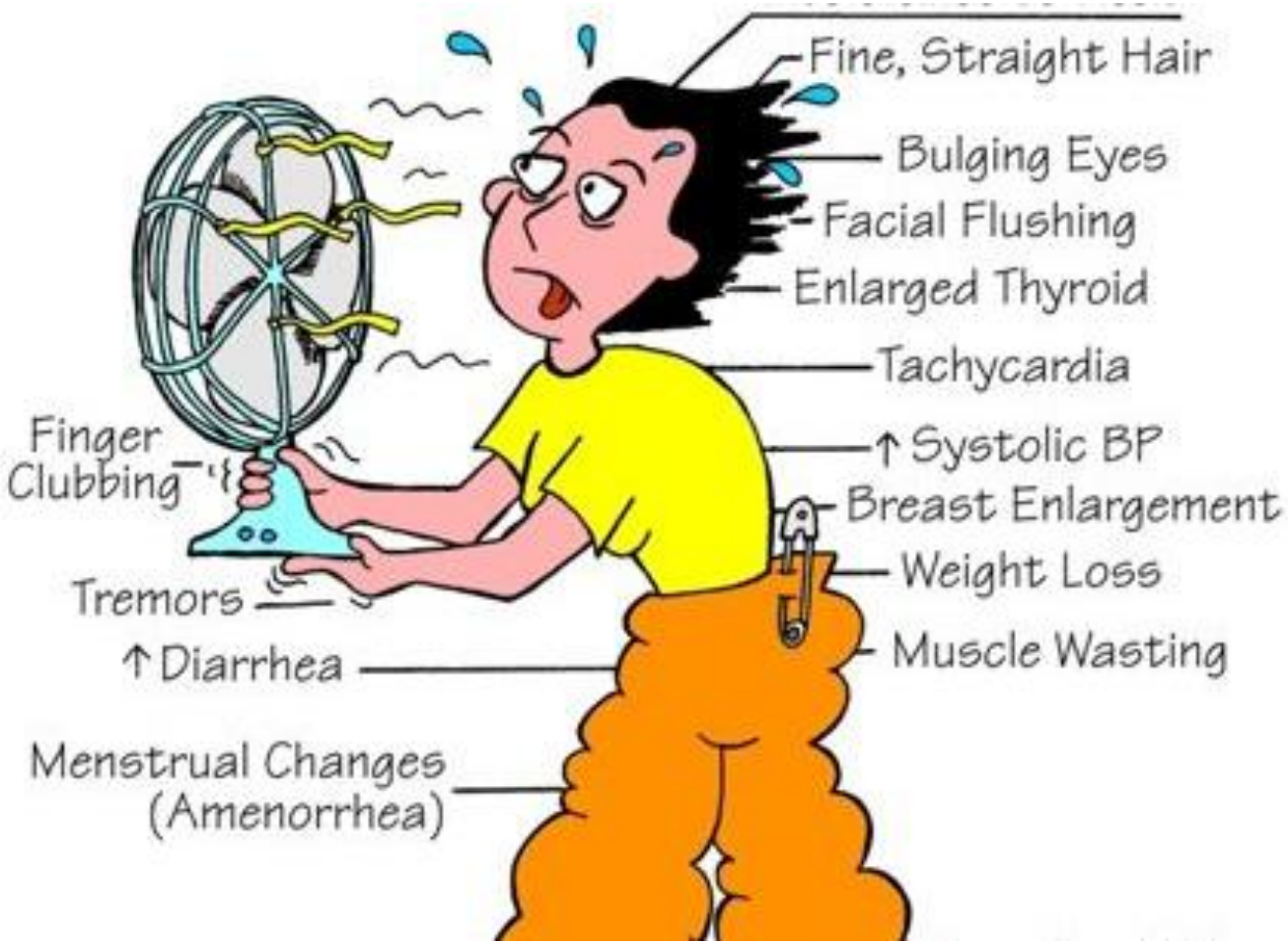
Thyroid storm

People with hyperthyroidism may develop thyroid storm after experiencing one of the following:

- trauma
- surgery
- severe emotional distress
- stroke
- diabetic ketoacidosis
- congestive heart failure
- pulmonary embolism

SO: make sure you control their thyroid hormone levels if they have one of the above. If they undergo surgery make sure you correct their hormonal levels before the surgery

hyperthyroidism



Lab tests

- *The measurement of serum TSH is the most useful single screening test for hyperthyroidism,* because TSH levels are decreased even at the earliest stages, when the disease may still be subclinical

- Once the diagnosis of thyrotoxicosis has been confirmed measurement of radioactive iodine uptake by the thyroid gland often is valuable in determining the etiology

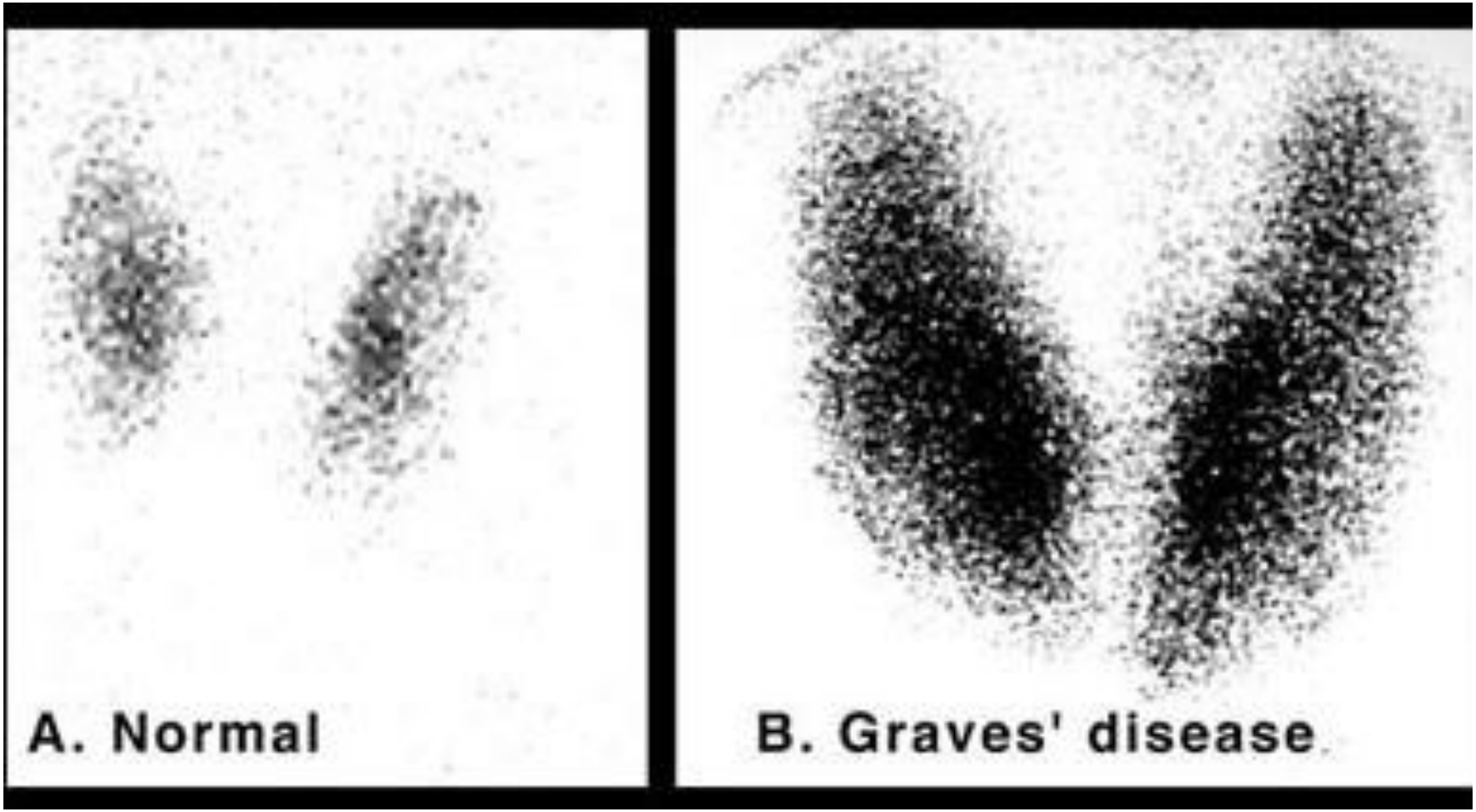
For example, such scans may show :

a. Diffusely increased (whole-gland) uptake in Graves disease,

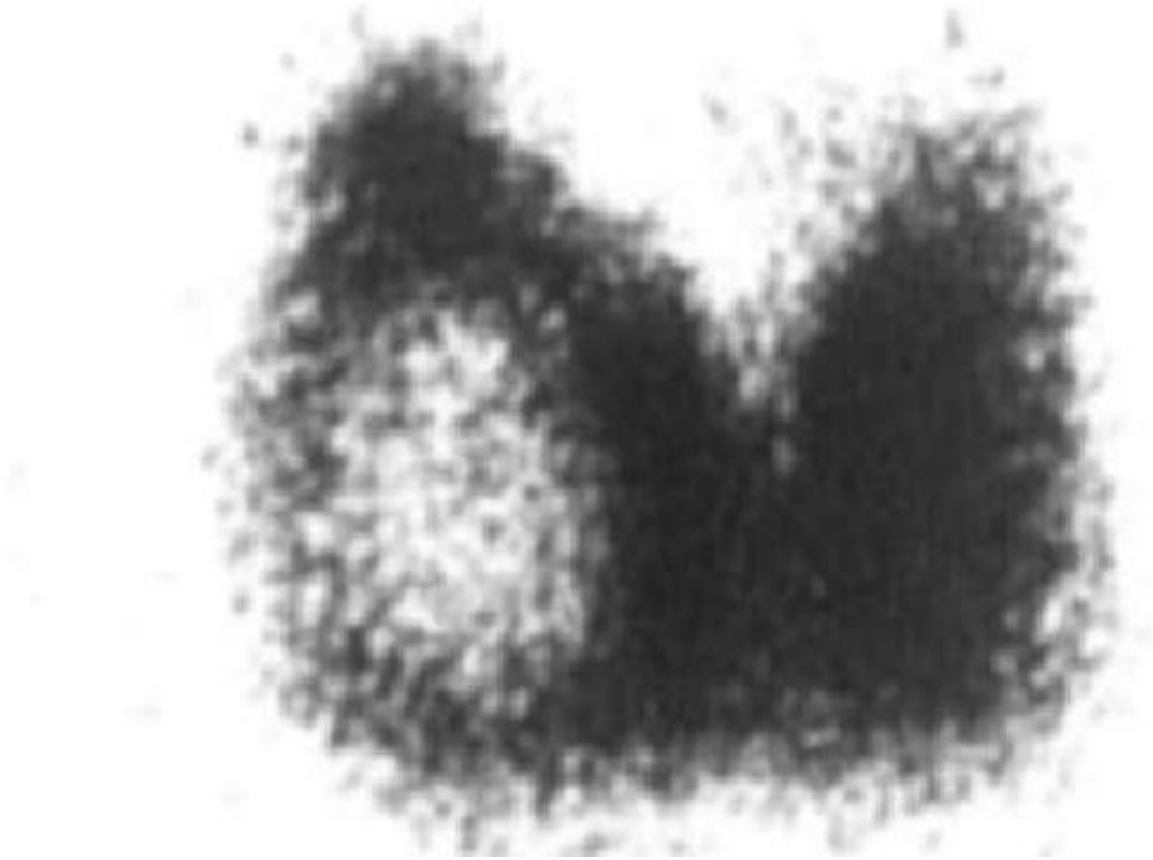
b. Increased uptake in a solitary nodule in toxic adenoma

c. Or decreased uptake in thyroiditis.

Iodine scans.. Black color shows how much iodine is the gland is taking.. More iodine means more activity in producing hormones



Cold nodule



HYPOTHYROIDISM :

Primary causes

a. - Worldwide, the most common cause of hypothyroidism is dietary deficiency of iodine.

b. In most developed countries, autoimmune diseases predominate such as Hashimoto thyroiditis

c. Genetic defects such as *Thyroid dysgenesis or*

Congenital biosynthetic defect (dyshormogentic goiter).

