Clinically discrete thyroid swelling & Carcinoma of thyroid

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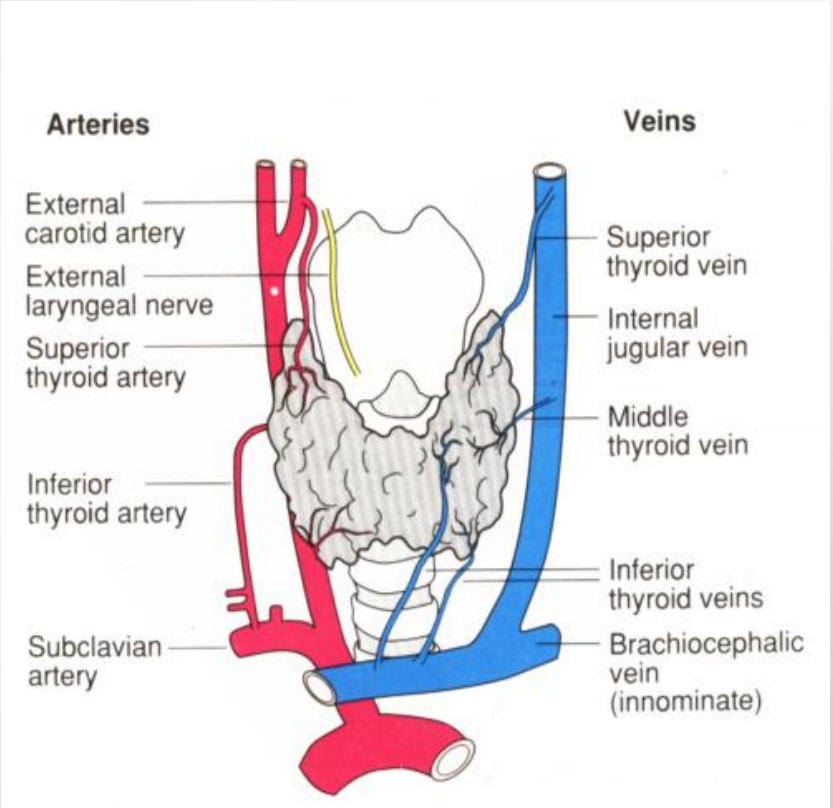
Anatomy

- Weight: 20-25 gms
- Arterial supply
  - superior thyroid arteries
  - inferior thyroid arteries
- Venous drainage
  - superior thyroid veins
  - middle thyroid veins
  - inferior thyroid veins
- Lymphatic drainage
  - pretracheal lymph nodes
  - paratracheal lymph nodes



Clinically discrete swellings

Types

- Isolated or solitary (70%)
  - swelling in an otherwise impalpable gland
- Dominant (30%)
  - swelling with clinical evidence of abnormality in the form of a palpable contralateral lobe or generalized mild nodularity

