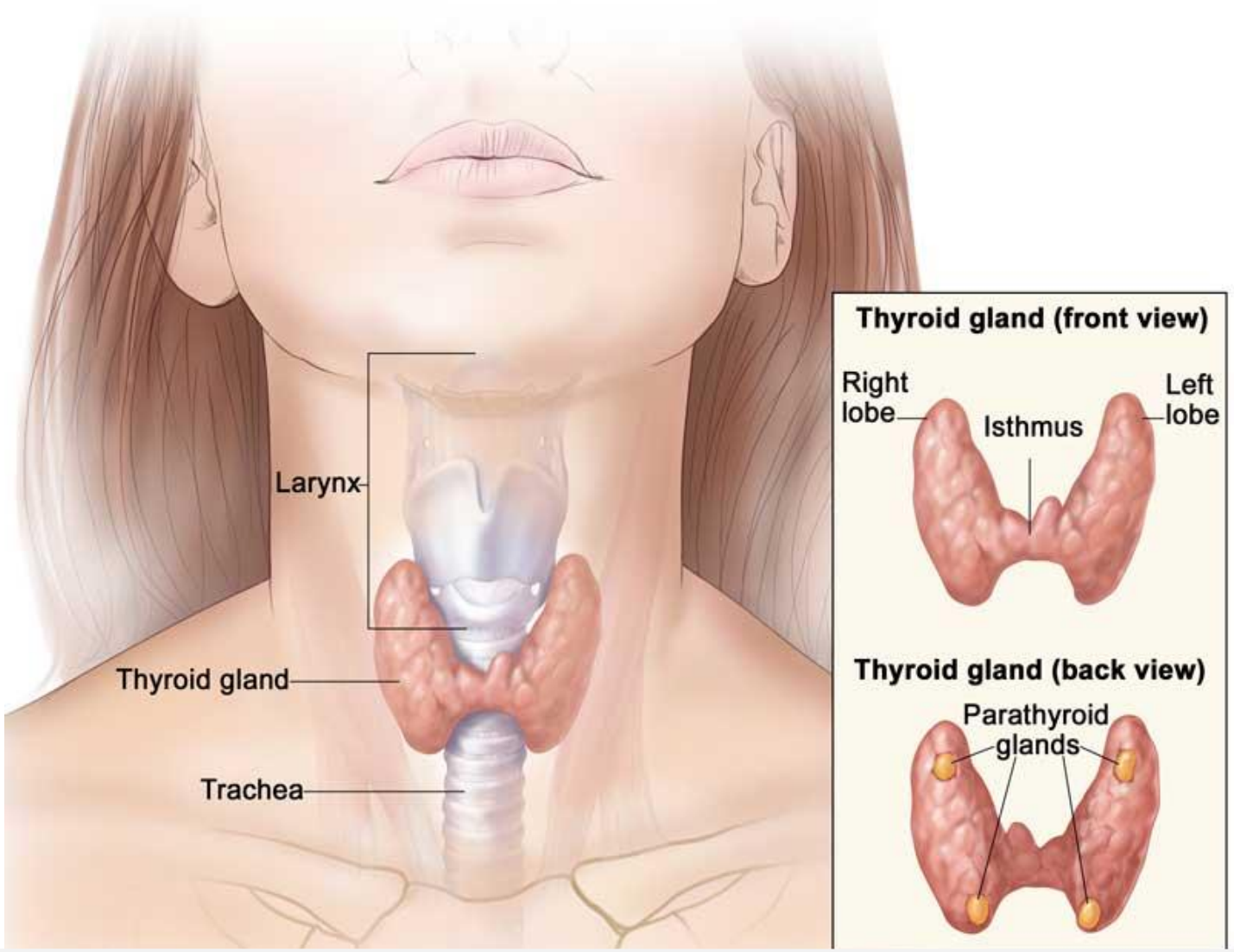
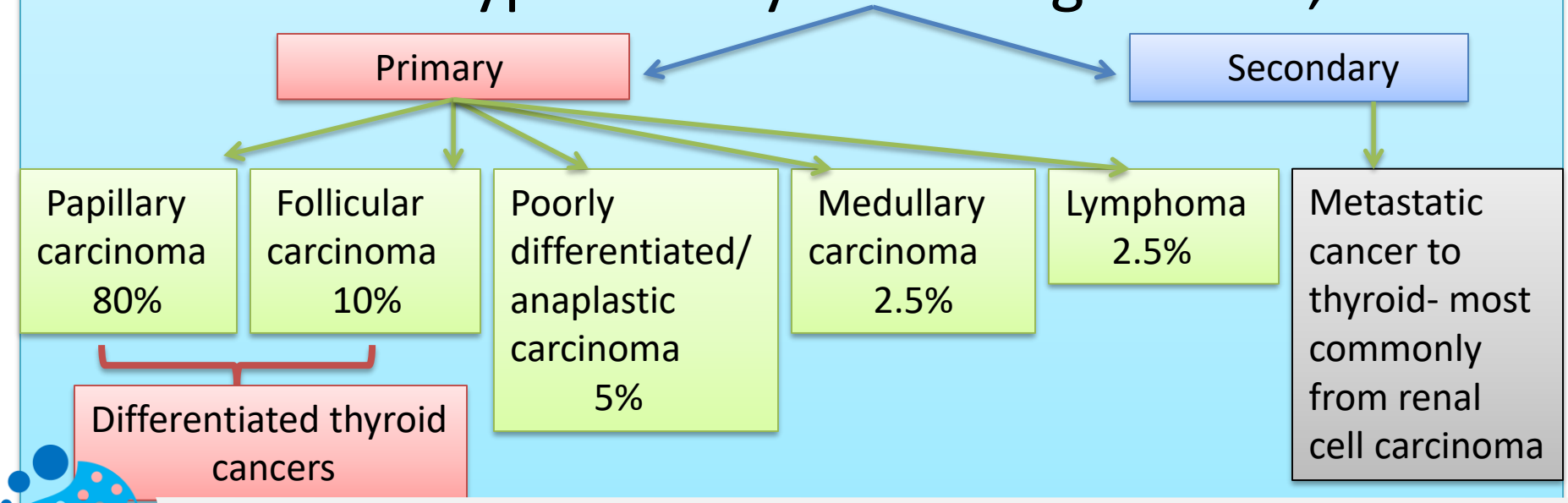
Thyroid Malignancies