Secondary causes: Pituitary or hypothalamic disorder

HYPOTHYROIDISM

HAIR LOSS

APATHY

LETHARGY

DRY SKIN (COARSE & SCALY)

MUSCLE ACHES & WEAKNESS

CONSTIPATION

HAIR LOSS

APATHY

LETHARGY

DRY SKIN (COARSE & SCALY)

MUSCLE ACHES & WEAKNESS

CONSTIPATION

INTOLERANCE TO COLD

RECEDING HAIRLINE

FACIAL & EYELID EDEMA

DULL-BLANK EXPRESSION

EXTREME FATIGUE

THICK TONGUE-SLOW SPEECH

ANOREXIA

BRITTLE NAILS & HAIR

MENSTRUAL DISTURBANCES

LATE CLINICAL MANIFESTATIONS

- SUBNORMAL TEMP
- BRADYCARDIA
- WEIGHT GAIN
- ↓ LOC
- THICKENED SKIN
- CARDIAC COMPLICATIONS

C.J. MILLER

hypothyroidism

It causes:

- Cretinism.. Hypothyroidism in infancy and early childhood
- Myxedema… hypothyroidism in older children and adults

Cretinism :*R*efers to hypothyroidism developing in infancy or early childhood

1. Endemic cretinism: in dietary iodine deficiency is endemic, including mountainous areas (the Himalayas)
2. *Sporadic cretinism.* Caused by enzyme defects that interfere with thyroid hormone synthesis

Clinical features of cretinism include:

- Impaired development of skeletal system- short stature,
- Coarse facial features, protruding tongue, umbilical hernia.
- Central nervous system problems , with mental retardation

M*yxedema.* or Gull syndrome :

a. cold intolerance and obesity

b. Generalized apathy and mental sluggishness that in the early stages of disease may mimic depression

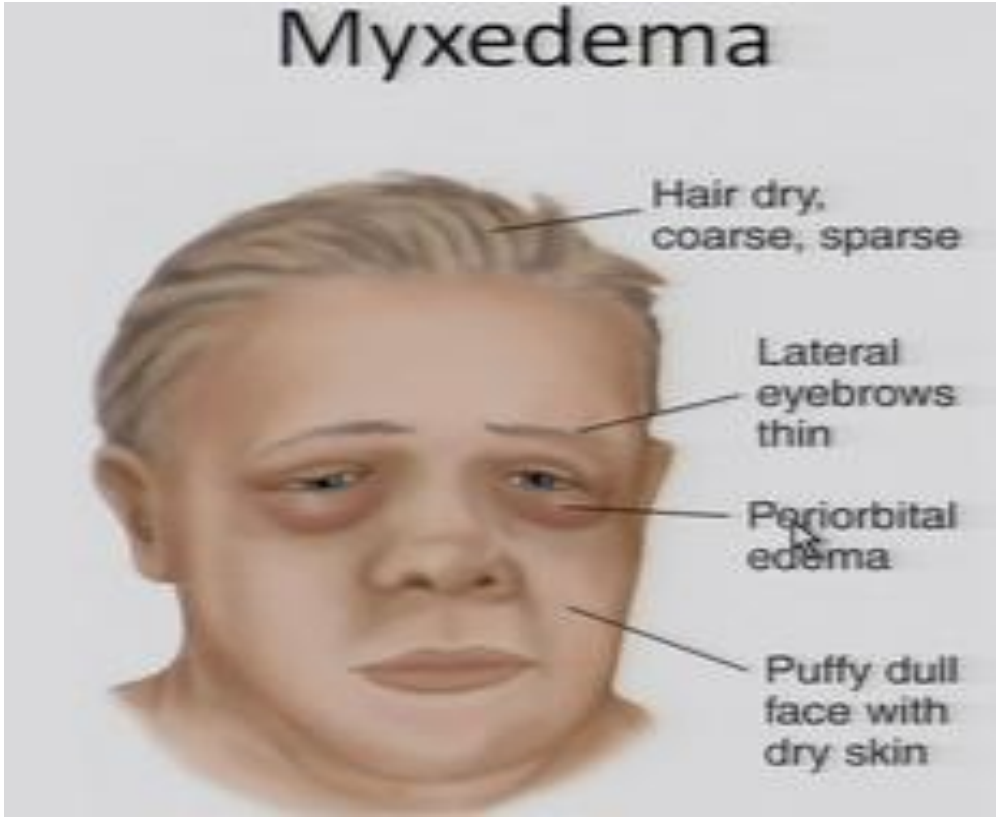
c. Broadening and coarsening of facial features

d. Enlargement of the tongue, and deepening of the voice.

e. Bowel motility is decreased, resulting in constipation.

f. Pericardial effusions are common; in later stages, the heart is enlarged, and heart failure may supervene.

g. Mucopolysaccharide-rich edematous fluid accumulates in skin, subcutaneous tissue, and number of visceral sites


Myxedema
Hair dry, coarse, sparse
Lateral eyebrows thin
Periorbital edema
Puffy dull face with dry skin

Lab tests

Serum TSH is the most sensitive screening test .

a. The serum TSH is increased in primary hypothyroidism

b. The TSH is not increased in persons with hypothyroidism caused by primary hypothalamic or pituitary disease.

c. Serum T_4 is decreased hypothyroidism of any origin.

thyroiditis

- = inflammation of the thyroid gland
- Several types:
- 1. Chronic Lymphocytic (Hashimoto) Thyroiditis
- 2.Subacute Granulomatous (de Quervain) Thyroiditis
- 3. Subacute Lymphocytic Thyroiditis
- 4.Riedel thyroiditis

Chronic Lymphocytic (Hashimoto) Thyroiditis

- *Is the most common cause of hypothyroidism in areas of the world where iodine levels are sufficient.*
- It is characterized by gradual thyroid failure secondary to autoimmune destruction of the thyroid gland
- It is most prevalent between the ages of 45 and 65 years and is more common in women than in men

***NOTE: ALL THYROID DISEASES ARE MORE IN WOMEN**

- It can occur in children and is a major cause of non-endemic goiter in children

PATHOGENESIS :-

Caused by breakdown in self-tolerance to thyroid antigens

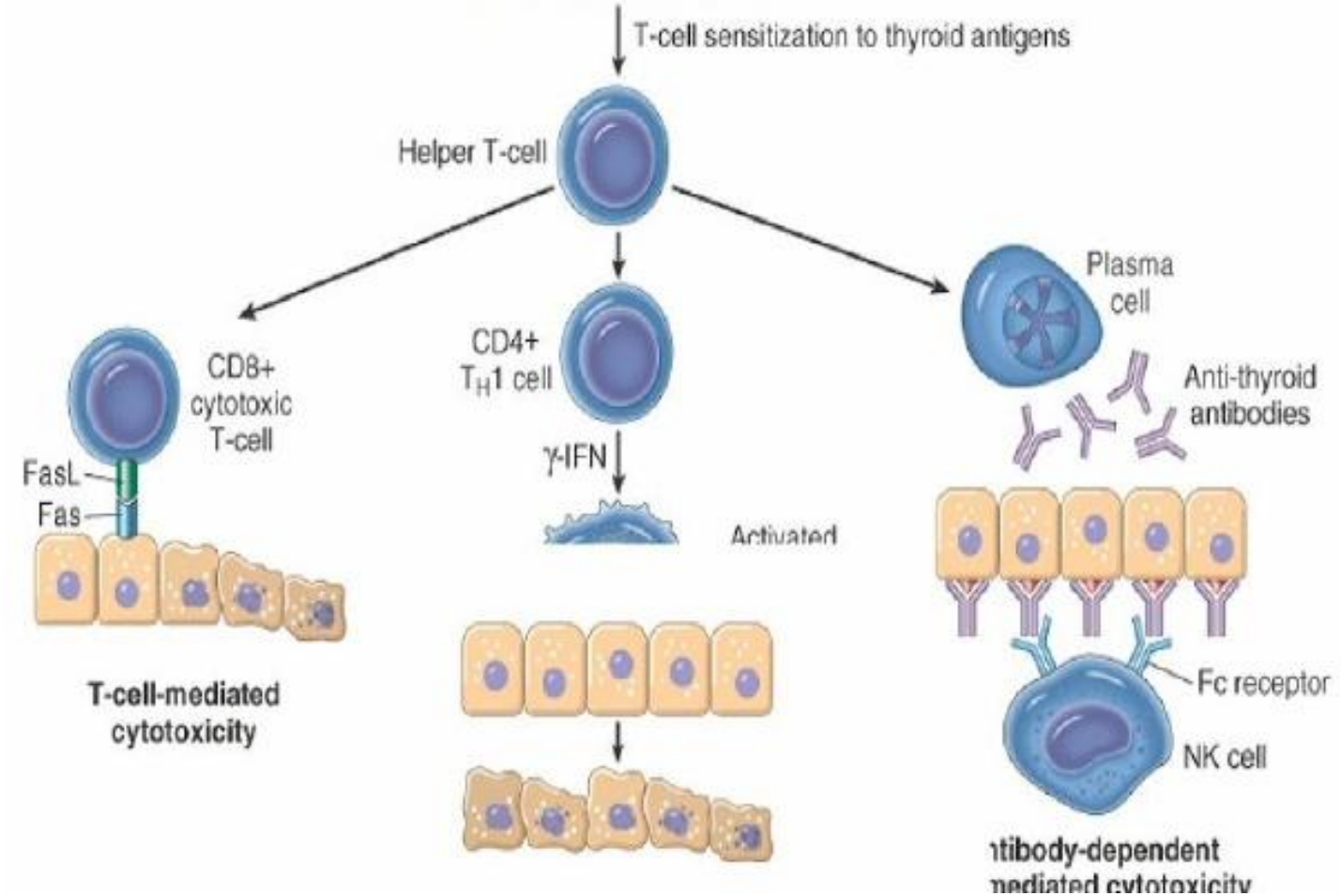
- Circulating autoantibodies against thyroid antigens are-present in the vast majority of patients
- Multiple immunologic mechanisms may contribute to thyroid damage ,

I. Cytokine-mediated cell death: Excessive T cell activation leads to the production of inflammatory cytokines such as IFN-γ in the thyroid with resultant recruitment and activation of macrophages and damage to follicles .

II. Binding of anti-thyroid antibodies (antithyroglobulin, and antithyroid peroxidase antibodies), followed by antibody-dependent cell-mediated cytotoxicity

III. T cell mediated cytotoxicity.

HASHIMOTO


T-cell sensitization to thyroid antigens
Helper T-cell
CD8+
cytotoxic
T-cell
FasL
Fas
T-cell-mediated
cytotoxicity
CD4+
T_H1 cell
γ-IFN
Activated
Plasma
cell
Anti-thyroid
antibodies
Fc receptor
NK cell
ntibody-dependent
nediated cytotoxicity

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HASHIMOTO

- A significant genetic component is supported by the

a. Concordance of disease in 40% of monozygotic twins,

b. the presence of circulating antithyroid antibodies in 50% of asymptomatic siblings of affected patients .