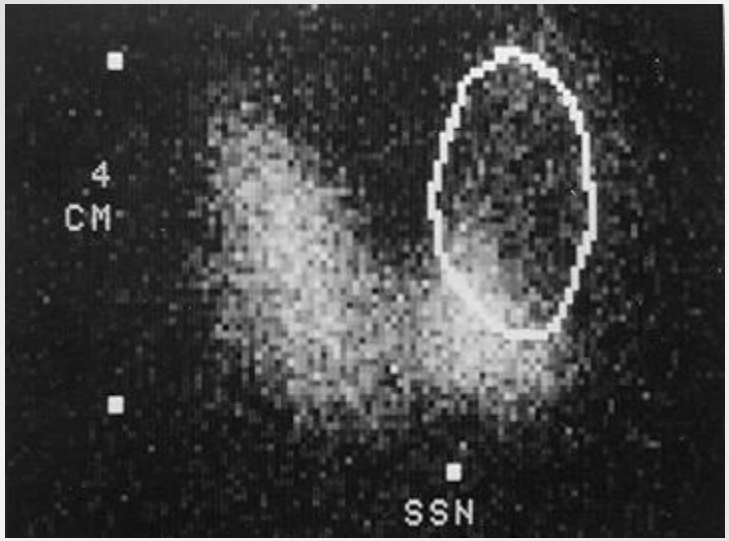
Risk of neoplasia

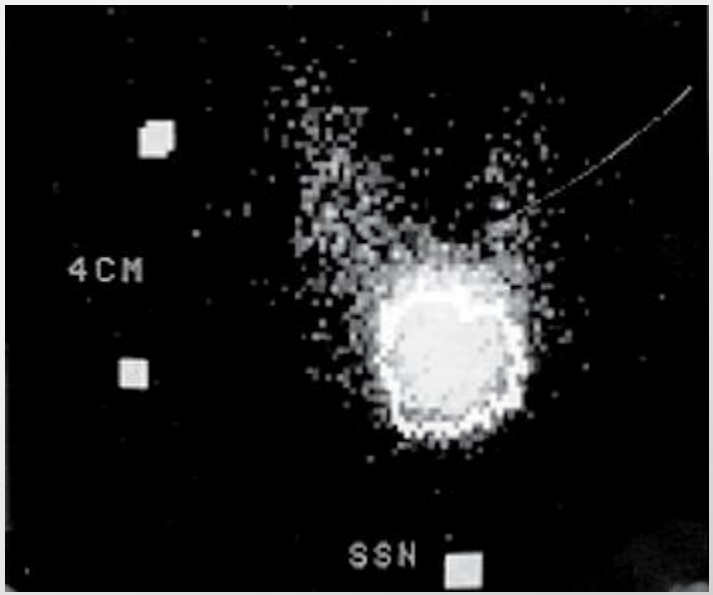
- 15% of isolated swellings prove to be malignant
- Additional 30-40% are follicular adenomas.
- Incidence of malignancy or follicular adenoma in dominant swellings is approx. half that of isolated swellings

Investigations

- Thyroid function tests
- Autoantibody titers
  - Determine which swellings is a manifestation of chronic lymphocytic thyroiditis.
- Ultrasonography
  - Determine the physical characteristics of thyroid swellings.

- Isotope scan
  - Determine the functional activity relative to the surrounding gland.





Fine-needle aspiration cytology (FNAC)

- Has excellent patient compliance, is simple and quick to perform in the OPD and is readily repeated.
- It aids in the diagnosis of colloid nodules , thyroiditis, papillary carcinoma , medullary carcinoma, anaplastic carcinoma and lymphoma.
- FNAC cannot distinguish between a follicular adenoma and follicular carcinoma as this distinction depends not on cytology but on histological criteria, which include capsular and vascular invasion.
- FNAC is less reliable in cystic than in solid swellings.

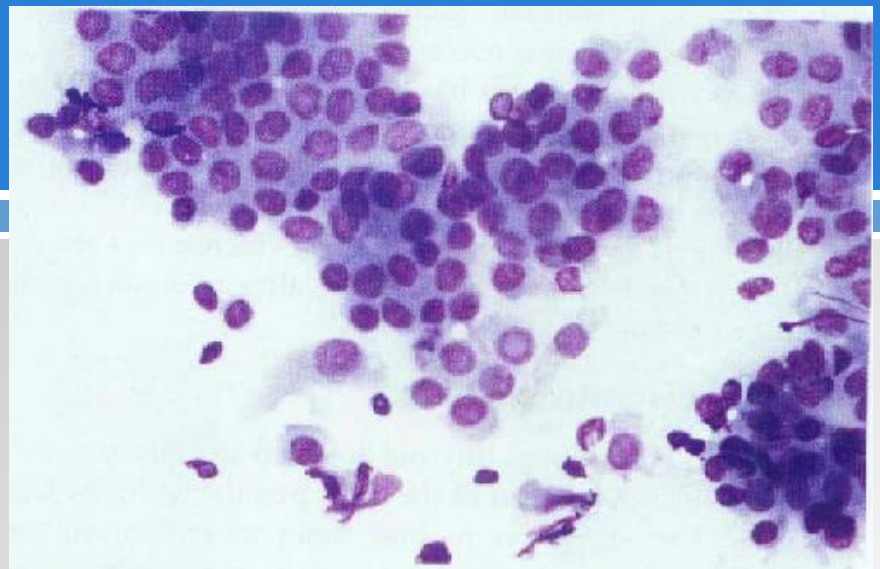


Fig. 44.17 Aspiration cytology. Papillary carcinoma with typical cellular variability and nuclear inclusions (*courtesy of Dr M. McKean, Aberdeen, Scotland*).

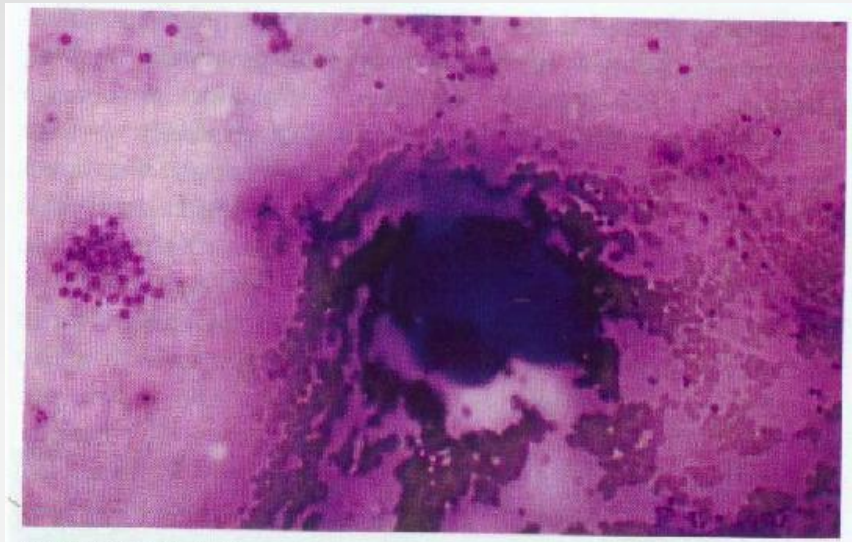


Fig. 44.16 Aspiration cytology – non-neoplastic appearances with scanty normal follicular cells together with colloid (= colloid nodule).

