Chapter

15

# Management of Thyroid Swelling

## What is a goiter?

The term goiter means enlarged and palpable thyroid gland (Fig. 4.1). The normal weight of the thyroid gland is 18 gm in females and 25 gm in males. The thyroid gland becomes palpable when the volume of the gland is more than double normal and the thyroid gland is visible when the volume becomes more than three times of normal.

## Describe the anatomy of the thyroid gland.

- There are two lateral lobes, measure 2 × 1 × 1 inches.
- They are connected by isthmus which is 1.5 × 1 inches.
- Extent of the lateral lobe is from mid of side of thyroid cartilage to 6th tracheal ring.
- The isthmus covers 2nd, 3rd and 4th tracheal ring.
- The pyramidal lobe triangular projection that projects from the left side of upper border of the isthmus and is connected to the hyoid bone by fibrous band or a muscle slip called levator glandule thyroidae.
- Lateral lobes are roughly triangular in shape.
- Their superficial surface is covered by infra-hyoid muscles or ribbon muscles the sterno-mastoid overlapping.
- The medial surface related to tracheal and oesophagus, inferior constrictor, crico-thyroid muscle and two nerves (recurrent laryngeal nerve and external laryngeal).
- Posterior surface overlaps common carotid and covers terminal part of inferior thyroid artery.

## Blood Supply of Thyroid

- Superior thyroid artery: It is a first branch from anterior surface of external carotid. Runs down wards to enter the upper pole. There it breaks up in branches to front of gland, back of gland and a branch to anastomose with its fellow of opposite side along upper border of the isthmus. It mainly supplies the connective tissue and capsule of thyroid gland.
- Inferior thyroid artery is a branch of thyro-cervical trunk (arises from first part of subclavian artery).
- Enter the gland from deep or posterior surface.
- Supplies the parenchyma of gland.
- Also gives ascending cervical, inferior laryngeal artery.
- It is related to RLN which lies behind or in front of vessels just before artery enters in gland.
- RLN must be identified and protected from injury before artery is ligated.
- Thyroid IMA artery: An occasional vessel from arch of aorta or the innominate.
- When present it enters the lower part of the isthmus.
- Acessory thyroid arteries are branches from small vessels to oesophagus and trachea.

## Veins of Thyroid Gland

- Superior thyroid vein: Leaves upper part of gland, runs along outer border of omohyoid muscle, crosses common carotid and terminate in internal jugular vein.
- Middle thyroid vein: Arises from middle of gland. Follows the inner border of omohyoid and enters internal jugular vein.
- It is short vessel of large diameter to be ligated first during thyroid surgery as it bleeds profusely if torn.
- Inferior thyroid vein: Leaves isthmus at its lower border.
- Runs down in front of trachea to end in the innominate vein of same side.

- Both inferior thyroid vein may join the left innominate vein.
- Large vessels should be divided in the end of subtotal thyroid removal after ligation of thyroid arteries to avoid venous congestion of gland.
- 4th thyroid of Kocher passing between middle and inferior thyroid vein.

### Nerves in Relation to Thyroid Gland

- External laryngeal nerve: It is a nerve to cricothyroid and branch of superior laryngeal nerve. It runs along superior thyroid vessels.
- Just before 1 cm of entrance of superior thyroid artery into gland, the nerve turns medially and enters cricothyroid muscle.
- Damage to this nerve results in weakness and huskiness of voice. Patients are not able to raise the pitch of the voice.

### Recurrent Laryngeal Nerve (RLN)

- Ascends on either side of trachea
- Lies lust lateral to the ligament of Berry (condensation of pre-tracheal fascia).
- In 25% it is contained in ligament of Berry as enters the gland.
- Right RLN is 1 cm lateral to tracheoesophageal groove at lower pole but it is in groove in mid-portion of thyroid. Nerve can be anterior or posterior to inferior thyroid artery at mid-portion of thyroid lobe.

### Lymphatics of Thyroid Gland

- Medially they drain into central compartment pre-tracheal, pre-laryngeal, para-tracheal tracheoesophageal groove lymph nodes and superior mediastinal nodes.
- Lymphatic drainage from superior third of gland is in lateral compartment.

### What is a WHO classification of goiter?

This classification is used mainly for survey of endemic goiter in community.

Goiter can be classified as per WHO classification

- *Grade 0*: No goiter is found (the thyroid impalpable and invisible)
- *Grade 1*: Neck thickening is present as a result of enlarged thyroid, palpable, however, not visible in normal position of the neck; the thickened mass moves upwards during swallowing. Grade 1 also includes nodular goiter if thyroid enlargement remains invisible.
- *Grade 2*: Neck swelling, visible when the neck is in normal position, corresponding to enlarged thyroid—found on palpation.

### Is the normal thyroid gland visible?

The normal thyroid gland is not visible except in young thin women when the isthmus may be visible.

### Discuss examination of a thyroid case.

#### *General Physical Examination*

*General inspection*.

Does the patient look ill, tense, agitated, irritable or sluggish?

*Appearance of patient*: Puffiness of face in hypothyroidism or anxious look in hyperthyroid.

Is the patient excessively sweating or feeling cold?

Is he or she appropriately dressed for weather?

Pre-tibial myxedema/generalized oedema (non-pitting)

Listen for a stridor, presence of which is suggestive of tracheal compression.

Dyspnea

Hoarse voice, slow speech

### Point to be Noted in Hands and Arms in a Thyroid Case

| ***Hypothyroid*** | ***Hyperthyroid*** |
|---|---|
| Bradycardia | Tachycardia—rapid/ bounding pulse |
| Cold skin | Atrial fibrillation |
| Dry skin | Hot, sweaty skin |
| Carpal tunnel syndrome | Clubbing (Graves') |
| Raynaud phenomenon | Onycholysis |
| | Fine tremor |
| | Systolic hypertension |

### Points to be Noted in Face in a Thyroid Case

Look for signs of anaemia, central cyanosis, dyspnoea as well as:

| ***Hypothyroid*** | ***Hyperthyroid*** |
|---|---|
| Loss of outer eyebrow | Exophthalmos +/– ophthalmo-eyebrow plegia (paralysis of one or more of extra occular muscles) |
| Thinning hair (women!) | Graves' |
| Xanthelasma | Lid lag |
| Corneal arcus/arcus senilis | Lid retraction |
| Pale, puffy face 'Toad-like' | Corneal ulceration |

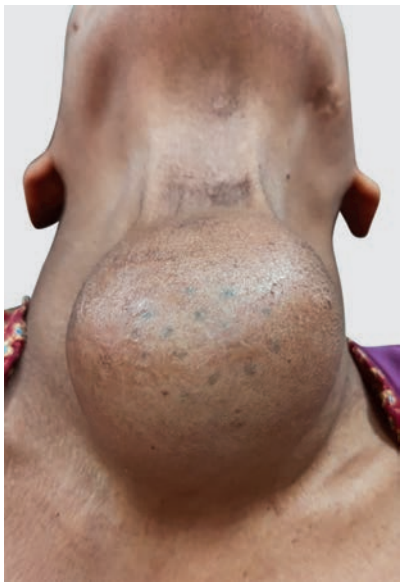


**Fig. 15.1:** Diffuse thyroid swelling

### Inspection of the Neck

Inspection begins by looking for any scar, asymmetry, or masses (Fig. 15.1). The inspection is best done from the side of the neck and from the front. A scar of previous thyroid surgery points to the potential thyroid disease in patients with non-specific symptoms. The redness or erythematic skin overlying a tender swelling is seen in acute suppurative thyroiditis.