- Gross :

- Diffuse and symmetric enlargement of the thyroid but localized enlargement may be seen in some cases to raise suspicion for neoplasm

Microscopic examination reveals

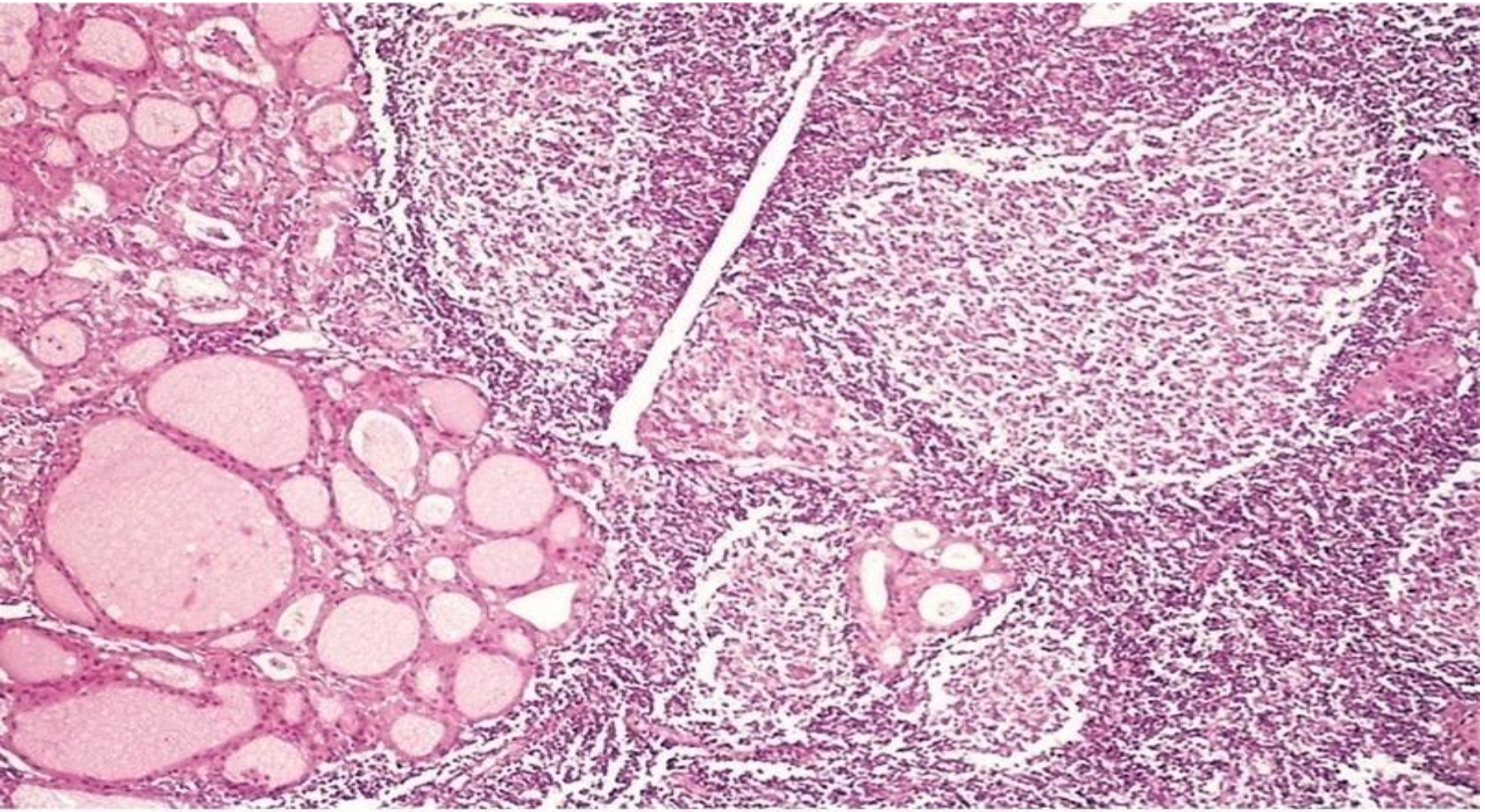
1. Infiltration by small lymphocytes, plasma cells, and well-developed germinal centers
2. The thyroid follicles are atrophic
3. Some follicles are lined by epithelial cells with abundant eosinophilic, cytoplasm, termed Hürthle cells and these Hurthle cells have numerous mitochondria

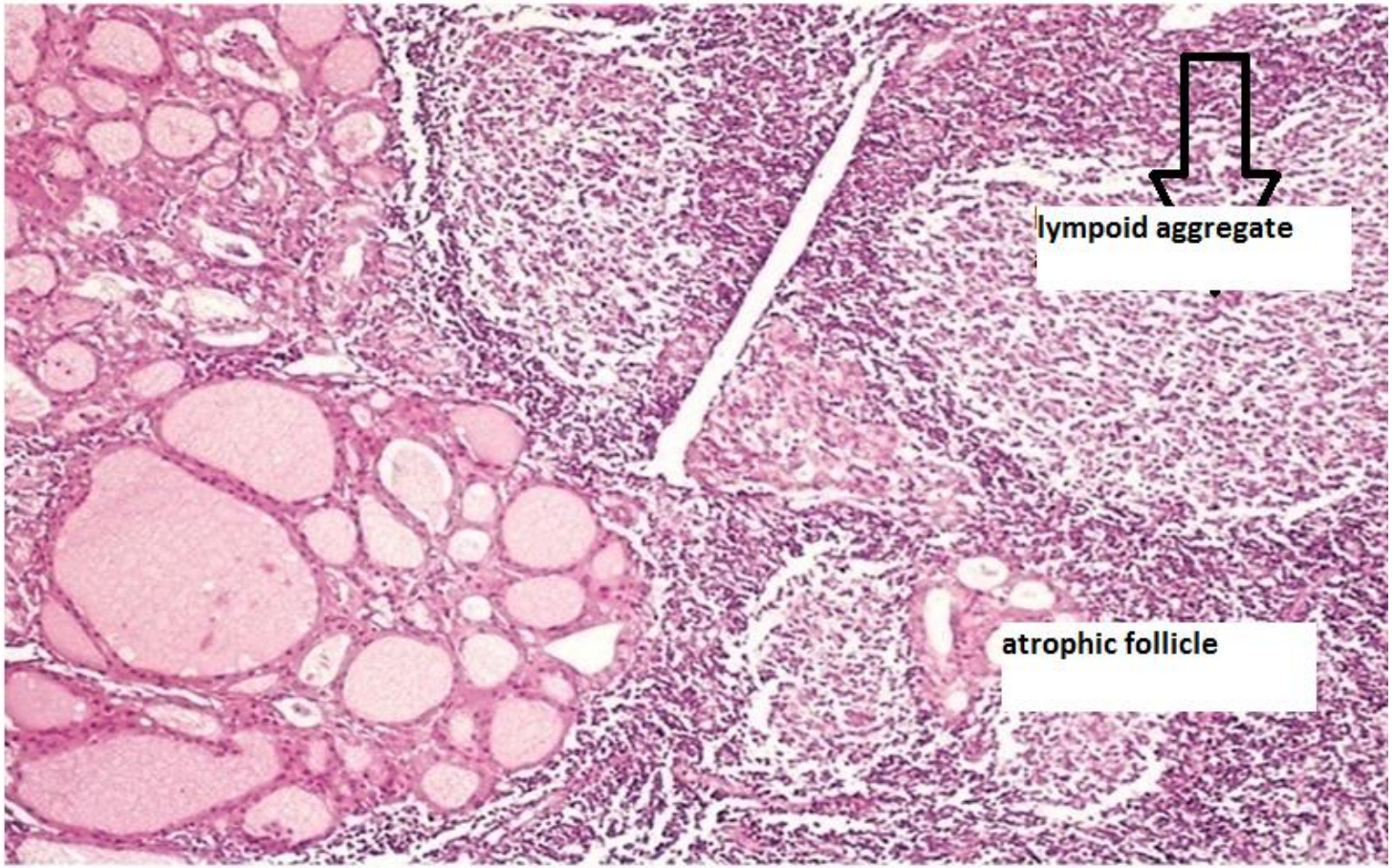
- ***Clinically*** ,

1. ***Painless*** *thyroid enlargement associated with some degree of hypothyroidism,*
2. - In the usual clinical course, hypothyroidism develops gradually.; however, it *may be preceded by transient thyrotoxicosis* due to disruption of thyroid follicles ,and secondary release of thyroid hormones (*hashitoxicosis*).

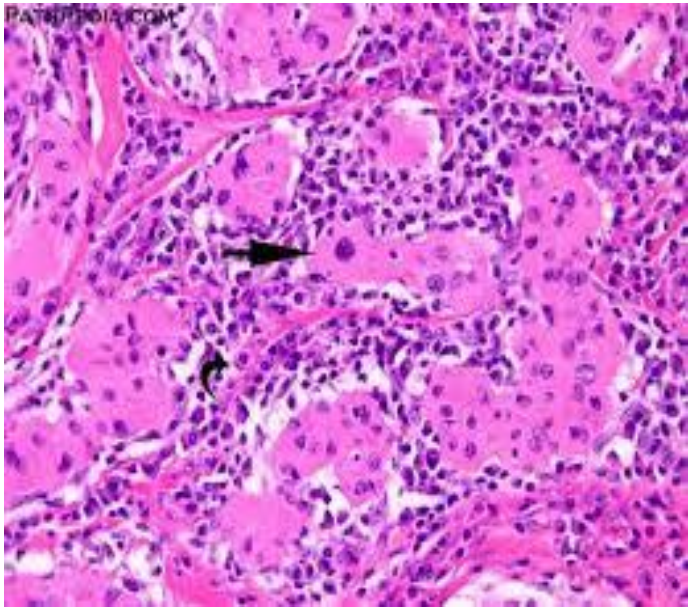
SO: at the beginning of the disease the destruction by autoimmune antibodies might cause increased release of thyroid hormones from the destructed follicles but later there is so much destruction and no new colloid is formed, resulting in hypothyroidism

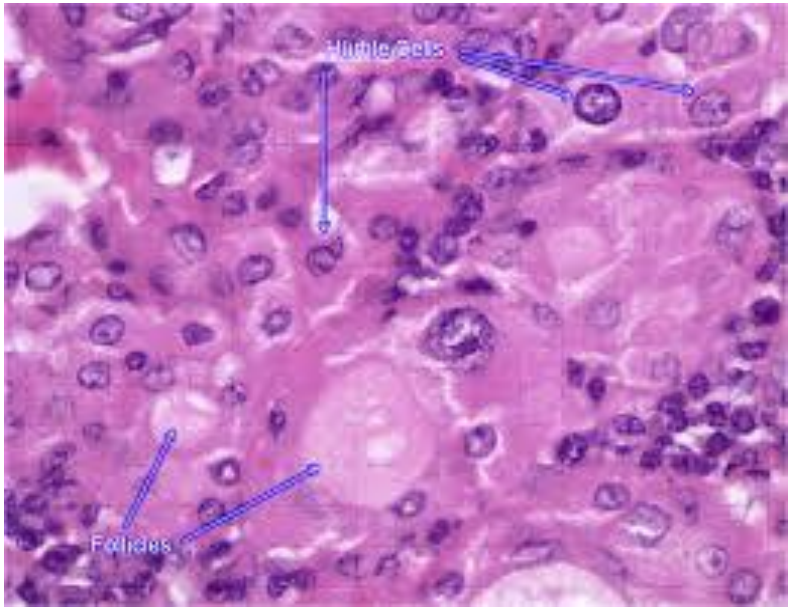
Hashimoto thyroiditis





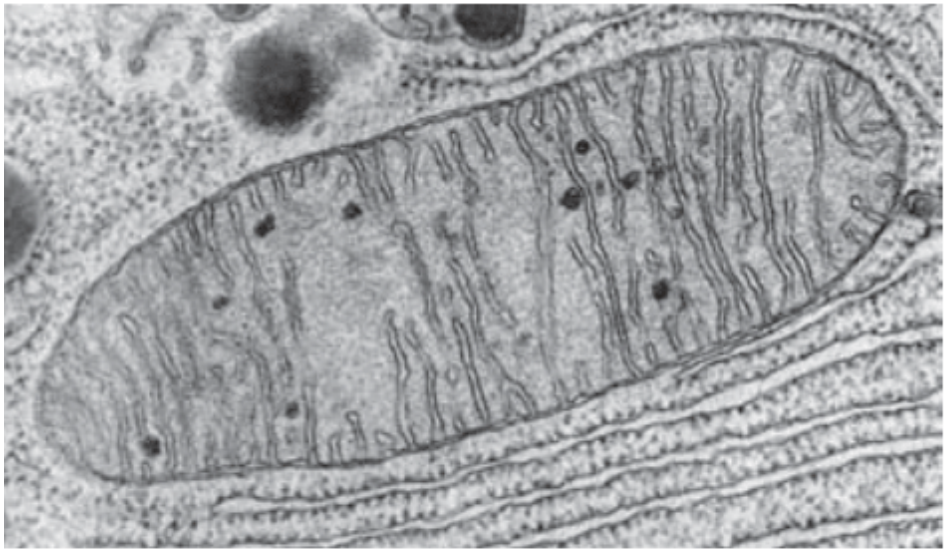
Hurthle cells: large cells with abundant eosinophilic cytoplasm, due to increased mitochondria





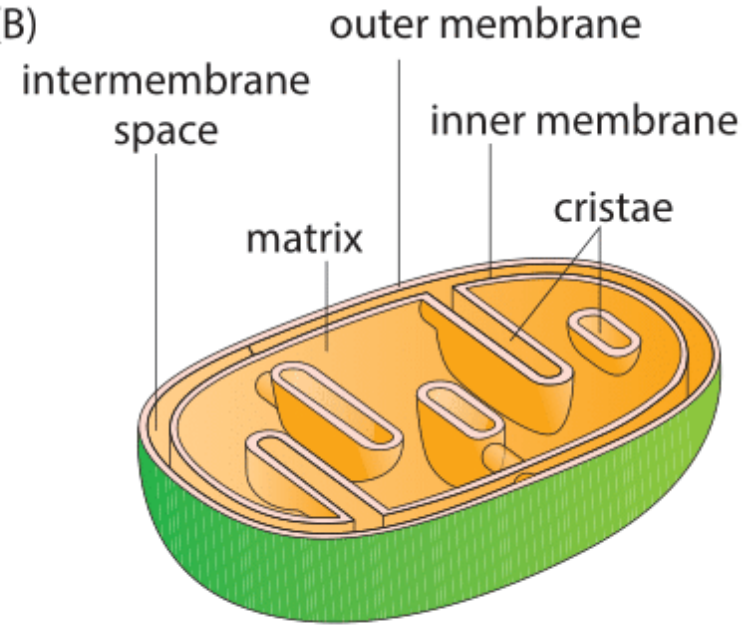
Hurthle cell cytoplasm is full of mitochondria

(A)



0.5 µm

(B)



3-D view of mitochondrion

- Patients with Hashimoto thyroiditis often :

1. Have *other autoimmune diseases*
2. .Are at *increased risk for the development of B cell non-Hodgkin lymphomas* within the thyroid gland.