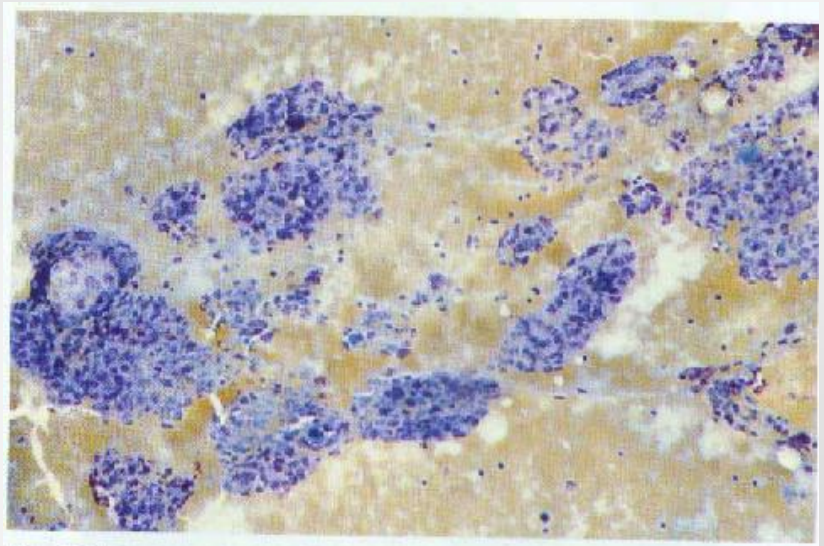
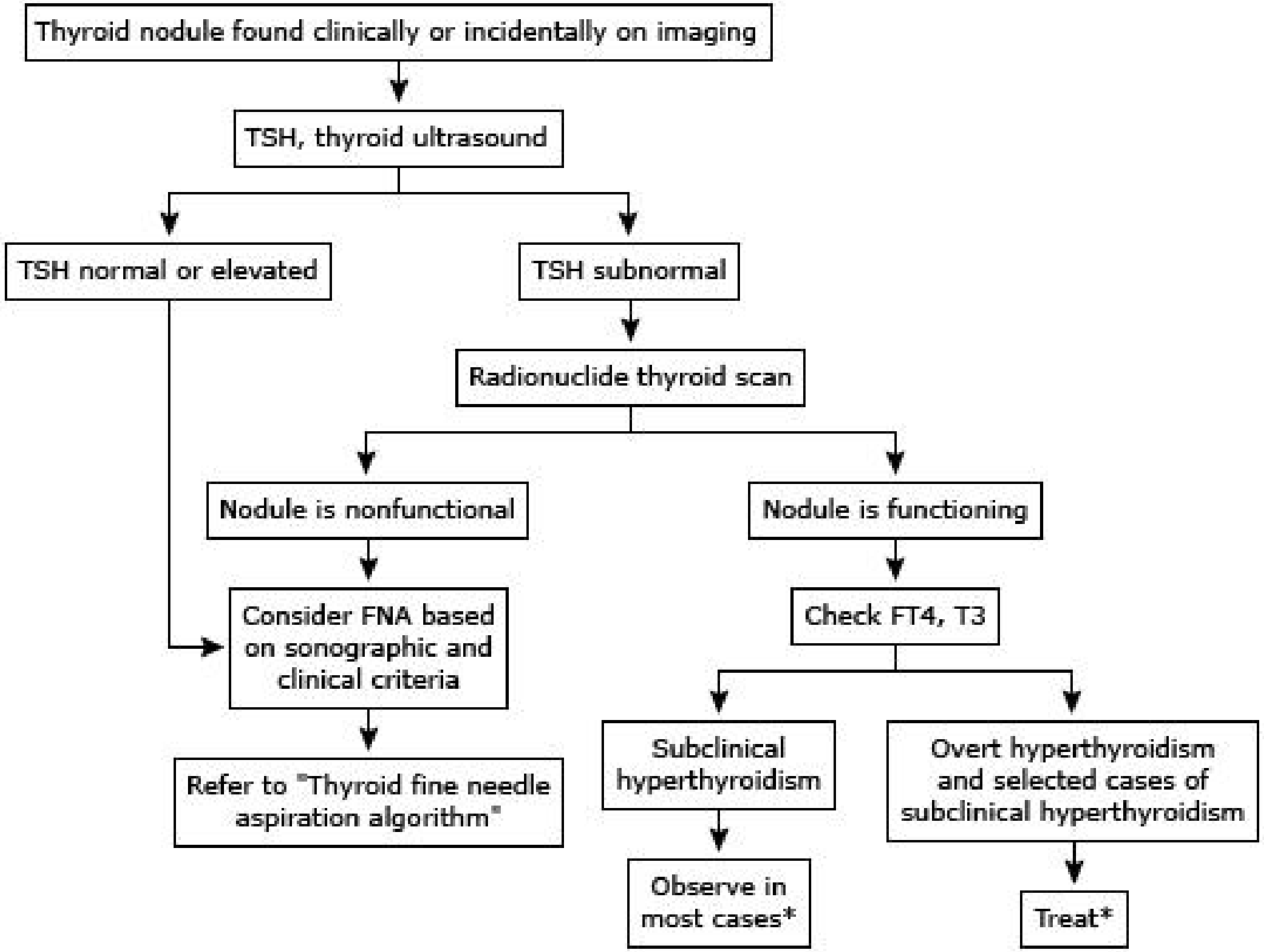