**Pizillo's technique:** This technique is used to make the thyroid more prominent in cases of short necked or obese people. The patient is asked to put the hands behind the occipital region and push the head backwards against the clasped hands behind the head to make thyroid more prominent.

### Signs of Thyroid Enlargement on Inspection

Assess the fullness on either side of the trachea below level of cricoid cartilage. To identify the thyroid gland find the laryngeal prominence of the thyroid cartilage which is the most conspicuous prominence in the neck. Next, locate the cricoid cartilage. The isthmus of the thyroid lies just below the cricoid cartilage. Next, ask the patient to extend the neck. This will lift the trachea and stretch the skin against the thyroid, allowing for better visualization. Then, inspect the patient's neck from the side. You should see a straight line from the cricoid cartilage to the sternal notch. If there is an anterior bowing of this line, this suggests a goiter is present.

During inspection look for any tracheal deviation if it is obvious, otherwise, deviation of trachea is confirmed on palpation. Inspect the swelling when the patient is swallowing water. Normally during swallowing the trachea and thyroid move upwards from 1.5 to 3.5 cm and then hesitates momentarily before coming back to normal position. A neck swelling is likely not to be thyroid if it does not move with swallowing, or does not hesitate with trachea before coming down to the original position or move in an asynchronous manner in relation to thyroid or trachea.

### When will thyroid not move with swallowing?

a. When the thyroid is too big and has occupied the extensive space in the neck.
b. If there is fixation to surrounding structures as in:
   - Invasive carcinoma
   - Riedel's thyroiditis
   - Lymphoma.

### Why does thyroid move with swallowing?

The following anatomical reasons are responsible for movement of thyroid with deglutination:

1. The pre-tracheal fascia splits to enclose the thyroid gland. The upper limit of attachment of pretracheal fascia is on oblique line of thyroid cartilage and upper border of cricoid cartilage where the thyropharyngeal muscle and cricopharyngeal muscle (parts of inferior constrictor) are attached. Thyropharyngeal muscle and cricopharyngeal muscle pulls the thyroid cartilage and cricoid cartilage upwards along with the structures attached to it.
2. The pre-tracheal fascia gets thickened to form ligament of Berry. The ligament of Berry fixes the thyroid to trachea. The trachea moves upwards during second phase of deglutition.

### What are the causes of breathlessness in relation to thyroid swelling?

a. Retrosternal goiter
b. Compression of trachea in long standing MNG due to collapse of tracheal rings resulting from pressure atrophy
c. Bilateral recurrent laryngeal nerve involvement due to malignancy or after surgery.

d. Erosion of trachea in malignancy
e. Congestive heart failure in thyrotoxicosis

### What is pseudo-goiter?

This refers to apparent thyroid enlargement when no true goiter is present. This pseudo-goiter can be seen in the following situations:

a. In thin patients, thyroids lying high in the neck over thyroid cartilage may appear enlarged when actually there is no enlargement. These glands are actually of normal size on palpation. This situation commonly arises when the thyroid gland is placed more than 10 cm above the suprasternal notch.
b. Presence of other cervical masses like adipose tissue (diffuse or localized), cervical lymph-adenopathy, brachial cleft cyst, or pharyngeal diverticulum that may simulate the appearance of goiter.
c. Modigliani syndrome is defined as a thyroid that appears enlarged when the person actually has an exaggerated cervical lordosis. This is named after the painter whose subjects demonstrated similar neck anatomy.

### In which subgroup of patient's palpation of thyroid is difficult?

Presence of kyphosis and emphysema in elderly may pose difficulties in palpation of thyroid as the cricoid bone is often displaced behind the sternum in these patients.

### What is the normal size of each normal lobe?

Each normal lobe is estimated to the size of the distal phalanx of the individual thumb.

### What are the different methods of palpation of thyroid gland?

a. The classical method of palpation of thyroid gland is to palpate from behind. The clinician stands behind the patient and palpates with both hands on front. The first step is to identify the cricoid cartilage and palpate the isthmus of thyroid gland which lies horizontally just below cricoid cartilage. The isthmus can be palpated by thumb then both the lateral lobes are palpated together. Ask the patient to flex the neck slightly forward to relax the sternocleidomastoid muscles and place the three fingers of both hands on the patient's neck so that your index fingers are just below the cricoid cartilage, then ask the patient to sip and swallow water as before. Feel for thyroid isthmus rising up under the finger pads.
b. *Lahey's method*: The examiner stands in front of the patient. To palpate left lobe, the thyroid is pushed to the left from side by left hand so that left lobe becomes prominent. The left lobe is palpated by right hand and vice versa.
c. *Crile method of palpation*: Thyroid examination is done while patient is swallowing water. For palpating left lobe clinician stands on the right side. The left thumb is used to palpate the left lobe of thyroid. For palpating right lobe two fingers of right hand or the right thumb can be used.

### What are the signs and symptoms of tracheal obstruction?

a. In a partially obstructed trachea a harsh noise is heard (stridor) as the patient breathes. If the obstruction is mild, one has to listen in a quiet room.
b. Later on as the obstruction becomes more obvious breathlessness cyanosis and restlessness become obvious.
c. The Kocher's test is used to detect tracheomalacia or tracheal obstruction. The slight push on lateral lobes will produce stridor. However, this test is mentioned to condemn as it can cause acute respiratory distress due to collapse of tracheal rings by pressure of examiners finger.

### What thyroid conditions give rise to tracheal obstruction?

a. Thyroid malignancy directly infiltrating into the lumen of trachea especially anaplastic carcinoma.
b. Retrosternal goiter
c. Long standing multi-nodular goiter giving rise to an atrophy of tracheal rings
d. Riedel's thyroiditis

### What is the consistency of normally thyroid gland and in various other conditions?

The consistency of normal thyroid gland is described as rubbery. In patients with Graves' disease thyroid gland feels softer than normal and is typically described as spongy and malleable. In Riedel's thyroiditis there is woody consistency.