Thyroid Malignancies

- Thyroid malignancies arise from;
  - Follicular cells
  - Para-follicular cells
  - Lymphatic tissues
- There are 2 types of thyroid malignancies;



Epidemiology

- The annual incidence is about 0.6 per million of the population and the sex ratio is three females to one male
- These tumors are responsible for 400 deaths annually in the UK
- There is an annual incidence of 30 000 cases in the USA, over 75% occur in women
- The incidence of papillary thyroid cancer is increasing rapidly across the world. This is mostly due to increased rates of imaging detecting previously occult disease

Aetiology

- The great majority of thyroid cancers have no known aetiological factor
- The most important identifiable aetiological factor in differentiated thyroid carcinoma (particularly papillary) is irradiation of the thyroid under 5 years of age
- Short latency aggressive papillary cancer is associated with the ret/PTC3 oncogene and later developing, possibly less aggressive, cancers with ret/PTC1

Aetiology

- The incidence of follicular carcinoma is high in endemic goitrous areas, possibly due to TSH stimulation
- Malignant lymphomas sometimes develop in autoimmune thyroiditis, and the lymphocytic infiltration in the autoimmune process may be an aetiological factor

Risk factors

High suspicious

- Family history of thyroid malignancy or multiple endocrine neoplasia
- Rapid tumour growth
- Very firm nodules
- Fixation to adjacent structures
- Vocal cord paralysis
- Cervical lymphadenopathy
- Distant metastasis (lungs or bones)

Moderate suspicious

- Age <20 years or >60 years
- Male sex
- Solitary nodule
- Nodule > 4 cm
- History of head and neck irradiation
- Compressive symptoms

Clinical Features

Thyroid swelling	• Most common presenting symptom
Enlarge cervical lymph nodes	• May be the presentation of papillary carcinoma
Recurrent laryngeal nerve paralysis	• Suggestive of locally advanced disease
Pain	• Often referred to the ear • Is suggestive of nerve involvement from infiltrating tumours

Clinical Features

- Anaplastic growths are usually;
  - hard
  - irregular
  - infiltrating
- A differentiated carcinoma may be suspiciously firm and irregular, but is often indistinguishable from a benign swelling
- Small papillary tumours may be impalpable, even when lymphatic metastases are present

Papillary Carcinoma

- Papillary carcinoma (PTC) is the **most common thyroid malignancy** and common in **females**
- Many patients live with this disease undetected
- The disease is known for its propensity for lymph node metastases
- These are more common in **younger patients**, in whom they do not affect the otherwise excellent survival