Fig. 44.18 Aspiration cytology. Follicular neoplasm showing increased cellularity with a follicular pattern (*courtesy of the late Dr V.M.M. Williams, Aberdeen, Scotland*).

Initial evaluation of a patient with a thyroid nodule

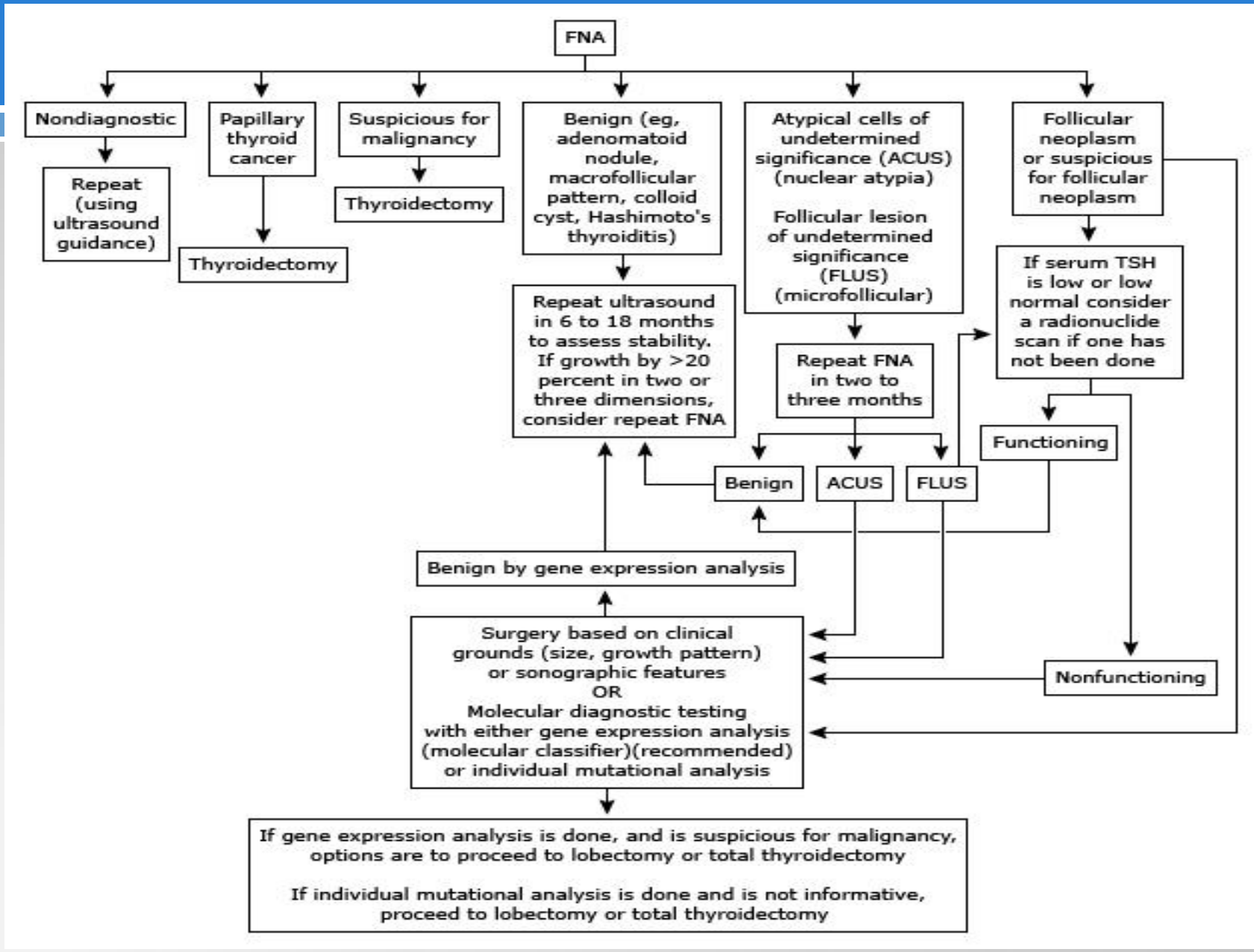


Treatment

- **The main indication for operation is the risk of neoplasia which includes follicular adenoma as well as malignant swellings.**