Note:

- The relationship between Hashimoto disease and thyroid epithelial cancers remains controversial, with some morphologic and molecular studies suggesting a predisposition to papillary carcinomas

Subacute Granulomatous (de Quervain) Thyroiditis

- Is much less common than Hashimoto disease
- Is most common between the ages of 30 and 50 and,
- More frequently in women than in men.
- Is believed to be caused by a viral infection and a majority of patients have a history of an upper respiratory infection just before the onset of thyroiditis.

Gross- The gland has intact capsule, and may be unilaterally or bilaterally enlarged.

Histologic examination reveals

1. Disruption of thyroid follicles, with extravasation of colloid

leading to a neutrophilic infiltrate, which is replaced by lymphocytes, plasma cells, and macrophages.

2. The extravasated colloid provokes a granulomatous reaction with giant cells that contain fragments of colloid.

3. Healing occurs by resolution of inflammation and fibrosis.

- Clinical Features :

-Acute onset characterized by neck pain (with swallowing)

- Fever, malaise, and variable enlargement of the thyroid.
- Transient hyperthyroidism may occur as a result of disruption of follicles and release of excessive hormones.
- The leukocyte count is increased.
- With progression of disease and gland destruction, a transient hypothyroid phase may ensue.
- The condition typically is self-limited, with most patients returning to a euthyroid state within 6 to 8 weeks

Subacute Lymphocytic Thyroiditis :

- Also is known as *silent* or *painless* thyroiditis;
- And in a subset of patients the onset of disease follows - pregnancy (*postpartum thyroiditis*).
- Most likely to be autoimmune because circulating antithyroid antibodies are found in a majority of patients
- It mostly affects middle-aged women, who present with a- *painless* neck mass or features of thyrotoxicosis

Riedel thyroiditis,:

A rare disorder of unknown etiology,

- Characterized by extensive fibrosis involving the thyroid and contiguous structures simulating a thyroid neoplasm
- May be associated with idiopathic fibrosis in other parts of the body, such as the retroperitoneum
- The presence of circulating antithyroid antibodies in most patients suggests an autoimmune etiology

GRAVES DISEASE

The most common cause of endogenous hyperthyroidism with a peak incidence in women between the ages of 20 and 40.

Triad of manifestations:

A. Thyrotoxicosis, All patients

B. Localized, infiltrative dermopathy (pretibial myxedema), minority of cases and involves the skin overlying the shins, and manifests as scaly thickening

C. Infiltrative ophthalmopathy with resultant exophthalmos in 40% of patients

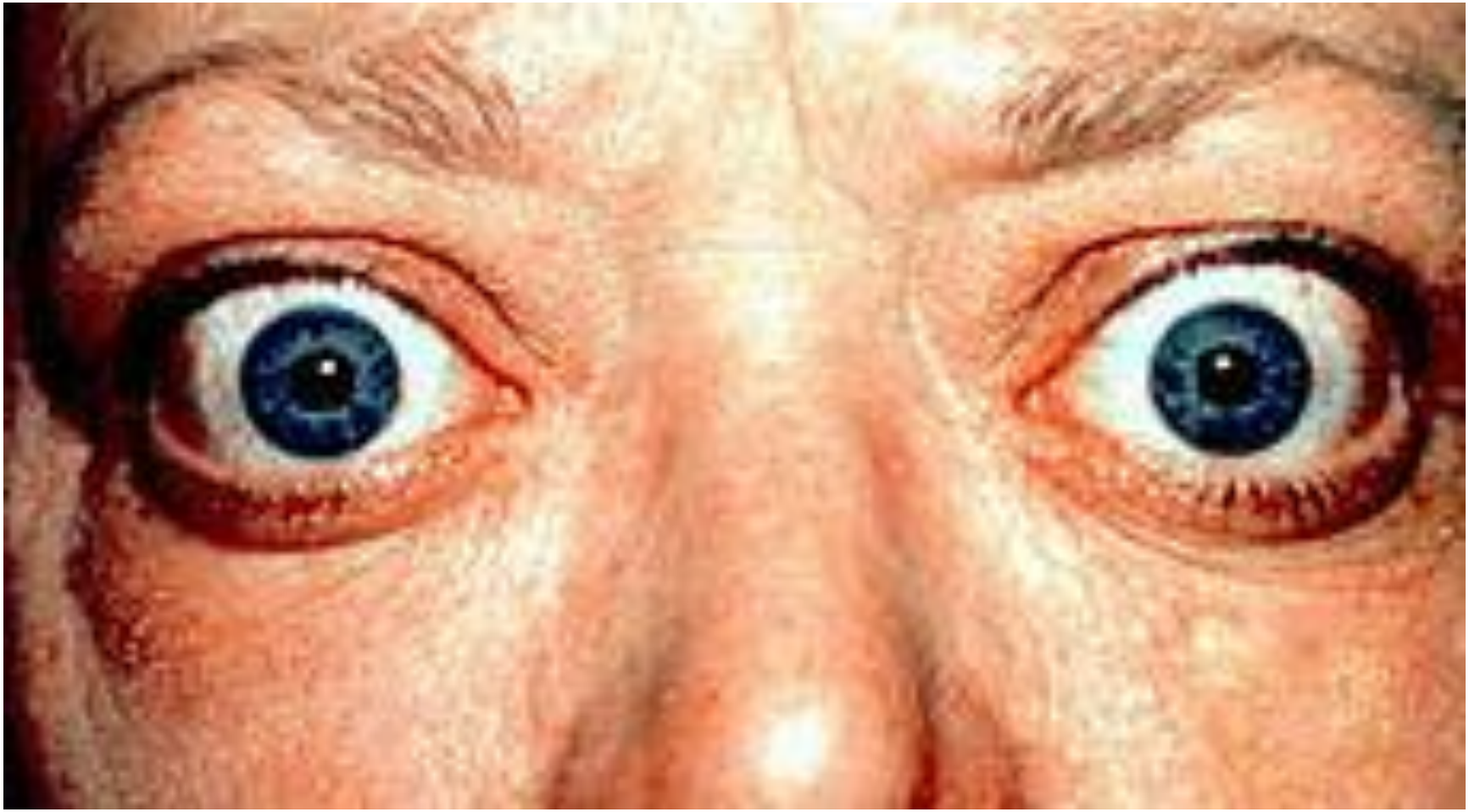
Exophthalmos is the result of increased volume of the retro-orbital connective tissues by

1. Marked infiltration of T cells with inflammatory edema
2. Accumulation of glycosaminoglycans
3. Increased numbers of adipocytes (fatty infiltration).

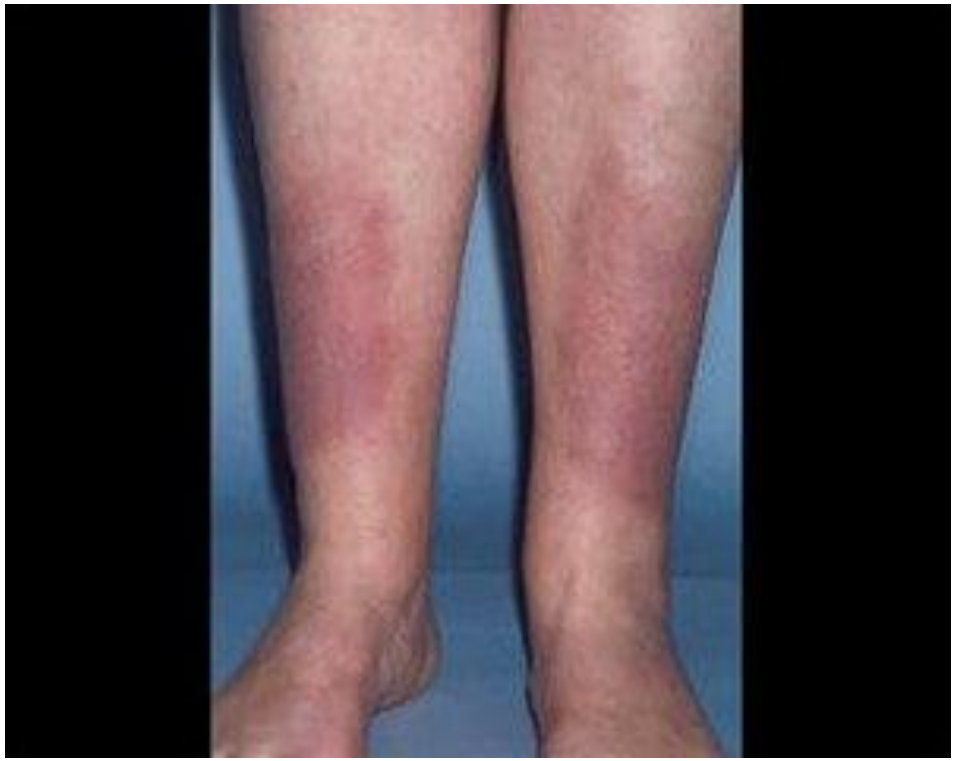
- These changes displace the eyeball forward, potentially interfering with the function of the extraocular muscles

- Exophthalmos may persist after successful treatment of the thyrotoxicosis, and may result in corneal injury.

exophthalmus



Pretibial myxedema



PATHOGENESIS :- Genetic factors are important in the causation of Graves disease, the incidence is increased in relatives of affected patients, and the concordance rate in

monozygotic twins is 60%.

- A genetic susceptibility is associated with the presence of

  HLA-DR3,

- it is characterized by a breakdown in self-tolerance to thyroid autoantigens, and is the production of multiple autoantibodies

Autoantibodies in GRAVES :

1. Thyroid-stimulating immunoglobulin:

- An IgG antibody binds to the TSH receptor and mimics the action of TSH, with resultant increased hormones

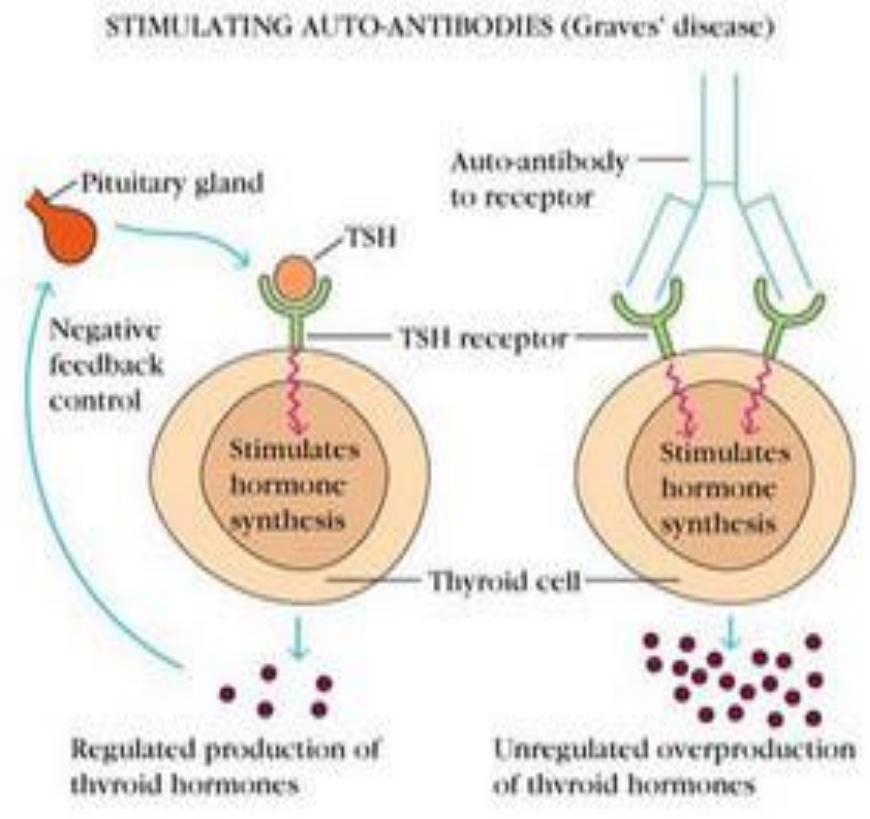
2. Thyroid growth-stimulating immunoglobulins:

- Directed against the TSH receptor, and have been implicated in the proliferation of follicular epithelium

3. TSH-binding inhibitor immunoglobulins:

- Prevent TSH from binding to its receptor on thyroid cells and in so doing may actually inhibit thyroid cell function, a finding explains why some patients with Graves spontaneously develop episodes of hypothyroidism.