In malignancy and lymphoma the consistency is stony hard. Hard consistency can also be seen in calcification of nodule and hemorrhage into a nodule. Hashimoto's glands are firmer in consistency due to extensive fibrosis.

### What is the accuracy of clinical examination in palpating nodules?

In only 6% of nodules less than 0.5 cm are palpable and about 50% of nodules more than 2 cm diameter are reliably detected by experienced examiner.

### What are the signs of toxicity of goiter on clinical examination? (Rule of T)

Signs of toxicity in a goiter are the following:

a. Tachycardia especially increased sleeping pulse rate
b. Tremors in the hands or tongue. These are fine tremors.
c. Thrill (bruit) over the goiter.
d. Toxic eye signs

### What is Delphian node?

The Delphian node drains the thyroid gland and larynx. It lies anterior to the cricothyroid ligament just above the isthmus. The word Delphian refers to the ancient Greek "Delphi". Delphi was the site of the Delphic oracle, the most important oracle in the classical Greek world, and it was a major site for the worship of the God Apollo. The node is called "Delphian" because it is the first lymph node of the anterior neck structures exposed in surgery. It often heralds thyroid carcinoma, just as the oracle at Delphi in ancient Greek mythology foretold the future. Involvement of this node is the earliest sign of metastatic papillary carcinoma. It may also be enlarged in laryngeal cancer, subacute granulomatous thyroiditis, Graves' disease and rarely in Hashimotos's thyroiditis.

### What are different methods to ascertain the possibility of retrosternal extension?

The retrosternal extension on clinical examination can be ascertained by the following methods:

a. Inability to feel the lower border of thyroid or lower border only palpable at the peak of deglutition.
b. Dullness on percussion of manubrium sterni.
c. *Positive Pemberton sign*: The sign named after Hugh Spear Pemberton, an English physician (1890–1956), was described in a brief communication in the Lancet in 1946. Pemberton's sign is defined as the development of facial plethora, cyanosis, and distension of neck veins while raising both arms simultaneously. A positive test indicates thoracic inlet obstruction. This sign was originally described in patients with retrosternal goiter, but may also be seen in lung carcinoma, lymphomas, thymomas, dermoid cysts, or aortic aneurysms.
d. *How to perform Pemberton's test*: Have your patient hold his arms above his head, with elbows touching his ears. A negative Pemberton's sign occurs when nothing happens for three minutes. A positive sign is a sensation of stuffiness, dizziness, congestion, or a "funny feeling" in the head. The face can become dusky as well. When the arms rise anteroposterior diameter of thoracic inlet decreases as the thoracic inlet get raised by bilateral contraction of sternal heads of sternocleidomastoid muscles, and, if a retrosternal goiter or other similar enlargement is present, obstruction can occur.

### What are the signs of malignancy on clinical examination of thyroid?

a. History of rapid increase in size of goiter.
b. History of radiation to the head and neck or thorax.
c. Presence of hard nodules
d. If the goiter is not moving with deglutition.
e. Involvement of recurrent laryngeal nerve leading to difficulty in breathing or hoarseness of voice.
f. Palpable cervical lymph nodes along with goiter.
g. *Berry's sign positive*: The positive Berry's sign means that the carotid pulsation are not palpable on the side of goiter as the malignant goiter engulfs the carotid sheath and the structures in it. On the other hand, benign enlargement of thyroid pushes the carotid pulsation laterally.

### What questions one should be able to answer at the end of clinical examination of thyroid case?

a. The type of goiter, i.e. diffuse, multi-nodular, solitary nodular.
b. Functional status of thyroid gland, i.e. hyper-functioning, hypo-functioning or euthyroid on the basis of clinical examination.
c. Any feature of malignancy as discussed above.
d. Is there any feature of retrosternal extension as discussed above?

### What is the pathology of eye signs in Graves' disease? (Adapted from Institute of Ophthalmology, USA)

In patients with Graves' disease, eye signs may precede, coincide with or follow the hyperthyroidism.

Activated T cells infiltrate orbital contents and stimulate fibroblasts, leading to:

1. Enlargement of extra ocular muscles
2. Cellular infiltration of interstitial tissues
3. Proliferation of orbital fat and connective tissue.

Enlargement of extra ocular muscles occurs by following mechanism:

a. The stimulated fibroblasts produce glycosaminoglycans (GAGs) which cause the muscle to swell.
b. Muscle size may increase by up to 8 times.
c. The swollen muscles occupy orbital space and can compress the optic nerve.
d. These swollen muscles can cause a forward propulsion of the globe (proptosis) so that the eyelids do not cover well and eyes dry out, causing exposure keratopathy.

### Five Main Clinical Manifestations

1. Soft tissue involvement
2. Eyelid retraction
3. Proptosis
4. Optic neuropathy/exposure keratopathy
5. Fibrosed muscles

#### *Soft Tissue Involvement*

*Symptoms*

a. Variable grittiness
b. Photophobia
c. Lacrimation

*Signs*

a. Periorbital and lid swelling
b. Conjunctiva hyperemia—sensitive sign of disease activity
c. Chemosis (oedema of the conjunctiva)
d. Severe cases: Conjunctiva prolapses over lower eyelid—watery eyes

#### *Eyelid Retraction*

1. Retraction of both upper and lower eyelids occur in 50% of patients
2. Normally, upper eyelid rests about 2 mm below the limbus, with lower eyelid resting at the inferior limbus.
3. When retraction occurs, the sclera (white) can be seen. Causes cosmetic problems.
4. Pathogenesis is due to spasm of Muller's muscle fibers which are supplied by sympathetic nerve.
5. May be due to contraction of the levator muscle by fibrosis, or be chemically induced by high thyroid hormone levels.
6. If persists when disease is inactive, can be helped by eyelid surgery.

#### *Eyelid Retraction* (Fig. 15.2)

**Clinical features**

*Clinical signs:*

a. Lid retraction in 1° (front) gaze
b. Lid lag, i.e. delayed descent of upper lid in downgaze
c. Staring appearance of the eyes.

*Proptosis is axial:*

- Thyroid eye disease is the most common cause of both bilateral and unilateral proptosis in adults
- Proptosis is uninfluenced by Rx of hyperthyroidism and is permanent in 70% of cases
- Severe proptosis prevents adequate lid closure, and may lead to severe exposure keratopathy and corneal ulceration.

### Optic Neuropathy

- Serious complication affecting about 5% of patients
- Caused mainly through direct compression of the optic nerve or its blood supply by enlarged and congested rectus muscles at the orbital apex

**Fig. 15.2:** Exophthalmos in hyperthyroidism

- May occur in the absence of proptosis
- Can cause severe but preventable visual impairment
- An early sign is decreased colour vision
- Slow progressive impairment of visual acuity
- Visual defects, especially central scotomas
- Optic atrophy in chronic advanced cases.