- **Clinical criteria includes:**
  - **Hard texture**
  - **irregular swelling**
  - **apparent fixity**
  - **recurrent laryngeal nerve paralysis**
  - **Deep cervical lymphadenopathy**

Management of thyroid nodules based upon results of FNAC



THYROID NEOPLASMS

Classification

- Benign
  - Follicular adenoma
- Malignant
  - Primary
    1. Follicular epithelium, differentiated
       - Follicular carcinoma
       - Papillary carcinoma
    2. Follicular epithelium, undifferentiated
       - Anaplastic
    3. Parafollicular cells
       - Medullary carcinoma
    4. Lymphoid cells
       - Lymphoma
  - Secondary
    - Metastatic
    - Local infiltration

Benign Tumors

- Follicular adenomas present as clinically solitary nodules
- Distinction between a follicular carcinoma and an adenoma can only be made by histological examination
- In the adenoma there is no invasion of the capsule or of pericapsular blood vessels.

Treatment of Benign Tumors

- Wide excision — preferably a lobectomy.
- The remaining thyroid tissue is normal so that prolonged follow up is unnecessary.

Malignant Tumors

- The vast majority of primary growths are carcinomas subdivided into follicular and papillary.
- Secondary growths are rare but blood-borne metastases can occur
  - from primary carcinomas of breast, colon and kidney and
  - from melanomas.

Relative incidence of primary malignant tumors

Relative incidence	%
Papillary carcinoma	60
Follicular carcinoma	20
Anaplastic carcinoma	10
Medullary carcinoma	5
Malignant lymphoma	5

Etiology of malignant thyroid tumors

- Differentiated thyroid carcinoma, esp. papillary, frequently follows accidental irradiation of the thyroid in childhood.
- The incidence of follicular carcinoma is high in endemic goitrous areas
- Malignant lymphomas can present in a patient known to have autoimmune thyroiditis, so that the lymphocytic infiltration in the autoimmune process may be an etiological factor.

Clinical features of thyroid neoplasms

- The annual incidence is about 3.7 per 100 000
- Sex ratio is three females to one male.
- The mortality is about 2-3 per cent.

- The commonest presenting symptom is a thyroid swelling

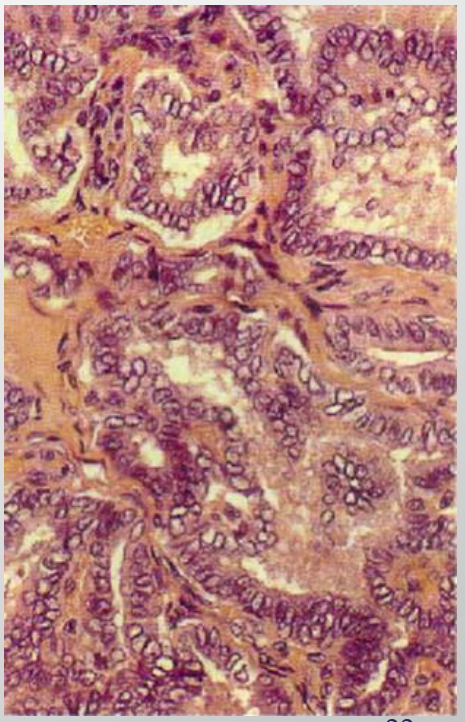
- Enlarged cervical lymph nodes may be the presentation of papillary carcinoma.

- Recurrent laryngeal nerve paralysis may be a presenting feature of locally advanced disease.
- Anaplastic growths are usually hard, irregular and infiltrating.
- Pain, often referred to the ear, is frequent in infiltrating growths.

Pathology

Papillary carcinoma

- Histologically the tumor shows papillary projections and characteristic pale, empty nuclei (Orphan Annie-eyed nuclei)
- very seldom encapsulated.
- Multiple foci may occur in the same lobe as the primary tumor or, less commonly, in both lobes.
  - They may be due to lymphatic spread in the rich intrathyroidal lymph plexus, or to multicentric growth.
- Spread to the lymph nodes is common
- blood-borne metastases are unusual unless the tumor is extrathyroidal.