Note the autoantibodies in Grave's cause stimulation of hormone synthesis



Note: The coexistence of stimulating *and* inhibiting immunoglobulins in the serum of the same patient may explain why some patients with Graves disease spontaneously develop episodes of hypothyroidism

.Gross: Symmetrical enlargement of the thyroid gland with intact capsule,

On microscopic examination,

a. The follicular cells in untreated cases are tall, and more crowded and may result in formation of small papillae

b. Lymphoid infiltrates, consisting predominantly of T cells, with few B cells and plasma cells are present throughout the interstitium; with formation of germinal centers

Laboratory findings and radiologic findings

- Elevated serum free T_4 and T_3 and depressed serum TSH
- Because of ongoing stimulation of the thyroid follicles radioactive iodine uptake is increased, and radioiodine scans show a *diffuse uptake* of iodine.

DIFFUSE AND MULTINODULAR GOITER

- Enlargement of the thyroid, or *goiter,* is the most common manifestation of thyroid disease

Mechanism :

- *The goiters reflect impaired synthesis of thyroid hormone* often caused by dietary iodine deficiency and this leads to to a compensatory rise in the serum TSH, which in turn causes hyperplasia of the follicular cells and, ultimately, gross enlargement of the thyroid gland .,

Goiters can be endemic or sporadic.

Endemic goiter :Occurs in geographic areas where the soil, water, and food supply contain little iodine.

- The term *endemic* is used when goiters are present in more than 10% of the population in a given region.
- Such conditions are common in mountainous areas of the world, including the Himalayas and the Andes but with increasing availability of iodine supplementation, the frequency and severity of endemic goiter have declined

Sporadic goiter : Less common than endemic goiter.

- The condition is more common in females than in males, with a peak incidence in puberty or young adulthood,

when there is an increased physiologic demand for T_4.

- It may be caused by several conditions, including the:

a. Ingestion of substances that interfere with thyroid hormone synthesis , such as excessive calcium and vegetables such as cabbage, cauliflower, sprouts, .

b. Hereditary enzymatic defects that interfere with thyroid hormone synthesis *(dyshormonogenetic goiter).*

-In most cases, the cause of sporadic goiter is not apparent.

MORPHOLOGY :

- Initially, the gland is diffusely and symmetrically enlarged (diffuse goiter) but later on it becomes multinodular goiter.

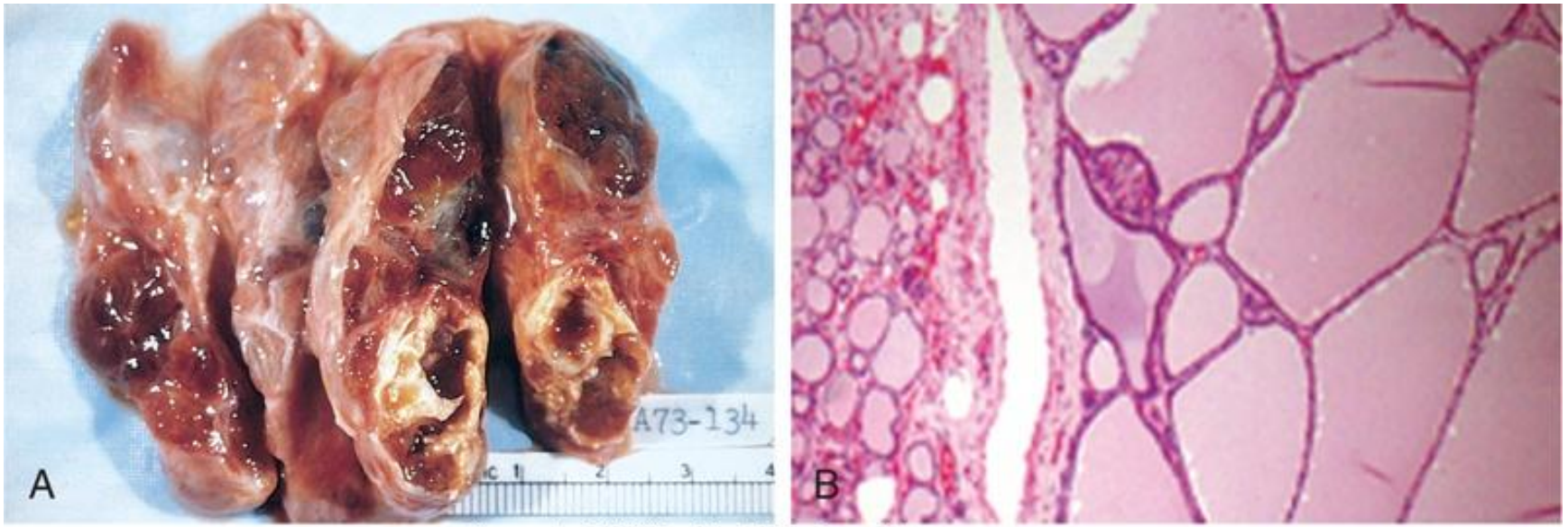
On microscopic examination,

a. The follicular epithelium may be hyperplastic in the early stages of disease or flattened and cuboidal during periods of involution.

b. Colloid is abundant in the latter periods (colloid goiter).

c. With time, recurrent episodes of hyperplasia and involution produce a more irregular enlargement of thee thyroid, termed multinodular goiter and virtually all long-standing diffuse goiters convert into multinodular goiters.

Multinodular Goiter



Kumar et al: Robbins Basic Pathology, 9e.

- Multinodular goiters cause multilobulated, asymmetrically enlarged glands which attain massive size and old lesions often show fibrosis, hemorrhage, calcification
- Multinodular goiters typically are hormonally silent,
- 10% of patients can manifest with thyrotoxicosis due to the development of autonomous nodules producing hormone independent of TSH stimulation and this condition, called toxic multinodular goiter or **Plummer syndrome**

Clinical Features :

a. The dominant features are *mass effects* of the goiter

b. may cause airway obstruction, dysphagia, and compression of large vessels in the neck and upper thorax

c. The incidence of malignancy in long-standing multinodular goiters is low (less than 5%) but not zero and concern for malignancy arises with goiters that demonstrate sudden changes in size or associated symptoms (hoarseness)

Thyroid tumors :

-present as solitary nodules.

- the majority of solitary nodules of the thyroid prove to be benign :

a. Follicular adenomas

b. A dominant nodule in multinodular goiter

c. Simple cysts or foci of thyroiditis

- Carcinomas of the thyroid, are uncommon, accounting for much less than 10% of solitary thyroid nodules.

- Several clinical criteria provide a clue to the nature of a given thyroid nodule:

a. Solitary nodules, in general, are more likely to be neoplastic than are multiple nodules.

b. Nodules in younger patients are more likely to be neoplastic than are those in older patients.

c. Nodules in males are more likely to be neoplastic than are those in females.

d. Nodules that take up radioactive iodine in imaging studies (*hot nodules*) are more likely to be benign than malignant.

Follicular adenomas

- Are benign neoplasms derived from follicular epithelium.
- solitary.
- The tumor is demarcated and compressed the adjacent thyroid parenchyma by a well-defined, intact capsule
- - cold nodules on scanning but might be functional.

.

Microscopic examination of follicular adenoma,

- The cells are arranged in follicles and its variants

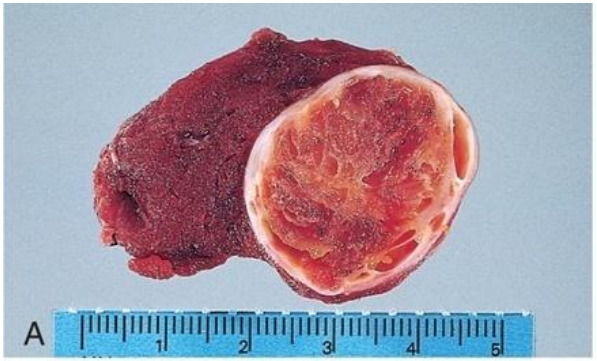
a. Hurthle cell adenoma:

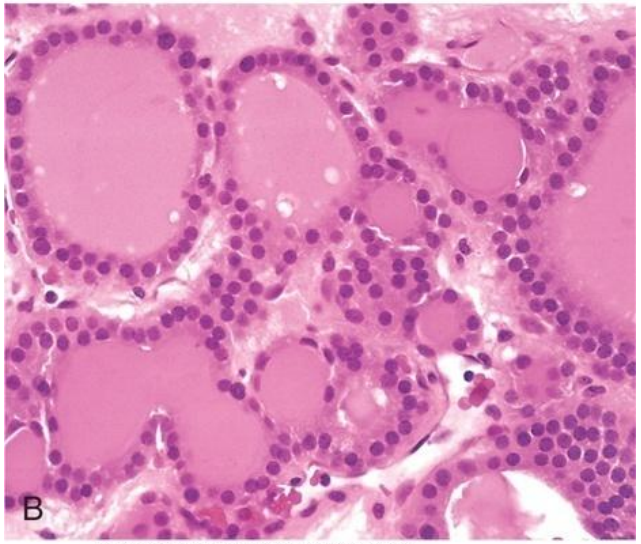
- The neoplastic cells show oxyphil or Hürthle cell change) and its behavior is not different from those of a conventional adenoma.

b. Atypical adenoma: The neoplastic cells exhibit focal nuclear atypia, (endocrine atypia);and these features do not constitute evidence of malignancy

**NOTE: endocrine atypia can occur in any benign neoplasm of any endocrine gand.

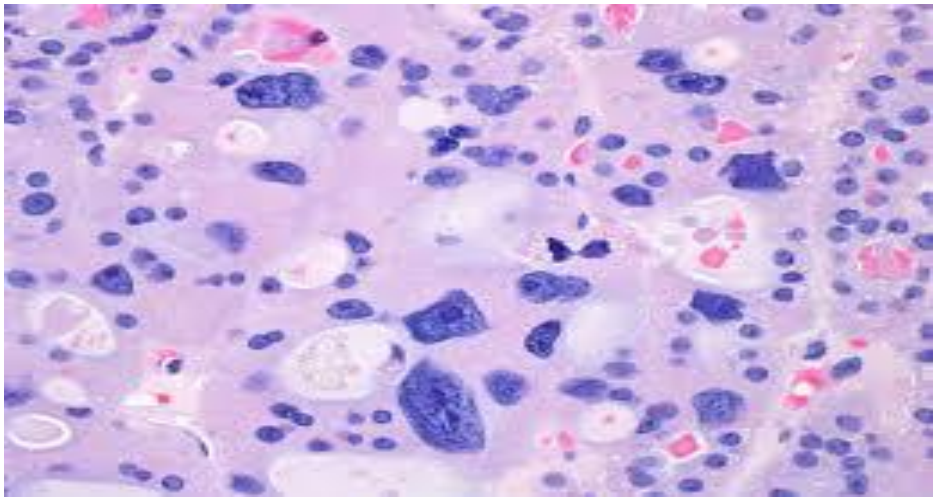
Follicular adenoma





Endocrine atypia

- Note these large and pleomorphic cells in a thyroid adenoma. This is endocrine atypia that doesn't necessarily mean the lesion is malignant



- Thyroid adenomas :

a. Carry an excellent prognosis
b. and do not recur or metastasize
c. and are *not* forerunners to carcinomas (not premalignant)

- About 10% of *cold* nodules prove to be malignant and by contrast, malignancy is rare in *hot* nodules

Carcinomas :

- Accounting for about 1.5% of all cancers
- A female predominance has been noted among patients who develop thyroid carcinoma in the early and middle adult years
- **cases manifesting in childhood and late adult life are distributed equally between men and women**
- The major subtypes of thyroid carcinoma are are

1. Papillary carcinoma (for more than 85% of cases)
2. Follicular carcinoma (5% to 15% of cases)
3. Anaplastic carcinoma (less than 5% of cases)
4. Medullary carcinoma (5% of cases)

PATHOGENESIS: genetic and environmental factors play a role

A. Genetic factors: each type of thyroid carcinoma has a different genetic mutation

A. Papillary thyroid carcinomas**:**

1. rearrangements of *RET*
2. activating point mutations in *BRAF*

Note: RET rearrangements and *BRAF* point mutations are not observed in follicular adenomas or carcinomas.