## What are the causes of thyroid nodules?

### *Causes of Thyroid Nodules*

*Benign etiology*

- Multinodular (sporadic) goiter ("colloid adenoma")
- Hashimoto's (chronic lymphocytic) thyroiditis
- Cysts: Colloid, simple, or haemorrhagic
- Follicular adenomas
  - Macrofollicular adenomas
  - Microfollicular or cellular adenomas
  - Hurthle-cell (oxyphil-cell) adenomas

*Malignant aetiology*

- Papillary carcinoma
- Follicular carcinoma
- Minimally or widely invasive oxyphilic (Hurthle-cell) type
- Medullary carcinoma
- Anaplastic carcinoma
- Primary thyroid lymphoma
- Metastatic carcinoma

## What are different types of goiters?

The goiter can be diffuse, multinodular goiter (MNG) or solitary nodular goiter (SNG).

The diffuse goiter means both lobes of thyroid are enlarged and smooth surfaced.

The multi-nodular goiter means more than one nodule is palpable on the surface of thyroid gland.

The solitary nodular goiter means except one nodule nothing else is palpable in the region of thyroid.

The goiter can be hyper-functioning, hypo-functioning or euthyroid.

## Causes of Multinodular Goiter

- *Endemic or sporadic*: Endemic goiter is one when more than 10% of population is suffering from goiter.
- Iodine deficiency
- Environmental goitrogens
- *Dietary goitrogens*: Vegetables with goitrogenic effect contain thioglycosides or cyanogenic glycosides. In this context cigarette smoking is thought to be a cofactor for goitrogenesis, since it increases serum thiocyanate concentration.
- Genetic defects of thyroid hormone action like T4 receptor defects
- Genetic defects of thyroid hormone synthesis
- *Goitrogenic drugs*: Lithium, carbutamide, amino-glutehiemide and fluoride
- *Thyroiditis syndrome*: They give rise to acute development of goiter. This inflammatory thyroid disease may be painful as in acute thyroiditis or subacute thyroiditis of de Quervain. Pain in acute MNG gives rise to suspicion of granulomatous thyroiditis such as sarcoidosis or tuberculosis.
- TSH producing pituitary adenoma

## Clinical Symptoms of Multinodular Goiter

- Feeling of tightness or feeling of foreign body are non-specific and are independent of actual thyroid volume or nodules.
- Dysphagia and urge to cough are usually caused by retrotracheal thyroid tissue and usually detected during surgery.
- Hoarseness is due to functional impairment of recurrent laryngeal nerve resulting from pressure.
- Dyspnea and stridor are usually due to tracheal compression or by dislocation of trachea by episternal or intra-thoracic goiter
- Venous obstruction

## What is the rate of enlargement of benign non-toxic MNG?

There is linear relationship between age, thyroid volume and nodularity with an average yearly increase of 4.5% of thyroid volume.

## Enumerate different causes of solitary nodular goiter (SNG).

Causes of SNG are

a. *Dominant nodule*: In this condition only one nodule is palpable and other nodules are small not clinically palpable. Dominant nodule is the cause of SNG in more than 50% of cases.
b. Papillary carcinoma
c. Follicular carcinoma

d. Anaplastic carcinoma
e. Follicular adenoma
f. Hemorrhage in one of the necrotic nodules of MNG and become large
g. If only one lobe is enlarged in Hashimoto's thyroiditis.

### How much is the prevalence of cancer in thyroid nodules?

Clinical importance of thyroid nodules lies in excluding thyroid cancer, which accounts for 4.0 to 6.5% of all thyroid nodules in non-surgical series. Non-palpable nodules have the same risk of malignancy as palpable nodules.

### In which subgroup of patient the prevalence of cancer is high in thyroid nodules?

The prevalence of cancer is higher in the following groups:

- Children
- Adults less than 30 years or over 60 years old
- Patients with a history of head and neck irradiation
- Patients with a family history of thyroid cancer
- Serum TSH is an independent risk factor for predicting malignancy in a thyroid nodule. The prevalence of malignancy is around 29.7% for patients with serum TSH >5.5 mU/L. When cancer is diagnosed, a higher TSH is associated with a more advanced stage of cancer.

On the other hand, the prevalence of cancer is lower in nodules in multi-nodular goiters. All autonomously hyper-functioning ("hot") nodules are practically benign.

### What is molecular factors which have incriminated in thyroid malignancy?

*Molecular genetics*

Various genes (proto-oncogenes and tumour suppressor genes) are incriminated in development of thyroid cancers:

1. **RET proto-oncogene:** This gene is present on chromosome 10 in tissues derived from embryonic nervous and excretory system and encodes for receptor tyro kinase which binds to several growth factors. Germline mutations in RET proto-oncogene predisposes to MEN 2A, MEN 2B and familial MTC.
2. **BRAF mutations:** These are associated with more aggressive thyroid malignancy, larger tumour size, invasion and lymphadenopathy; it occurs in 50% of patients with papillary cell carcinoma.
3. **P53 mutations:** These are common in undifferentiated thyroid cancers.
4. **Peroxisome proliferator activated receptor gamma (PPAR gamma):** They play an important role in the development of follicular neoplasms.
5. **Tumour suppressor genes p15 and p16:** They are more commonly mutated in thyroid cancer cell lines.

### What is thyroid nodule?

The thyroid nodule is an isolated lesion which looks different from the surrounding thyroid parenchyma on radiological examination. 10–15% of these thyroid nodules prove to be malignant.

Nodules with high risk of malignancy are as follows:

- Age >70 years or <14 years: Nodules discovered during childhood have a 3–4-fold higher risk of malignancy than in adults
- Head and neck radiation during childhood has 33–37% chance of malignancy
- 18-FDG-PET positive solitary thyroid lesions have an increased risk of malignancy of approximately 30–50%; FDG-PET should be done in euthyroid solitary nodular goiter, if available
- History of thyroid cancer in the family
- Past history of genetic syndromes, such as MEN 2, familial papillary thyroid cancer and familial polyposis coli
- Fixed, hard, solid nodule, cervical lymphadenopathy and vocal cord paralysis
- Cold nodules on thyroid scan in a hyperthyroid patient
- Following findings on USG are suggestive for malignancy
- Microcalcifications
- Hypoechoic nodule
- Nodule with irregular border
- Nodular vascularity
- Follicles which are taller than wider on transverse view.