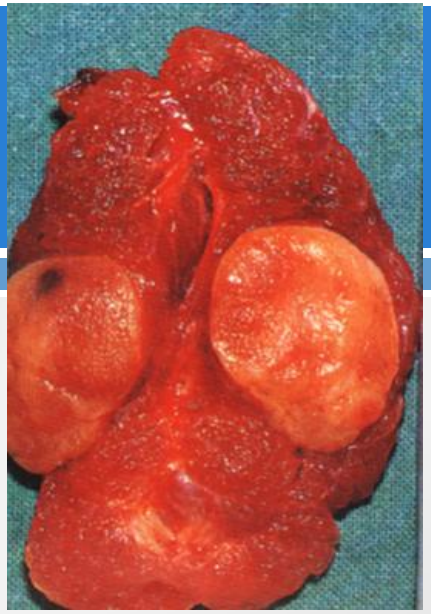


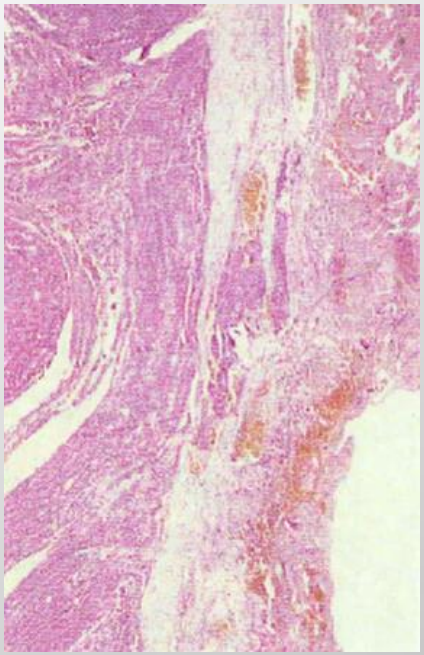
Occult carcinoma

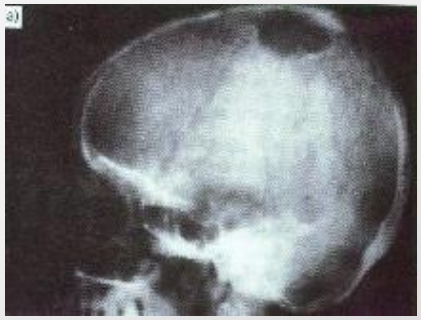
- Papillary carcinoma may present as an enlarged lymph node in the jugular chain with no palpable abnormality of the thyroid.
  - primary tumor may be no more than a few mms in size.
  - The term occult is now applied to all papillary carcinomas less than 1.5 cm in diameter.
- These have an excellent prognosis.

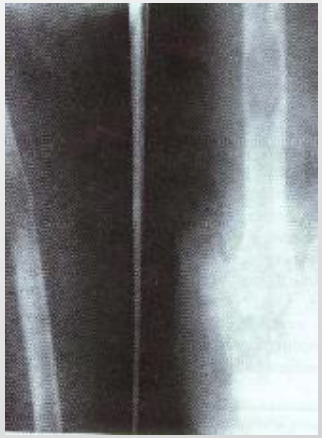
Follicular carcinoma

- macroscopically encapsulated but microscopically there is invasion of the capsule and of the vascular spaces in the capsular region
- Multiple foci are seldom seen
- Lymph node involvement is much less common than in papillary carcinoma.
- Blood-borne metastases are twice as common
- Mortality rate is twice as high.









Differentiated thyroid Ca: Risk group definitions

Low risk group

- Men of 40 years or younger, women of 50 years and younger without distant metastasis
- All older patients with intrathyroidal papillary carcinoma or follicular carcinoma with minor capsular involvement, in association with tumors <5 cm in diameter and no distant metastasis.

High risk group

- All patients with distant metastasis
- All older patients with extrathyroidal papillary carcinoma or follicular carcinoma with major capsular involvement and tumors 5 cm in diameter or larger regardless of extent of disease.

Differences b/w papillary & follicular carcinoma

	Papillary %	Follicular %
Male Incidence	**22**	**35**
Lymph node metastasis	**35**	**13**
Blood vessel invasion	**40**	**60**
Recurrence rate	**19**	**29**
Overall mortality rate	**11**	**24**
Distant metastasis	**45**	**75**
Local recurrence	**20**	**12**

Staging of thyroid cancers

Primary tumor (T)*

- **TX** Primary tumor cannot be assessed
- **T0** No evidence of primary tumor
- **T1** Tumor 2 cm or less in greatest dimension limited to the thyroid
  - T1a Tumor 1 cm or less, limited to the thyroid
  - T1b Tumor more than 1 cm but not more than 2 cm, limited to thyroid
- **T2** Tumor > 2 cm but not > 4 cm in greatest dimension limited to the thyroid
- **T3** Tumor > 4 cm limited to thyroid or any tumor with minimal extrathyroid extension (eg, extension to sternothyroid muscle or perithyroid soft tissues)
- **T4a** Moderately advanced disease
  - Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve
- **T4b** Very advanced disease
  - Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels
- All **anaplastic carcinomas** are considered T4 tumors
  - T4a Intrathyroidal anaplastic carcinoma
  - T4b Anaplastic carcinoma with gross extrathyroid extension