Papillary Carcinoma

- Only thyroid cancer in children
- Aetiology
  - Radiation- external / radio active iodine
- TSH or Hormone dependent tumour
- Frequently solitary and commonly multi nodular type
- 80% multifocal
- Spread is ;
  - Slowly progressive
  - Less aggressive
  - Direct
  - Lymphatic- cervical LN
  - Usually no blood spread
- Compressive features are uncommon

Papillary Carcinoma

- Metastatic disease confers a poor outcome
- One contentious finding in patients with PTC is a high rate of occult micrometastases
- Distant metastases are uncommon in PTC
- Papillary microcarcinoma is used to describe PTC that is <10 mm in size.These lesions are common and not associated with adverse outcomes
- Prognosis is good, one of the curable malignancy

Investigations

- USS
- FNAC- diagnostic investigation
- Papillary carcinoma is confirmed with;
  - Psammoma bodies
  - Orphan annie nuclei

Follicular Carcinoma

- Common in females
- Can occur from pre existing MNG
- 2 types
  - Non invasive
  - Invasive
- Unifocal in 90%

Follicular Carcinoma

- Spread- more aggressive tumour
  - Mainly blood spread
    - Bones
    - Lungs
    - Liver
    - Lymph nodes
- Bone spread
  - Vascular
  - Warm
  - Pulsatile
  - Localized
  - Common sites- skull, long bones and ribs

Follicular Carcinoma

Clinical features

- Firm or hard nodule
- Tracheal compression- common
- Recurrent laryngeal nerve palsy
- Berry's sign- positive
- Pulsatile skull lump

Investigations

- Follicular carcinoma can normally only be differentiated from follicular adenoma by the architecture on histology
- FNAC- inconclusive.Lacking capsular and angio invasion
- Frozen section
- Investigations for secondaries

Hurthle cell cancer

- Variant of follicular cancer
- Consists of oxyphilic cells
- Occur commonly in older females. Usual age is 60-75 years
- Spreads more commonly to regional LN than follicular cancer
- Does not take up I 131
- Poor prognosis than follicular carcinoma

Management of Differentiated thyroid cancers

Surgery

- Thyroidectomy
- Lymph node dissection

Adjuvant treatment

- Radioactive iodine
- TSH suppression therapy

Surgery

- For the vast majority of patients, outcome is excellent irrespective of the extent of surgery
- The aim of surgery is to rid the patient of macroscopic disease and minimise the chance of recurrence and death
- In high-risk patients with nodal or distant metastases, total thyroidectomy will be performed to eradicate disease in the thyroid and prepare the patient for radioactive iodine
- For low-risk patients with a single focus of disease limited to the thyroid, a thyroid lobectomy can be offered

Surgery for Papillary Thyroid Cancer

- Papillary thyroid cancer > 1cm
  - Total thyroidectomy
- Papillary thyroid cancer ≤ 1 cm
  - Hemithyroidectomy if the lesion is
    - Well differentiated
    - Unifocal
    - Intrathyroidal
- Total thyroidectomy if there is any
  - History of head and neck irradiation
  - Familial papillary thyroid cancer
  - Evidence of cervical lymph node metastasis

Surgery for follicular thyroid cancer

- Hemithyroidectomy
  - if follicular lesion with atypia or follicular neoplasm in FNAC
- Completion thyroidectomy if carcinoma is confirmed on histology
- The exceptions are
  - Unifocal tumour
  - Low risk (minimally invasive)
  - Intrathyroidal
  - Node negative tumour
  - Tumour < 1 cm

Surgery for follicular thyroid cancer

- Total thyroidectomy
  - Lesion is > 4cm
  - Marked atypia on FNAC
  - Family history of thyroid cancer
  - History of radiation exposure to head and neck
  - Bilateral nodal disease
  - Patient's wish

Lymph node dissection

- Central lymph node dissectionwhen there are clinically apparent metastasis
- Lateral lymph node dissectionwhen FNAC proven lymph node metastasis in clinically or sonographically suspicious lymph nodes

Thyroxine

- Following surgery, thyroid cells (both normal and malignant) can be suppressed using high doses of thyroxine
- Following surgery, patients can be considered high or low risk
- For those patients who had a total thyroidectomy at high risk from disease, thyroxine will be prescribed at levels which suppress TSH without making the patient biochemically hyperthyroid

Thyroxine

- In contrast, low-risk patients who have had lobectomy may be considered for thyroxine replacement at physiological levels
- In particular, long-term TSH suppression can result in cardiac arrhythmia and osteoporosis
- As such the treating team should consider all risks during follow-up to strike this balance