GENETIC FACTORS

B. Follicular thyroid carcinomas:

a. Gain-of-function point mutations of *RAS,*

b. Loss-of-function mutations of *PTEN,* a suppressor gene

c. A unique (2;3) translocation presents in one third to one half of follicular carcinomas,

GENETIC FACTORS

C. Anaplastic carcinomas:

Inactivation of *TP53*, restricted to anaplastic carcinomas and may also relate to their aggressive behavior

GENETIC FACTORS

D. Medullary thyroid carcinomas:

- Arise from the C cells (Para-follicular cells)

a. Familial medullary thyroid carcinomas occur in multiple endocrine neoplasia type 2 (MEN-2) and are associated with germe line *RET* proto-oncogene mutations .

b. RET mutations are also seen in approximately one half of nonfamilial (sporadic) medullary thyroid cancers.

B. Environmental Factors.

a. The major risk factor to papillary thyroid cancer is exposure to ionizing radiation, during the first 2 decades of life.

b. Deficiency of dietary iodine: and by extension, an association with goiter is linked with a higher frequency of follicular carcinomas.

Papillary Carcinoma :

Is the most common form

- accounts for the majority of thyroid carcinomas associated with previous exposure to ionizing radiation.
- May occur at any age,

Gross: Either solitary or multifocal lesions

- Some are well circumscribed and even encapsulated; others infiltrate the adjacent parenchyma and the definitive diagnosis is made by microscopic examination

Microscopically:.

1. The nuclei of papillary carcinoma cells show:

a. optically clear nuclei, or "Orphan Annie eye" nuclei , seen on histological but not cytological preparations (formalin artefact)

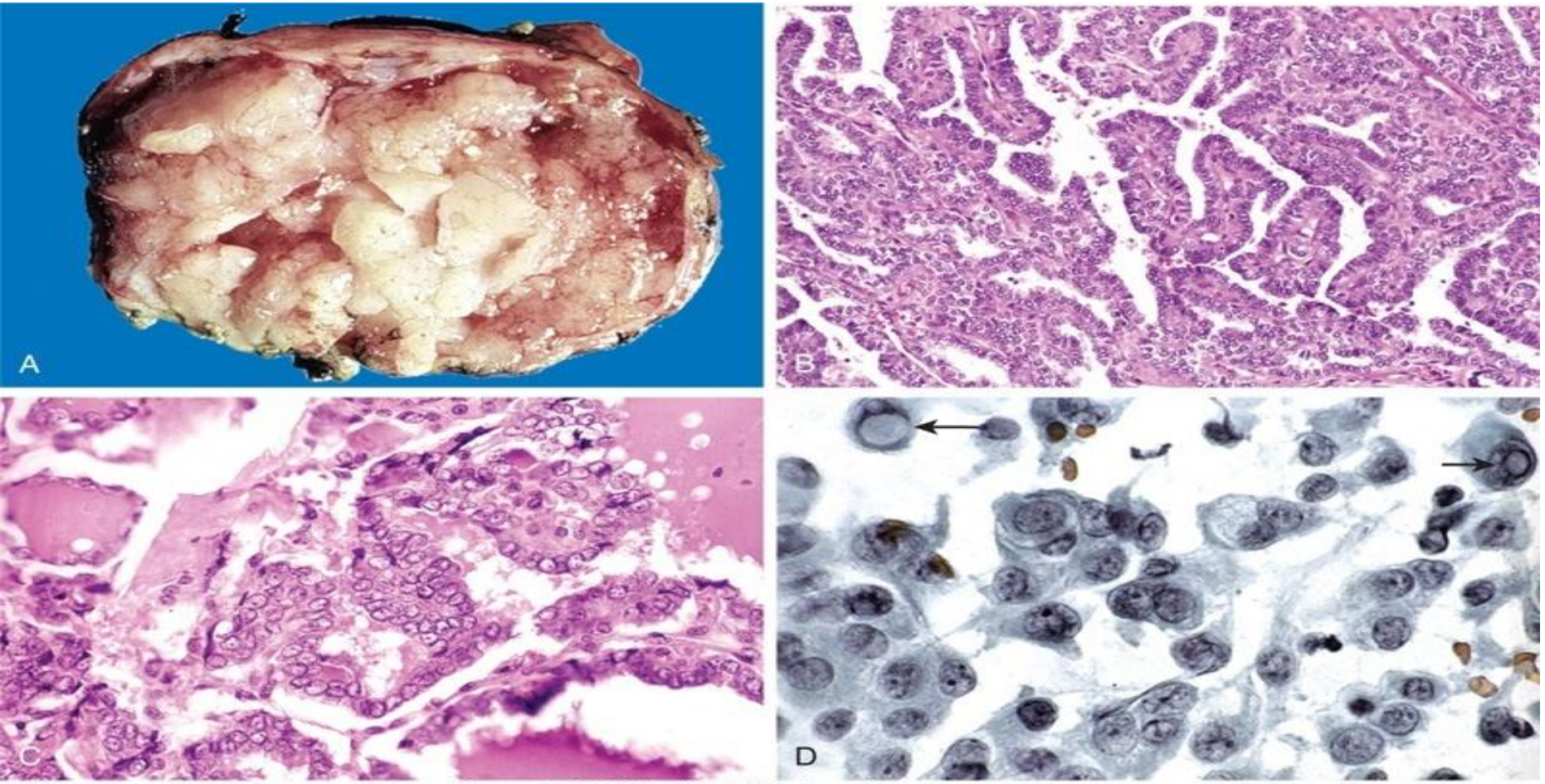
b. Have invaginations of the cytoplasm to the nucleus (pseudoinclusions)

2. papillary architecture is common

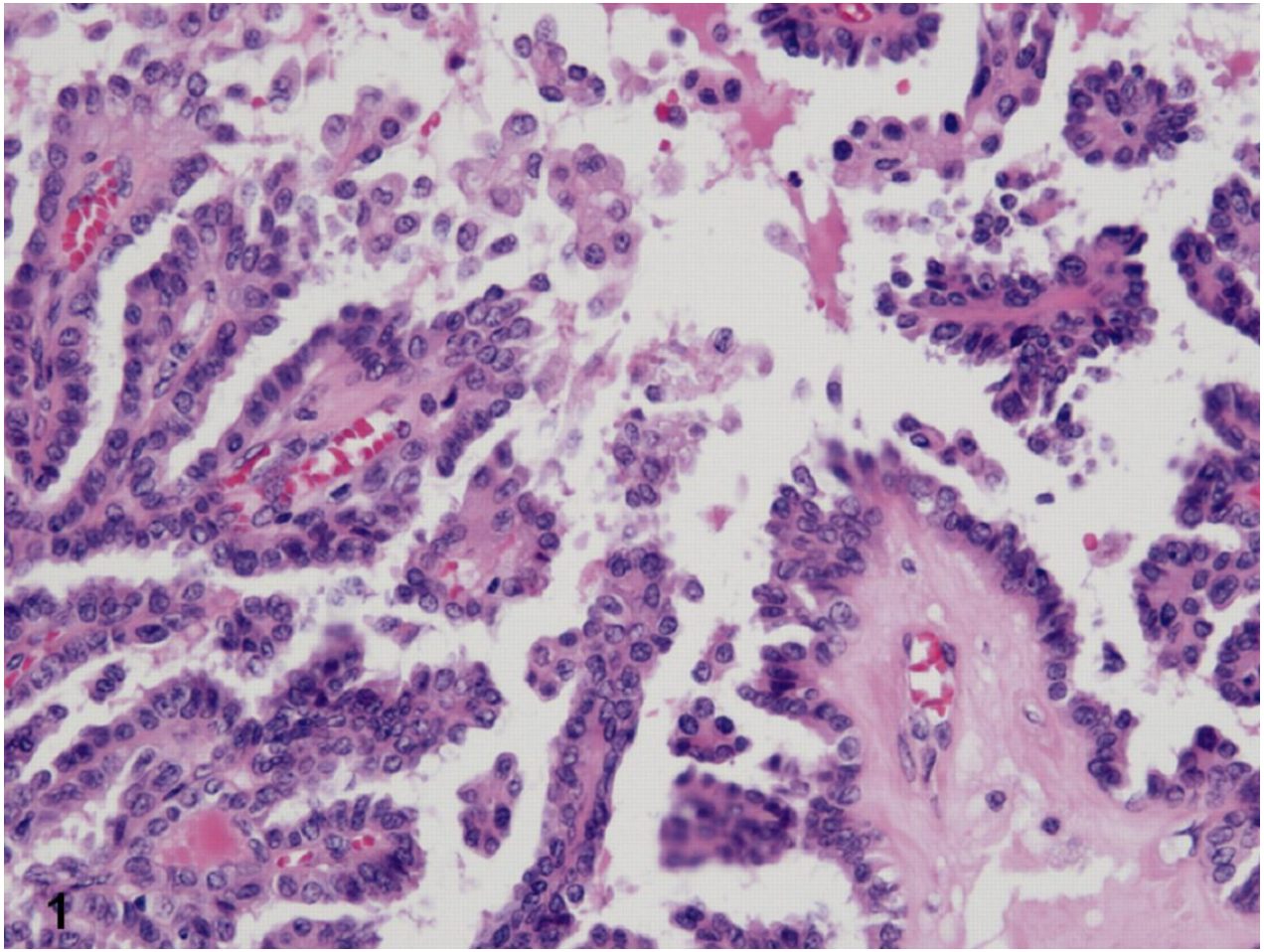
3. Concentrically calcified structures (psammoma bodies)