- **Regional lymph nodes (N)**
  - NX — Regional lymph nodes cannot be assessed
  - N0 — No regional lymph node metastasis
  - N1 — Regional lymph node metastasis
    - N1a — Metastasis to Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)
    - N1b — Metastasis to unilateral, bilateral, or contralateral cervical (Levels I, II, III, IV, or V) or retropharyngeal or superior mediastinal lymph nodes (Level VII)
- **Distant metastasis (M)**
  - M0 — No distant metastasis
  - M1 — Distant metastasis

Diagnosis of thyroid neoplasms

- Diagnosis is obvious on clinical examination although Riedel's thyroiditis is indistinguishable.
- Failure to take up radio-iodine is characteristic of thyroid carcinomas, but occurs also in degenerating nodules and all forms of thyroiditis.
- Thyroid antibody titers are often raised in carcinoma.
- FNAC
- No diagnostic test is absolutely certain, and exploration with excision eg lobectomy is essential when in doubt.
- In an anaplastic and obviously irremovable carcinoma, however, incisional or needle biopsy is justified.

Treatment

- Initial treatment
- Management of persistent or recurrent disease
- Long-term management

Initial treatment

Guidelines

- Surgery is the primary mode of therapy for differentiated thyroid cancers.
  - The surgical approach depends upon the extent of the disease, the patient's age, and the presence of comorbid conditions.
- After initial surgery, patients are managed by endocrinologists specialized in the treatment of thyroid cancer.
  - Radioiodine therapy
  - Thyroid hormone suppression
  - External beam radiotherapy

Surgery

- **Unilateral lobectomy and isthmusectomy**
  - when a unifocal tumor is < 1.0 cm in dia (microcarcinoma) and confined to one lobe.
  - appropriate for patients whose pathology reports subsequently show multifocal papillary microcarcinomas with fewer than five foci.
- **Total thyroidectomy**
  - if the primary tumor is 1.0 to 2.0 cm in diameter, or
  - if extrathyroidal extension or metastases are present, or
  - when multifocal papillary cancer is appreciated preoperatively.
- **More extensive resection with invasion of neck structures such as the esophagus, trachea, or strap muscles**
  - central (Level VI) neck dissection (with total thyroidectomy) in papillary cancer, only if there is clinical evidence of nodal involvement.
  - Prophylactic central neck dissection in advanced papillary cancer (>4 cm and/or extrathyroidal extension) even in the absence of clinical evidence of nodal involvement.

Radioiodine therapy

3 uses in the post-thyroidectomy patients with DTC:

- adjuvant ablation of residual thyroid tissue and microscopic residual cancer,
- imaging for possible metastatic disease, and
- treatment of known residual or metastatic thyroid cancer.
  - Radioiodine (**131-I**) is the most effective adjuvant treatment for papillary cancer.

- Radioiodine uptake depends on adequate stimulation by TSH and is reduced by the presence of excess iodide.
  - Therefore, whenever radioiodine imaging and treatment are planned, the patient should be instructed to avoid all iodine-containing medications and to limit dietary intake of iodine for at least one week.

Thyroid hormone suppression

- After initial thyroidectomy, whether or not radioiodine therapy is given, levothyroxine therapy is required to prevent hypothyroidism and to minimize potential TSH stimulation of tumor growth.
  - For low risk disease – serum TSH can be maintained between 0.1 and 0.5 mU/L.
  - For high risk disease – serum TSH should be less than 0.1 mU/L.

External beam radiotherapy

- useful in patients with DTC who have metastatic disease that is refractory to radioiodine or patients whose tumors do not concentrate radioiodine.
- adjuvant therapy
  - after macroscopically complete surgical excision to prevent recurrence,
  - after incomplete surgical resection or local recurrence to provide regional tumor control,
- palliative therapy for distant metastases.

Systemic chemotherapy

- Tyrosine kinase inhibitor
  - Sorafenib, Vandetanib, Sunitinib
  - patients require meticulous follow-up for potential toxicities, esp. hypertension, oral mucositis, hand/foot syndrome, diarrhea, and cutaneous lesions.

Bone metastases

- Pamidronate
  - may reduce bone pain from skeletal metastases.
- Denosumab
  - to prevent skeletal related events (pathologic fracture, or spinal cord compression) in patients with bone metastases.

Follow-up

- Patients with differentiated thyroid cancer require follow-up with physical examinations, biochemical testing (including serum thyroglobulin), ultrasound, and other imaging.