Radioiodine

- Thyroid tissue concentrates iodine
- For this reason, 131I can be given in order to deliver tumoricidal doses of radioactivity directly to thyroid tissue, both benign and malignant
- Radioiodine treatment is not an alternative to surgical resection for gross resectable disease

Radioiodine

- In order to effectively drive the radioiodine into cells, high levels of TSH are required
- This can be achieved by rendering the patient hypothyroid (off thyroxine) or by using recombinant TSH, which is injected prior to radioiodine administration.
- Following radioiodine administration, an uptake scan is performed
- This demonstrates areas of iodine uptake in the whole body and can be used to identify any metastatic disease not recognised on initial imaging

Prognostic risk classification for patients with differentiated thyroid carcinoma (AMES & AGES)

	LOW RISK	HIGH RISK
Age	<40 years	>40 years
Sex	Female	Male
Extent	Extent No local extension, intrathyroidal, no capsular invasion	Capsular invasion, extra thyroidal extension
Metastasis	None	Regional or distant
Size	<2 cm	>4 cm
Grade	Well differentiated	Poorly differentiated

MEDULLARY CARCINOMA

- These are tumours of the parafollicular (C cells) derived from the neural crest rather than the cells of the thyroid follicle as are other primary thyroid carcinomas
- Characteristic amyloid stroma is seen in histology
- Spreads mainly to lymph nodes (60%)

MEDULLARY CARCINOMA

- Classified as’
  - Hereditary- 25 %
    - Associated with MEN syndromes
    - Familial non-MEN syndromes
  - Sporadic- 75%
- Heraditary disease occurs in young age and the sporadic diseaseoccurs arround 4th decade. But it can occur at any age
- May associate with MEN 2 syndrome (Pheochromocytoma, hyperparathyroidism and mucosal neuromas)

MEDULLARY CARCINOMA

- High levels of serum calcitonin and carcinoembryonic antigen are produced by many medullary tumours.
- Calcitonin levels fall after resection and rise again with recurrence, making it a valuable tumour marker in the follow-up of patients with this disease
- Also secretes;
  - 5HT (Serotonin)
  - Prostaglandin
  - ACTH
  - VIP

Leads to cause diarrhoea is a feature in 30% of cases

MEDULLARY CARCINOMA

- Tumours are not TSH dependent and do not take up radioactive iodine
- The prognosis is variable and depends on the stage at diagnosis
- Even small tumours confined to the thyroid gland may have spread by the time of diagnosis, particularly in familial cancers
- The progression of disease may be very slow
- In familial cases of medullary thyroid cancer, genetic screening of relatives should be recommended

Management

- When medullary carcinoma is diagnosed, staging of the neck and chest should be performed
- For those patients with disease confined to the thyroid, total thyroidectomy is recommended to remove all C cells
- In addition, elective dissection of the central neck nodes is also performed to optimise the chance of cure
- If there is evidence of nodal metastases, cure is unlikely

Anaplastic thyroid carcinoma

- Aggressive malignancy
- Typically affects elderly women
- Usual presentation is with local symptoms
- Characterized by rapid growth, visceral invasion and distant metastases
- Distant spread is present in 90% of patients at the time of diagnosis most commonly to the lungs

Management

- FNAC is accurate in 90% of cases
- One of the indication for core biopsy because thyroid lymphoma can be incorrectly diagnosed as anaplastic cancer
- Very poor prognosis- Almost all patients will be dead within 6 months

Treatment

- Chemotherapy and radiotherapy (solid evidence is lacking)
- Surgery- rarely performed, tracheostomy for airway sign

Malignant lymphoma

- In the past, many malignant lymphomas were diagnosed as small round-cell anaplastic carcinoma
- Most lymphomas occur against a background of lymphocytic thyroiditis
- Hashimoto's disease is a strong risk factor
- Non-Hodgkin B-cell lymphoma is the most common pathology
- Generally presents in older patients
- Presentation- Rapidly enlarging painless neck mass, local compressive features

Management

- Diagnosis is established by biopsy
- Histology, immunohistochemistry and flow cytometry is the preferred means of diagnosis
- Response to irradiation is dramatic and radical surgery is unnecessary
- In patients with tracheal compression, isthmusectomy is the most appropriate form of biopsy although the response to therapy is so rapid that this should rarely be necessary unless there has been difficulty in making a histological diagnosis
- The prognosis is good, particularly if there is no involvement of cervical lymph nodes