## TNM-staging for Thyroid Malignancy

| | |
|---|---|
| **Primary tumour (T)** | |
| TX | Tumour cannot be evaluated, e.g. post-thyroidectomy patient |
| T0 | No primary tumour is detected but tumour found in cervical lymph nodes, e.g. lateral aberrant thyroid |
| T1 | Tumour less than or equal to 2 cm in maximum diameter and is confined to the thyroid |
| T1a | Tumour ≤1 cm, confined to the thyroid |
| T1b | Tumour >1 cm but ≤2 cm in greatest diameter, confined to the thyroid |
| T2 | Tumour more than 2 cm but less than or equal to 4 cm, confined to the thyroid |
| T3 | Tumour size more than 4 cm, confined to the thyroid or with minimal extension outside thyroid-like extension to sternothyroid muscle or parathyroid soft tissues |
| T4a | Tumour extension outside the thyroid capsule with invasion of subcutaneous soft tissues, larynx, trachea, oesophagus or recurrent laryngeal nerve |
| T4b | Tumour invading prevertebral fascia or encases carotid artery or mediastinal vessel |
| **Anaplastic carcinomas are kept in stage IV:** | |
| T4a | Anaplastic carcinoma confined to thyroid |
| T4b | Anaplastic carcinoma which has come out of thyroid grossly |
| **Regional lymph nodes (N)** | |
| Regional lymph nodes include the central compartment, lateral cervical, and upper mediastinal lymph nodes: | |
| NX | Local lymph nodes cannot be evaluated |
| N0 | Regional lymph nodes not involved |
| N1 | Regional lymph node involved in tumour |
| N1a | Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes) lymph nodes have metastasis |
| N1b | Involvement of 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 evidence of distant metastasis |
| M1 | Evidence of distant metastasis is present |

## Papillary Carcinoma

- These account for 80–85% of all thyroid cancers in iodine sufficient areas.
- It is a predominant thyroid malignancy in children and in individuals exposed to external radiation.
- Male: female ratio is 1:2.
- The mean age of presentation is 30–40 years.
- Most patients are euthyroid at presentation.
- It presents as a slow growing painless mass.
- At later stages, dysphagia, dyspnea and dysphonia can occur.
- Lymph node enlargement may be the presenting symptom especially in pediatric age group and young population.
- They can present with lateral aberrant thyroid which simply denotes that the cervical lymph node has been evaded by metastatic cancer, in the absence of thyroid swelling.

## Diagnosis

1. FNAC of thyroid nodule/lymph node.
2. USG neck for lymph nodes and contralateral lobe.
3. Lymph nodes are involved in both lateral and central compartment.
4. Distant metastasis develops in 20% of patients in late stages.

## Pathology

1. On cut section, they are hard and whitish; they remain flat on cut surface but normal thyroid tissue of nodular goiter tends to bulge on sectioning with blade.
2. Microscopically, it exhibits papillary projections, or a mixed pattern of papillary and follicular structures, or a pure follicular pattern.
3. Characteristic pathological features are as follows:
   a. Cells which are cuboidal in shape and have abundant pale cytoplasm.
   b. Nuclei are crowded and may demonstrate 'grooving' and intranuclear cytoplasm inclusions classically known as Orphan Annie nuclei, which allows diagnosis by FNAB.
4. Psammoma bodies are microscopic, calcified deposits representing the clumps of sloughed cells.
5. Multifocality is seen in 85% of cases and has increased risk of cervical lymph node metastasis.

6. Papillary carcinoma rarely invades adjacent structures such as trachea, esophagus and recurrent laryngeal nerve.
7. Other variants of papillary cell carcinoma are as follows and account for less than one percent of cases are aggressive in nature and should be given RAI 131 therapy irrespective size
   a. Tall cell variant
   b. Insular
   c. Columnar
   d. Diffuse sclerosing
   e. Clear cell variety
   f. Trabecular type
   g. Poorly differentiated type

   These subtypes account for 1% of all papillary carcinomas and are associated with poorer prognosis.
8. Minimal or occult carcinoma refers to tumour of <1 cm with no evidence of local invasiveness through the thyroid capsule or angio-invasion and not associated with lymph node metastasis. It is present in 2–36% of thyroid glands removed at autopsy and is associated with a better prognosis than a larger tumour.

### Prognostic Indicators

Hay and colleagues in 1987 from Mayo clinic proposed the AGES system. Low risk patients are young, with well-differentiated tumour, no metastasis and small primary lesion.

**AGES:** Age, grade, extra thyroid spread and size.

**AMES:** Age (<40 years for females, <50 years for males), metastasis, extra thyroid spread, size of tumour (<5 cm).

**Degroot system of classification**

- Class I: Intrathyroidal
- Class II: Evidence of cervical node metastasis
- Class III: Extra thyroid invasion
- Class IV: Evidence of distant metastasis.

**Molecular and genetic markers indicating poor prognosis:**

1. Tumour DNA aneuploidy.
2. Decreased cAMP response to TSH.
3. Increased epidermal growth factor binding.
4. Presence of NRAS and GSP mutation.
5. Presence of p53 mutations.
6. Presence of BRAF V600E mutation which is an independent factor for tumour recurrence and tumour-related mortality.

**Patients with BRAF mutation should have the following:**

- More extensive initial surgical excision.
- High dose of post-operative radioactive iodine (RAI) therapy.
- Increased TSH suppression.
- Follow-up.

### Treatment

Total or near total thyroidectomy is performed for primary cancer >1 cm.

Thyroid lobectomy is carried out for the following:

1. Small <1 cm tumour.
2. Incidentally discovered small focus.
3. Low risk patient as per various classifications.
4. Unifocal intra-papillary carcinoma.

The central compartment of lymph node dissection is done in T3 and T4 tumours even when no lymph nodes are enlarged on prophylactic basis. It is not required for clinically node negative T1/T2 cases.

Modified radical neck dissection is done for biopsy-proven lymph node metastasis detected clinically or by imaging.

Dissection of posterior triangle lymph nodes or supra hyoid dissection is not necessary.

Prophylactic lateral node dissection is not required.

### Follicular Carcinoma

- These tumours account for 10% of all thyroid cancers which occur; more common in iodine depleted areas
- The mean age of presentation is 50 years and the male: female ratio is 1:3.
- They usually present as solitary nodular goiter and occasionally occur with history of rapid increase in size in a long-standing goiter.
- Cervical lymphadenopathy is uncommon at initial presentation (about 5%).
- In <1% of cases, follicular carcinoma may be hyperfunctioning and patients may present with signs and symptoms of thyrotoxicosis.
- FNAC cannot distinguish between benign follicular adenoma and follicular carcinoma. Jointly they are known as follicular neoplasm. However, large follicular tumors (>4 cm) are likely to be malignant in older males.

**Molecular markers to distinguish between benign and malignant follicular neoplasm are as follows:**

1. DNA-based markers, such as BRAF, RAS, RET/PTC and PAX/PPAR gamma abnormality. Presence of any of these mutations in FNAB sample is a strong indicator of cancer.
2. Micro RNAs are small non-coding RNAs associated with carcinogenesis. There is an upregulation of miR-197 and miR-346.
3. Peripheral blood levels of TSH-R mRNA are also able to predict malignancy.
4. Measurement of expression of 167 genes (veracyte).