5. Metastases to cervical lymph nodes in half of cases.

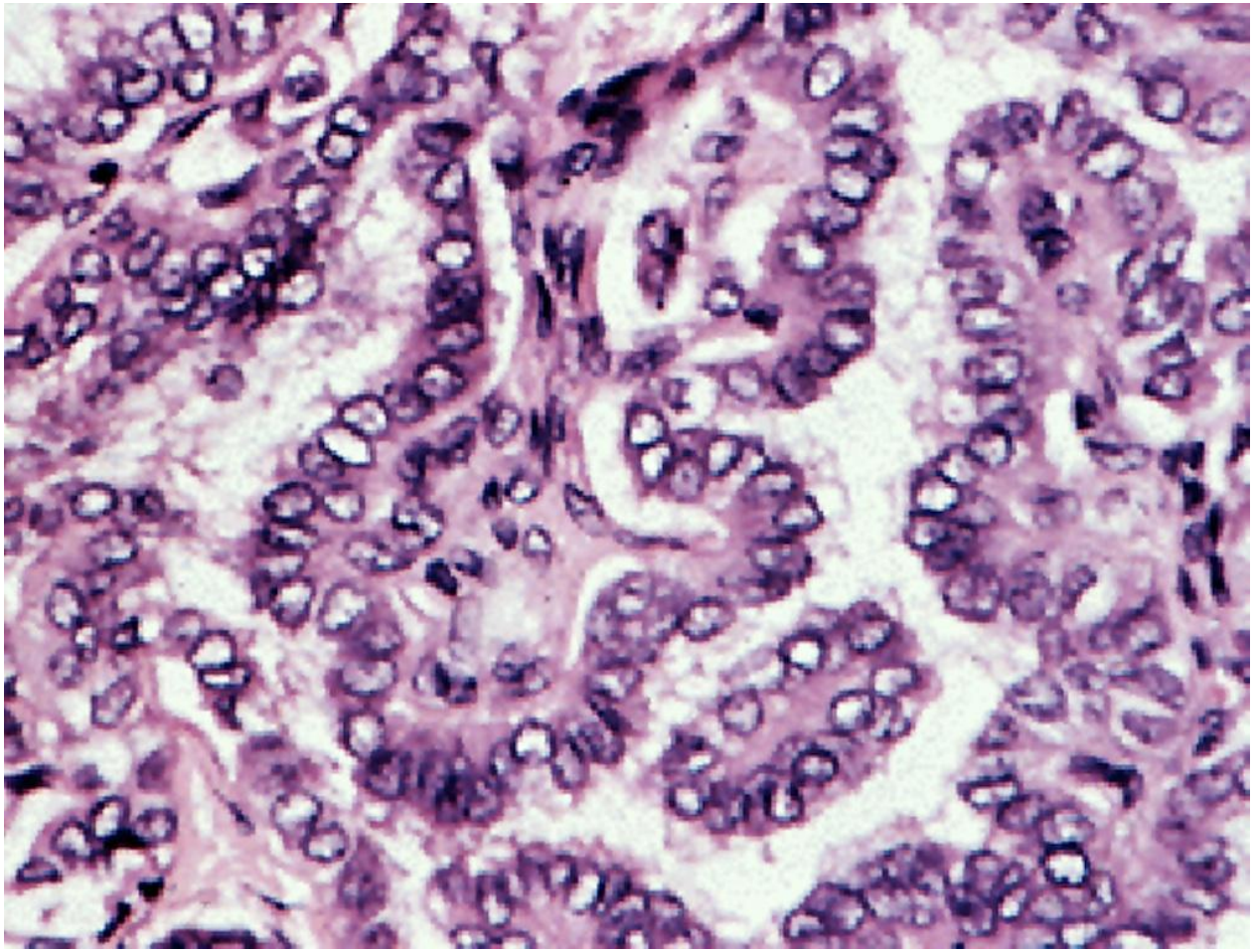
Papillary carcinoma



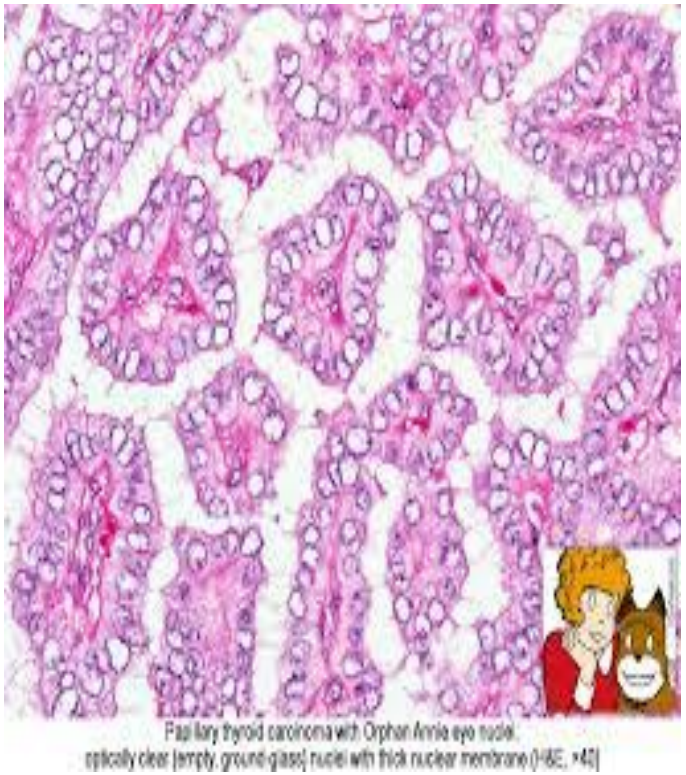
Papillary structures: projections with vascular core



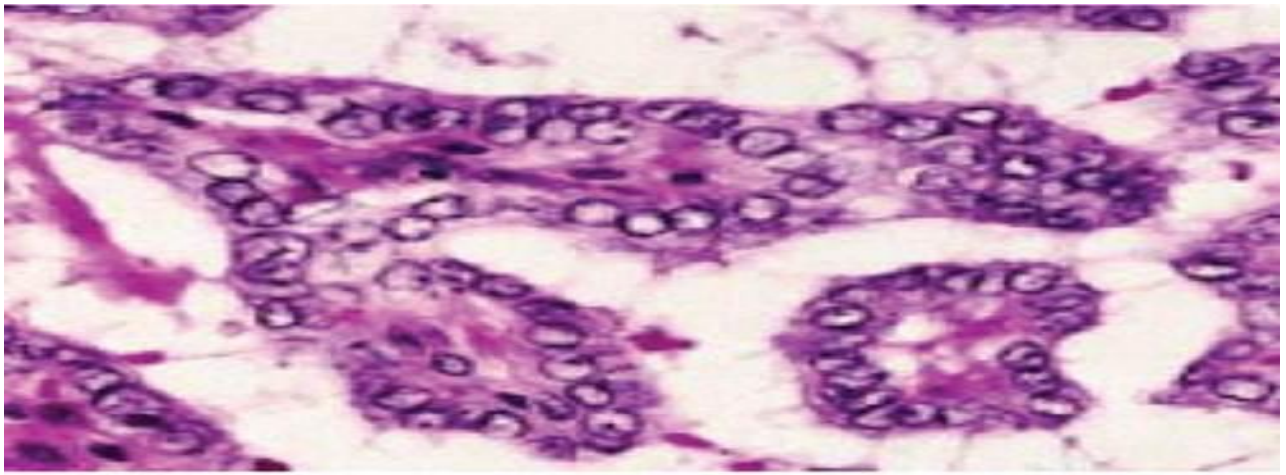
Clear nuclei: note the nuclei are whitish in color



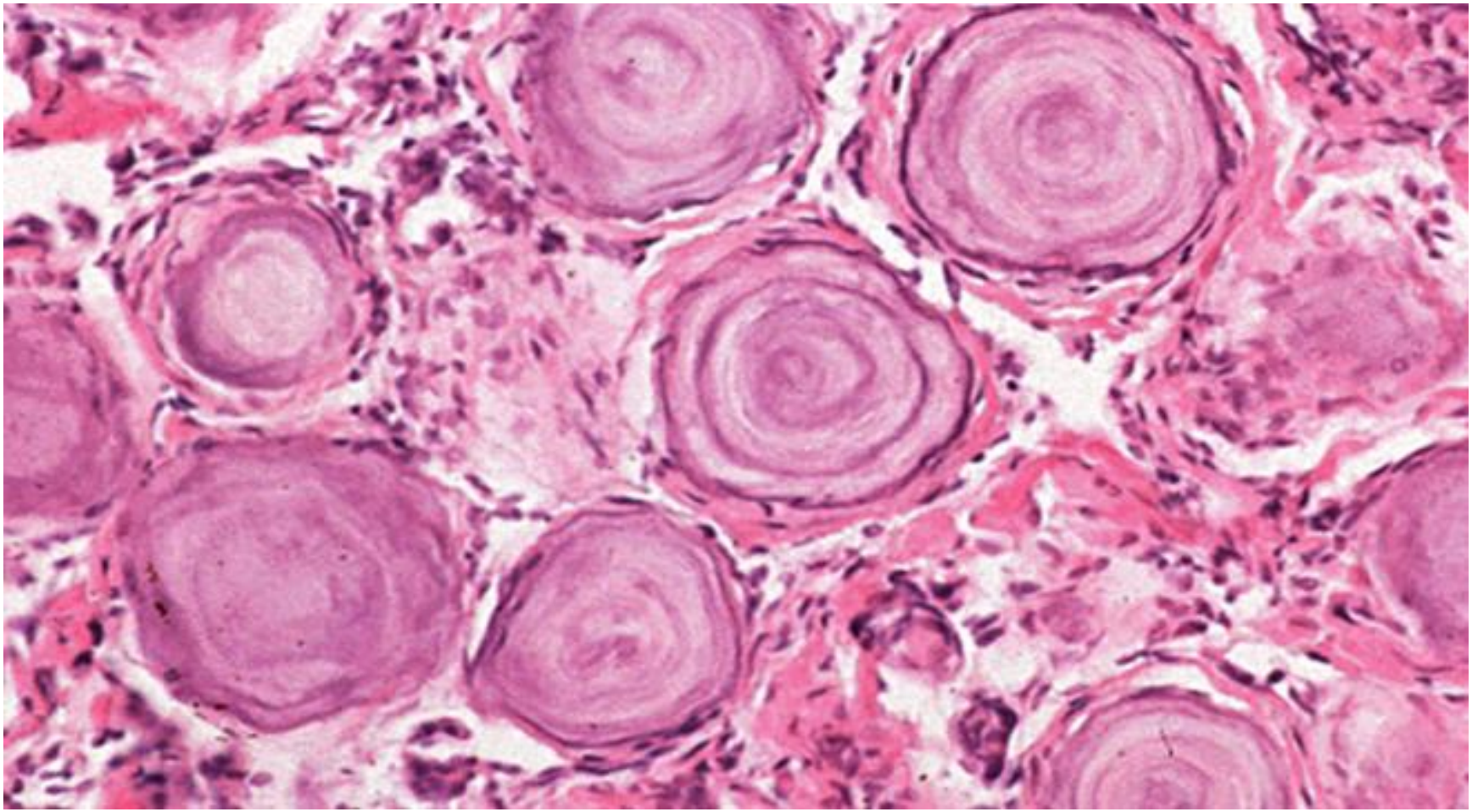
Orphan Annie eye! Because the nuclei are white and empty like Annie's character eyes!!



I know what you're thinking: pathological terms are funny.. You’re right



Psammoma bodies: calcification arranged in concentric pattern



Clinical Features of papillary carcinomas

a. nonfunctional tumors manifest as painless masses in the neck, either within the thyroid or as metastasis in a cervical lymph node

b. indolent lesions, with 10-year survival rates of 95%.

c. The presence of isolated cervical nodal metastases does not have influence on good prognosis of these lesions.

d. In a minority of patients, hematogenous metastases are present at the time of diagnosis, most commonly to lung.

Follicular Carcinoma :

-- More common in women and in areas with dietary iodine deficiency .
- The peak incidence between the ages of 40 and 60 years

On microscopic examination,

- Are composed of fairly uniform cells forming small follicles,
- In other cases, follicular differentiation is less apparent
- It may be

a. widely invasive, infiltrating the thyroid parenchyma and extrathyroidal soft tissues, or

b. Minimally invasive that may be impossible to distinguish from follicular adenomas on gross examination and the .

- **requires extensive histologic sampling to find capsular and/or vascular invasion**

Clinical Features

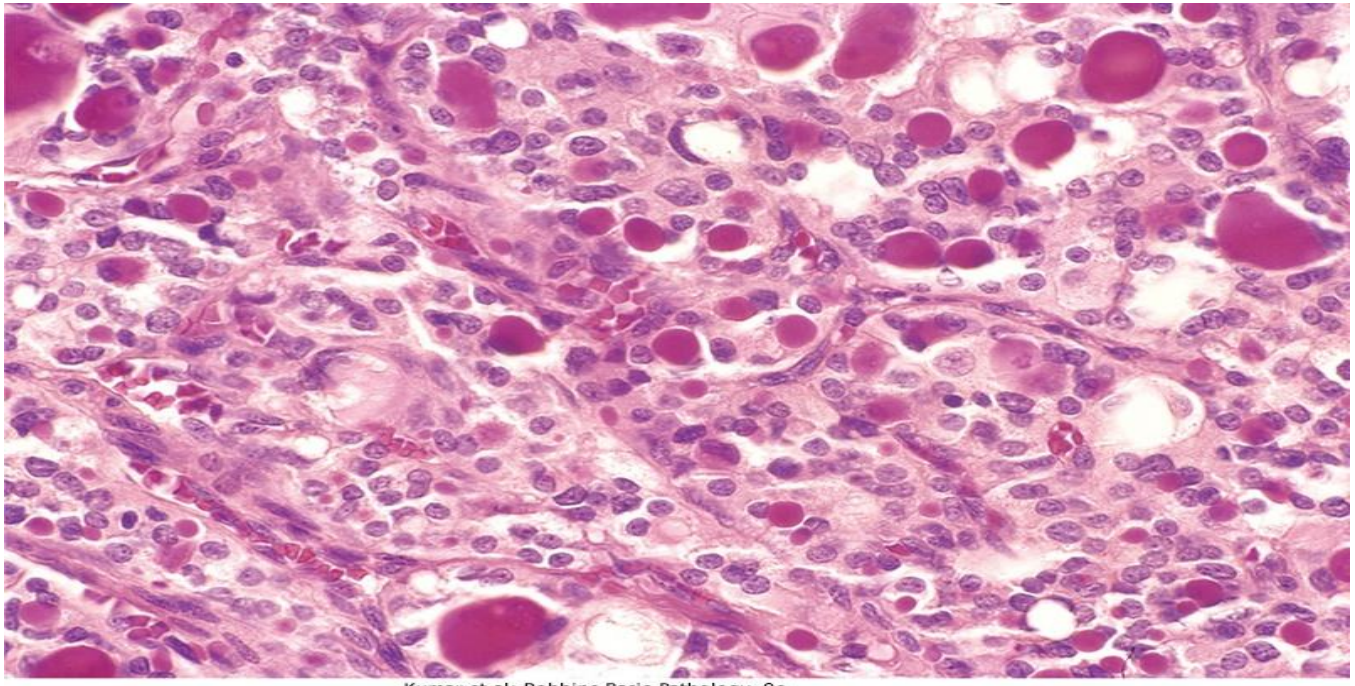
- Manifest most frequently as solitary *cold thyroid nodules.*
- Tend to metastasize through the bloodstream (*hematogenous dissemination*) to lungs, bone, and liver.
- Regional nodal metastases are uncommon .