Imaging

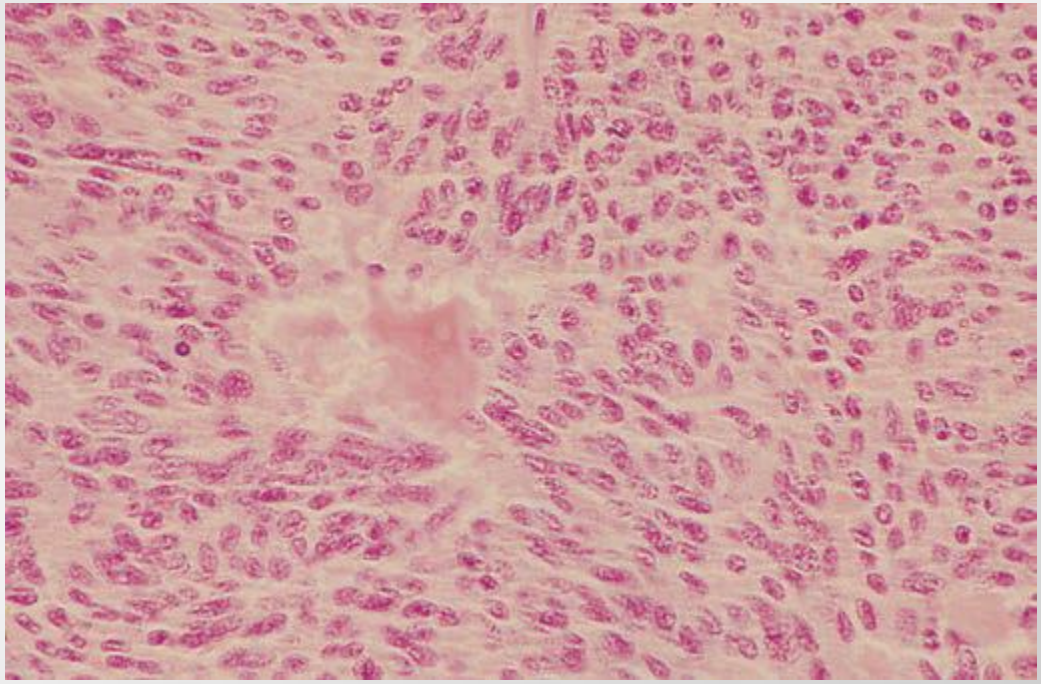
- Neck ultrasound is performed at 6 to 12 month intervals depending on risk assessment.
- If there is biochemical or ultrasound evidence of recurrence,
  - diagnostic whole body scan (radioiodine imaging on a low iodine diet with TSH stimulation), CT or MR imaging, skeletal x-rays, or skeletal radionuclide imaging.
- In patients with evidence of distant metastases, FDG-PET scanning may provide useful prognostic information.

Anaplastic carcinoma

- This occurs mainly in elderly women.
- Local infiltration is an early feature with spread by lymphatics and by the bloodstream.
- Some lesions present in an advanced stage with tracheal obstruction and they require urgent tracheal decompression by isthmusectomy. Tracheostomy is best avoided.
- Complete resection is justified if the disease appears confined to the thyroid and possibly the strap muscles.
  - Even then the survival rarely exceeds six months.
- Radiotherapy should be given in all cases and may provide a worthwhile period of palliation.

Medullary carcinoma

- These are tumors of parafollicular (C cells) derived from neural crest.
- There is a characteristic amyloid stroma.



- High levels of serum calcitonin and carcinoembryonic antigen are produced.
  - Calcitonin levels fall after resection and rise again with recurrence making it a valuable tumor marker in the follow up.
- Diarrhea is a feature in 30% of cases and this may be due to 5-hydroxytryptamine or prostaglandins produced by the tumor cells.

- Some (10-20%) tumors are familial.
  - MC may occur in combination with adrenal pheochromocytoma and hyperparathyroidism (due to hyperplasia) in multiple endocrine neoplasia type 2A (MEN-2A).
  - When the familial form is associated with prominent mucosal neuromas involving the lips, tongue and inner aspect of the eyelids, with a Marfanoid habitus, the syndrome is referred as MEN type 2B.
  - The familial form frequently affects children and young adults,

- Sporadic cases occur at any age with no sex predominance.

- Involvement of lymph nodes occurs in 50–60% and blood-borne metastases are common.
- Tumors are not TSH dependent and do not take up radioactive iodine.
- Prognosis is variable and depends on stage at diagnosis.
  - Any nodal involvement virtually eliminates the prospect of cure and, unfortunately, even small tumors confined to the thyroid gland may have spread by the time of diagnosis, esp. in familial cancers.
- In common with many endocrine tumors the progression is slow with an indolent course and long survival, even in the absence of cure.

Treatment

- Total thyroidectomy and either prophylactic or therapeutic resection of central and bilateral cervical lymph nodes.
- Familial cases are now detected by genetic screening
  - *RET* mutations identifies individuals who will develop medullary cancer later in life.
  - This is supplemented by estimating serum calcitonin levels in the basal state and after stimulation by either calcium or pentagastrin.
  - A rise in calcitonin levels should lead to thyroidectomy.
  - Prophylactic surgery is recommended for infants with genetic trait.

The End!