### Pathology

- Usually solitary lesions and surrounded by capsule.
- Histologically, follicles are present but devoid of colloid.
- If capsular/vascular invasion is present, it indicates malignancy.

### Surgical Treatment of Follicular Neoplasm

If a follicular neoplasm is diagnosed on FNAB, then hemithyroidectomy is performed as 80% of these will be benign adenomas.

Total thyroidectomy is indicated in the following patients:

1. Older male patients with follicular lesion >4 cm as 50% of these lesions will be malignant.
2. If atypical cells are seen on FNAB.
3. Family history of thyroid cancer.
4. History of radiation exposure.

If histopathology after lobectomy shows frankly invasive carcinoma or follicular carcinoma with angio-invasion, with or without capsular invasion, it requires complete thyroidectomy.

Prophylactic nodal dissection is not needed as lymph node involvement is infrequent.

Therapeutic nodal dissection should be done if nodes are involved.

Cumulative 10-year mortality for follicular carcinoma is 15% and 30% at 20 years.

**Poor prognosis is indicated by the following:**

1. Age >50 years at presentation.
2. Tumor size >5 cm.
3. Higher tumor grade.
4. Marked vascular invasion.
5. Extrathyroidal invasion.
6. Distant metastasis.

### Hurthle cell carcinoma

- Accounts for 3% of all thyroid cancers.
- Under WHO classification, it is a subtype of follicular thyroid cancer.
- Tumour contains sheets of eosinophilic cells packed with mitochondria which are derived from oxyphilic cells of the thyroid gland.

#### *Differences from follicular carcinoma*

- In high-risk group, maintain TSH levels between 0.1 and 0.5 mU/mL.

Thyroglobulin levels are measured every 6 months.

Thyroglobulin levels should be measured after T4 withdrawal or after recombinant TSH stimulation.

Thyroglobulin level of <0.5 ng/mL without antithyroglobulin antibody.

#### *Staging of thyroid cancers*

Stage I: All younger patients <45 years of age with papillary or follicular carcinoma are stage I unless distant metastasis are present.

In >45 years old patients following staging is applied

Stage I: Any papillary/follicular carcinoma <2 cm

Stage II: Any tumor >2 cm without nodal metastasis.

Stage III: Any tumor with nodal metastasis/extrathyroidal invasion.

Stage IV: Distant metastasis.

#### *In medullary thyroid carcinoma*

1. No age distinction.
2. Extrathyroidal invasion in stage II.

#### *Follow-up imaging*

*Low-risk patients*: Negative TSH stimulated thyroglobulin level and cervical USG not showing any lymph node, do not require any diagnostic whole-body radioactive scan.

Diagnostic whole-body radioactive scan is indicated in patients with high risk or intermediate risk.

USG neck is done at 6–12 months after thyroidectomy, then annually for 3–6 years.

18-FDG-PET is indicated in initial staging of patients with poorly differentiated thyroid cancer or Hurthle cell tumour or in patients with metastatic disease.

*Medullary carcinoma*

- Accounts for 5% of all thyroid malignancies.
- Arises from parafollicular C cells of thyroid.
- Parafollicular cells are derived from ultimobranchial bodies.
- These cells are concentrated superolaterally in the thyroid lobes, which is the site of development of medullary carcinoma.
- C-cells secrete:
- Calcitonin (32 amino acid polypeptide)
- Carcinoma-embryonic antigen (CEA)
- Calcitonin gene related peptide
- Histaminases
- Prostaglandin E2 and F2 alpha
- Serotonin
- 25% occur in familial pattern MEN 2A and MEN 2B. These occur secondary to germ line mutation in RET proto-oncogene.
- About 2–4% of patients develop Cushing syndrome as a result of ectopic production of ACTH.

**MEN 2A (MALPH)**

1. Medullary thyroid carcinoma
2. Pheochromocytoma
3. Hyperparathyroidism
4. Lichen planus
5. Amyloidosis

**MEN 2B (GMP)**

1. Medullary thyroid carcinoma
2. Pheochromocytoma
3. Marfanoid habitus
4. Ganglioneuromatosis

**Clinical features**

- Neck mass is common.
- It may be associated with palpable cervical lymphadenopathy (15–20%).
- Pain and aching is more common.
- Local invasion may produce dysphagia, dysphonia or dyspnoea.
- Distant blood-borne metastasis to liver, bone (frequently osteoblastic) and lung occur later.
- Female to male ratio is 1.5:1.
- Most patients present in 50–60 years of age, but patients with familial disease are present at a younger age.
- 80% of cases are unilateral.
- Multicentric in familial disease.
- Bilateral tumours occur in 90% of cases of familial tumours.
- Familial cases are associated with C-cell hyperplasia, which is a premalignant disease.
- The presence of amyloid is a diagnostic finding but immunohistochemistry for calcitonin is more commonly used as diagnostic tumour marker. These tumours are also positive for CEA and calcitonin gene-related peptide.
- 25% of patients have familial disease.
- All new patients of medullary thyroid cancer should be screened for RET point mutations, pheochromocytoma and hyperparathyroidism.
- CEA is a better predictor of prognosis.

**Treatment**

- USG neck to evaluate neck nodes and superior mediastinal nodes.
- Serum calcitonin, CEA and calcium levels should be measured.
- RET proto-oncogene mutation testing should be done.
- Presence of pheochromocytoma needs to be excluded.
- If the patient is found to have pheochromocytoma, it has to be operated first.

Total thyroidectomy is the treatment of choice because of the following:

- High incidence of multicentric nature
- More aggressive course.
- $I^{131}$ therapy usually not effective.
- Bilateral prophylactic central compartment neck node dissection should be routinely performed due to high incidence of involvement of central compartment nodes.
- If patient has palpable or image detected cervical lymph nodes or calcitonin levels >400 pg/mL:
- Chest CT and
- Triple phase abdominal CT is performed to assess metastatic disease
- In patients with no metastatic disease, bilateral lateral neck dissection is advised (IIA, III, IV and V).

**Targeted therapy**

1. Vandetamib inhibits both EGFR and VEGFR.
2. Anti-CEA monoclonal antibody (labetuzumab) has also been shown to have anti-tumour response.

***Prophylactic thyroidectomy***

- It is indicated in RET mutation carriers if the mutation is confirmed.

- In patients with less aggressive mutation, thyroidectomy may be delayed for >5 years.
- If there is normal annual serum calcitonin, normal USG neck, less aggressive family history or family preference, children with mutation at codon 634 are advised to undergo thyroidectomy at <5 years of age, and those with MEN 2B-related mutation should undergo thyroidectomy before 1 year of age.
- Central neck dissection is avoided in children who are RET-positive but have normal calcitonin level and normal USG neck. If calcitonin level is increased, prophylactic central neck dissection is indicated.