NOTE HOW THE ABOVE TWO FEATURES DIFFER FROM PAPILLARY CARCINOMA !!

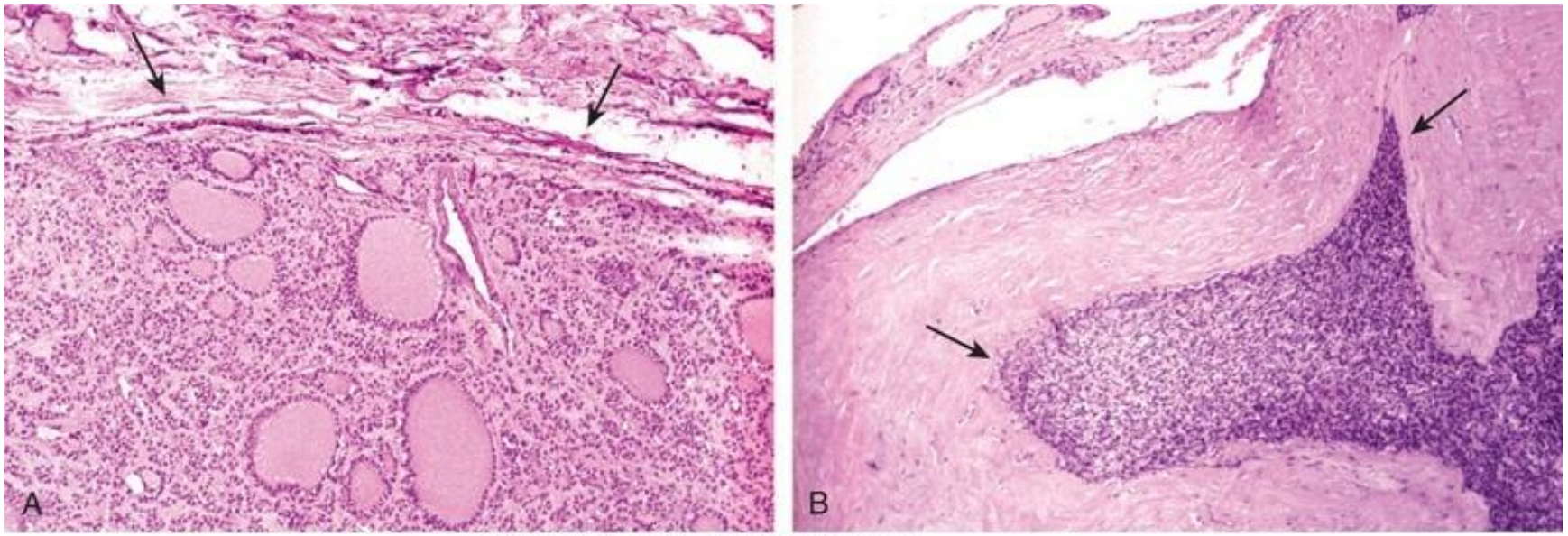
- As many as half of patients with widely invasive carcinomas succumb to their disease within 10 years, while less than 10% of patients with minimally invasive follicular carcinomas die within the same time span.

Follicular carcinoma:

- This pic looks like follicular adenoma, so can not diagnose carcinoma until the capsule is examined



Follicular carcinoma: capsular invasion



- SO : to diagnose follicular carcinoma you need
- Capsular invasion
- Or vascular invasion

3. Anaplastic Carcinoma

- Are undifferentiated tumors of the thyroid epithelium,
- The mean age of 65 years.
- They are aggressive, with a mortality rate of 100%.
- Metastases to distant sites are common, but death occurs in less than 1 year as a result of aggressive local growth which compromise of vital structures in the neck.

4. Medullary Carcinoma

- neuroendocrine neoplasms.
- Secrete **calcitonin**, the measurement of which plays an important role in the diagnosis and postoperative follow-up evaluation of patients.
- In some cases, the tumor cells elaborate somatostatin, serotonin, and vasoactive intestinal peptide (VIP)

- Are sporadic in about 70% of cases and the remaining 30% are *familial* cases

a. Occurring in the setting of MEN syndrome 2A or 2B,

b. or familial medullary thyroid carcinoma without an associated MEN syndrome

Note: Both familial and sporadic forms demonstrate activating *RET* mutations.

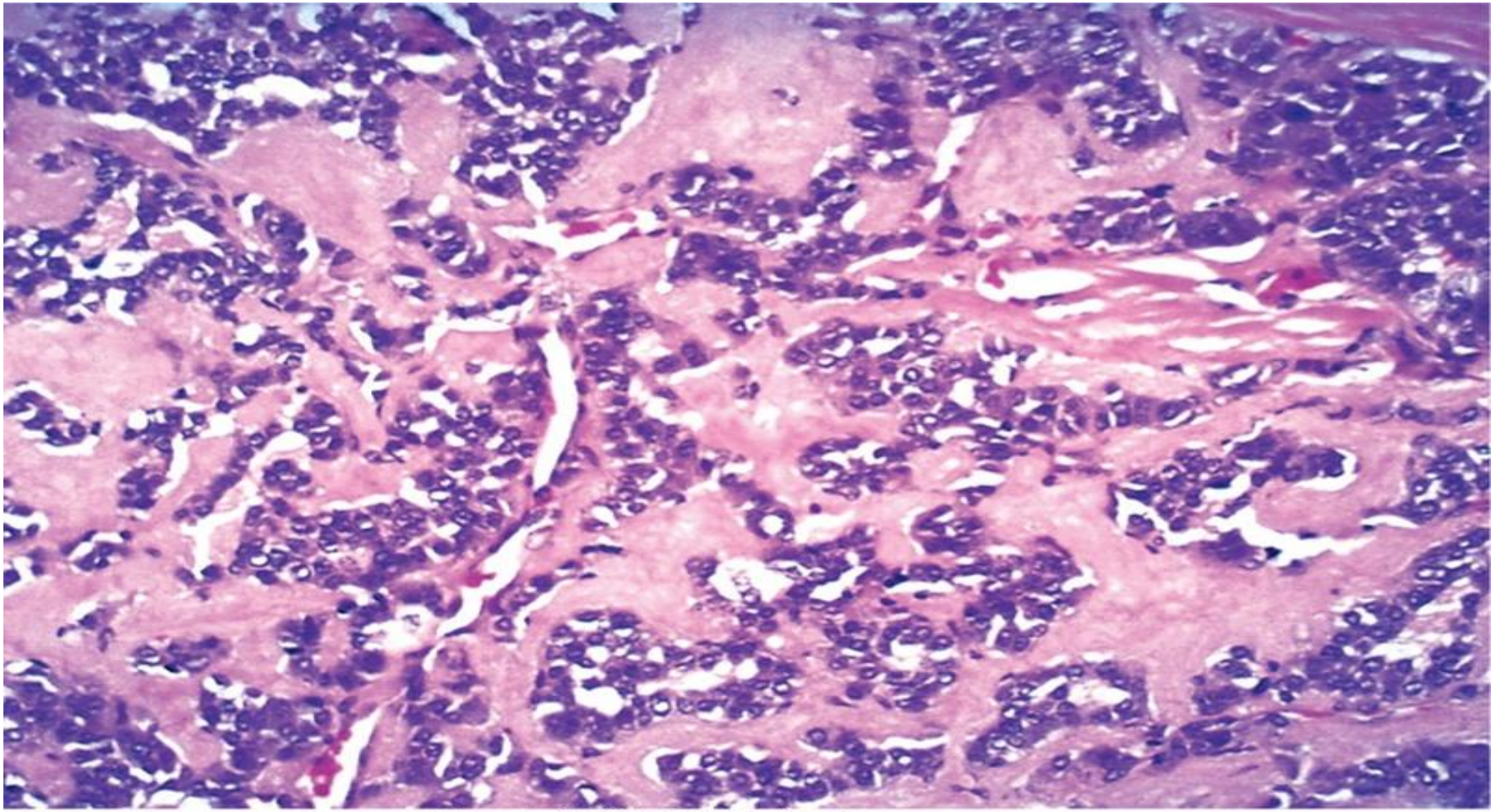
Cases associated with MEN-2A or MEN-2B show multicentric C cell hyperplasia in the surrounding thyroid parenchyma, a feature usually absent in sporadic lesions.

These foci are believed to represent the precursor lesions from which medullary carcinomas arise.

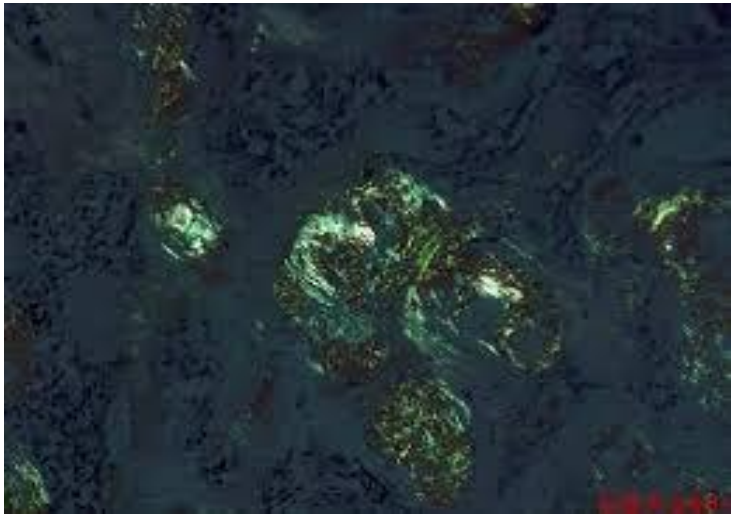
- The sporadic cases manifests most often as a mass in the neck, sometimes associated with compression effects such as dysphagia or hoarseness.

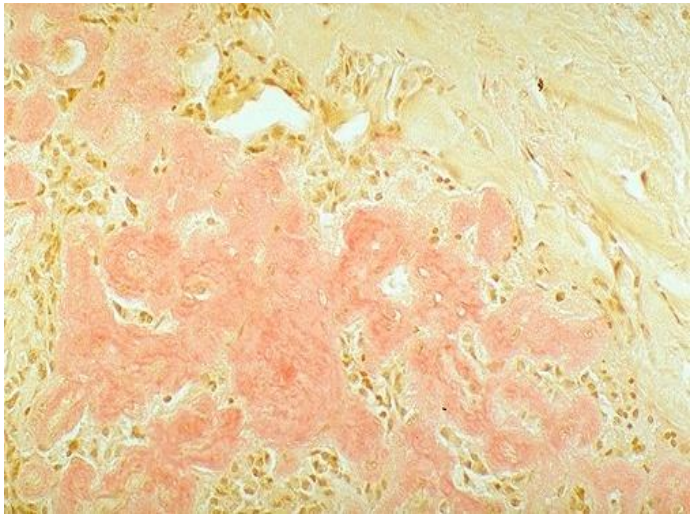
- AMYLOID STAIN IS POSITIVE IN THESE TUMORS= congo red stain

Medullary carcinoma



Congo red






Thank you!