### *Post-operative follow-up of medullary carcinoma*

- Annual CEA and calcitonin levels.
- Complete physical examination every year.
- USG neck every year; if positive, then CT/MRI/FDG-PET-CT.

10-year-survival is 80% in lymph node—negative patients, but decreases to 45% in lymph node—positive patients.

Survival is best in non-MEN familial medullary thyroid carcinoma.

Prognosis is worst in MEN 2B.

## Anaplastic Carcinoma

- Accounts for <1% of thyroid malignancy.
- More common in females.
- Most common age group is of seventh or eighth decade.
- Common presentation is rapidly growing painful neck mass.
- Associated symptoms such as dysphagia, dysphonia and dyspnoea are common.
- Tumour is large and often fixed to surrounding structures.
- It may ulcerate with areas of necrosis.
- Lymph nodes are usually involved at the time of presentation.
- Evidence of distant metastatic spread is often present.

### Diagnosis

- Diagnosis is confirmed by FNAC which shows giant and multi-nucleated cells.
- If spindle cell element is present, then diagnosis of sarcoma (primary or metastatic) should be considered.
- Core or incisional biopsy is indicated if there is necrotic material on FNAC.

### Pathology

- They are firm and whitish in appearance.

Three main histological types are seen:

- Spindle cell type
- Squamoid type
- Pleomorphic giant cell type.

### Treatment

- If the mass is confined to thyroid, total thyroidectomy or near total thyroidectomy with therapeutic lymph node dissection is performed.
- If extrathyroidal extension is present, en-block resection of all gross disease should be considered.
- Tracheostomy should be avoided unless there is impending airway obstruction.

## What investigations should be performed in a case of goiter?

*Serum TSH*: Thyroid function should be assessed in all patients with thyroid nodules. If the serum TSH concentration is low, it indicates overt or subclinical hyperthyroidism, the thyroid scintigraphy should be performed next.

If the serum TSH concentration is normal or elevated, then fine needle aspiration biopsy is indicated. The patients with a high serum TSH concentration also require an evaluation for hypothyroidism.

## Thyroid Ultrasonography

It should be performed in all patients with thyroid nodules. The nodularity in goiter can be due to varied aetiology like from Hashimoto's thyroiditis resulting from focal enlargement from lymphocytic infiltrates, TSH-induced hyperplasia of follicular tissue, or a thyroid tumour.

Ultrasonography may also help to distinguish among these possibilities.

It gives the following information:

- Gives information regarding size and anatomy of gland and adjacent structures.
- It provides much more information than physical examination and thyroid scan.
- Ultrasound findings can be used to select nodules for FNA biopsy.
- Ultrasound can identify nodules on posterior aspect of thyroid or predominantly cystic nodules.

- Thyroid volume can be calculated by USG using formula of ellipsoid with empirical correction factor of 0.479. Thickness, width and length of both thyroid lobes is measured and thyroid volume is corrected by following formula:

Length (a) × Width (b) × Thickness (c) × 0.479

a, b, c represent maximum length, maximum width and maximum thickness.

### Thyroid Scintigraphy

Thyroid scintigraphy determines the functional status of a nodule. A low serum TSH, indicating overt or subclinical hyperthyroidism, increases the possibility that a thyroid nodule is hyperfunctioning. Thus, thyroid scintigraphy should be performed in patients with a low serum TSH concentration.

Thyroid scintigraphy can be used to select nodules for FNA. Scintigraphy is done by using one of the radioisotopes of iodine (usually $^{123}I$) or technetium-99m pertechnetate, however, radioiodine scanning is preferred as 5% of thyroid cancers concentrate pertechnetate, but not radioiodine These nodules may appear hot or indeterminate ("warm") on pertechnetate scans and cold on radioiodine scans. The nodule may appear cold (non-functioning), warm or hot on scintiscan.

### Fine Needle Aspiration Cytology (FNAC)

The American Thyroid Association recommends FNA biopsy as the procedure of choice for evaluating thyroid nodules and selecting candidates for surgery. FNA biopsy has resulted in improved diagnostic accuracy, a higher malignancy yield at the time of surgery, and significant cost reductions.

### FNA

a. A simple and safe office procedure
b. In this procedure tissue samples are obtained for cytological examination using 23 to 27 gauge (commonly 25 gauge) needles with or without ultrasound guidance.
c. The adequate samples can be obtained in 90 to 97% of aspirations of solid nodules.

### Recommendations for FNA in Thyroid Nodules

a. Solid hypo-echoic nodules (palpable or non-palpable) measuring >1 cm in the absence of risk factors.
b. Solid nodules that are iso-echoic or hyper-echoic, if they are >1.0 to 1.5 cm.
c. Mixed cystic-solid nodules without suspicious features on ultrasound, if they are > 2.0 cm.
d. Spongiform nodules, defined as an aggregation of multiple micro-cystic components in more than 50% of the nodule volume, may not require FNA regardless of size, although it may be prudent to biopsy spongiform nodules >2.0 cm.
e. In presence of abnormal cervical lymph nodes all nodes should be biopsied.
f. Solid nodules with micro-calcification nodules more than 1 cm should be biopsied.

### In High-risk History all Nodules should be Biopsied

a. History of thyroid cancer in one or more first degree relatives;
b. History of external beam radiation as a child;
c. Exposure to ionizing radiation in childhood or adolescence;
d. Prior hemi-thyroidectomy with discovery of thyroid cancer;
e. 18FDG avidity on PET scanning;
f. MEN2/FMTC-associated RET proto-oncogene mutation;
g. Calcitonin >100 pg/mL

When cytologic results show follicular lesion/atypia or follicular neoplasm, the results are often called indeterminate. The risk of malignancy with these cytologic classifications ranges from 5 to 32% and the majority of these patients undergo thyroid surgery.

However, in most of these patients who undergo surgery, the pathology is found to be benign. There are two approaches to the molecular characterization of FNA aspirates that are commercially available: Identification of particular molecular markers of malignancy, such as BRAF and RAS mutational status, and use of high density genomic data for molecular classification (an FNA-trained mRNA classifier). The mRNA classifier measures the activity level of 167 genes within the nodule (using the FNA aspirate).

### What are the different approaches regarding treatment of goiter?

a. *Observation*: Patients with an asymptomatic non-toxic MNG can be safely observed without specific treatment. Growth preventing intervention is usually unnecessary, as benign nodules usually grow quite slowly.

b. *Iodine supplementation*: Iodine supplementation is usually effective in reducing thyroid size in children and adolescents living in iodine deficient areas.
c. *Thyroxine suppression*: Recent trials have shown a beneficial effect of thyroxine treatment for both diffuse goiters and thyroid nodules. A goiter reduction of 20–40% can be achieved, but results are variable. The suppression of the serum TSH level should be between 0.5 and 0.1 mIU/L without going below this limit. Thyroid nodule reduction has been achieved with TSH being kept in the lower part of the normal range to minimize potential side effect.
d. *Radioactive iodine therapy*: Radioiodine therapy of non-toxic goiters is commonly performed in Europe as it is a reasonable therapeutic option, especially in patients who are older or have a contraindication to surgery. Careful studies have shown a reduction in thyroid volume in nearly all patients after a single dose of therapy. Of patients with non-toxic diffuse goiter treated with radioactive iodine, 90% have an average of 50–60% reduction in goiter volume after 12–18 months, with a reduction in compressive symptoms. The decrease in goiter size has positively correlated with the dose of iodine-131. Reduction in goiter size is greater in younger patients and in individuals who have only a short history of goiter or who have a small goiter. Baseline TSH is not a predictor of response to radioactive iodine. Obstructive symptoms improved in most patients who received radioactive iodine. Adverse effects, including thyroiditis occurred, but no patient reported worsening of compressive symptoms requiring treatment. No long-term follow-up reports on patients treated with radioactive iodine exist. Patients should always be monitored clinically after 131I therapy, for evidence of goiter re-growth.

Transient hyperthyroidism is rare and typically occurs in the first 2 weeks after treatment. Only a small percentage (~20%) of patients with non-toxic goiter develop hypothyroidism after radioactive iodine treatment. Recombinant human TSH (rhTSH) may have a role in radioactive iodine treatment for nontoxic goiter. Pretreatment with rhTSH 24 hours prior to therapy can reduce the amount of radioiodine needed to shrink the goiter (up to a 50% reduction).

## Surgery

### *Indications of Surgery for Nontoxic MNG*

a. Cosmetic reasons
b. Compressive symptoms (tracheal or esophageal)
c. Retro-sternal goiter
d. Suspicious nodules

### *Type of Surgery*

Subtotal thyroidectomy is performed leaving normal amount of thyroid tissue on each side (8 gm). Care is taken to remove all visible nodules. Another option is Hartley Dunhill procedure in which total lobectomy is performed on the side which is mainly involved in the pathology and on less involved side partial lobectomy is done..

After bilateral subtotal thyroidectomy, all patients require thyroid hormone replacement therapy. The full replacement therapy should start immediately after surgery, with TSH levels checked 3–4 weeks postoperatively. Adjust thyroid hormone therapy, such as T4, to maintain a TSH level in the reference range. Some evidence exists that thyroid hormone replacement therapy prevents recurrence of non-toxic goiter after surgical removal.

## What is toxic nodular goiter?

A toxic nodular goiter (TNG) contains autonomously functioning thyroid nodules, with resulting hyper-thyroidism. TNG, also known as Plummer's disease, was first described by Henry Plummer in 1913. It is the second most common cause of hyperthyroidism after Graves' disease. In areas of endemic iodine deficiency, it is the most common cause of hyperthyroidism especially in elderly persons.

## What is the pathophysiology of TNG?

- There are single or multiple nodules in MNG which are autonomous and hyper-functioning.
- The single hyper-functioning nodule is known as toxic adenoma.
- The nodules become autonomous due to somatic mutation in the thyrotropin or TSH receptor.
- Autonomous nodules become toxic in 10% of patients particularly if the nodule is more than 2.5 cm in diameter.

## Discuss treatment of toxic nodular goiter.

As TNG is not an autoimmune disease so it rarely remits. All patients who have autonomously

functioning nodules should be treated definitely with radioactive iodine or surgery.

Radioactive 131I treatment (RAI): In the Western countries radioactive iodine is considered the treatment of choice for TNG. Except for pregnancy, there are no absolute contraindications to radioiodine therapy.

A fixed dose of using 370 megabecquerels is used. A single dose of radioiodine therapy has a success rate of 85–100% in patients. Radioiodine therapy may reduce the size of the goiter by up to 40%.

- Failure of initial treatment with radioactive iodine has been associated with increased goiter size and higher T3 and free T4 levels and suggests a need for higher doses of radioactive$^{131}$.
- A positive correlation exists between radiation dose uptake by the thyroid and decrease in thyroid volume. In patients with uptake of less than 20%, pretreatment with lithium, PTU, or recombinant TSH can increase the effectiveness of iodine uptake and treatment. This treatment may be valuable in elderly patients in whom surgery is considered high risk.

### Complications RAI

- Hypothyroidism occurs in 10–20% of patients.
- Tracheal compression due to thyroid swelling after radiation therapy is no longer considered to be a risk.
- In about 4% of patients clinically significant radiation-induced thyroiditis develop with features of mild hyperthyroidism. These patients should be treated symptomatically with beta-blockers.
- Elderly patients may have exacerbation of congestive heart failure.
- Thyroid storm is a rare complication which can develop in patients with rapidly enlarging goiters or high total T3 levels. Patients with these conditions should receive pretreatment with anti-thyroid drugs.

### Pharmacotherapy

Anti-thyroid drugs and beta blockers are used for short courses in the treatment of TNG; to make patients euthyroid in preparation surgery and in treating hyperthyroidism while awaiting full clinical response to radioiodine. Patients with subclinical disease at high risk of complications (e.g. atrial fibrillation, osteopenia) may be given a trial of low dose methimazole (5–15 mg/d) or beta-blockers and should be monitored for a change in symptoms or for disease progression that requires definitive treatment.

### *Surgical Therapy*

Surgical therapy is usually reserved for

- Young individuals
- Patients with 1 or more large nodules
- Patients with obstructive symptoms,
- In patients with dominant nonfunctioning or suspicious nodules,
- In patients who are pregnant,
- In patients in whom radioiodine therapy has failed.
- In patients who require a rapid resolution of the thyrotoxic state.
  - Subtotal thyroidectomy results in cure of hyperthyroidism in 90% of patients and allows for rapid relief of compressive symptoms.
  - Restoring euthyroidism prior to surgery is mandatory
  - Complications of surgery include the following:
    - In patients who are treated surgically, the frequency of hypothyroidism is similar to that found in patients treated with radioiodine (15–25%).
    - Complications include permanent vocal cord paralysis (2.3%), permanent hypoparathyroidism (0.5%), temporary hypoparathyroidism (2.5%), and significant postoperative bleeding (1.4%).
    - Other postoperative complications include tracheostomy, wound infection, wound hematoma, myocardial infarction, atrial fibrillation, and stroke.
    - The mortality rate is almost zero.

### How are tumours of the thyroid classified?

As per WHO 2010 the thyroid tumours can be classified as (Fig. 4.3):

- Primary
  - Epithelial
    - Follicular origin
      - Benign

- Follicular adenoma (conventional type)
- Follicular adenoma (oncocytic type)

- Uncertain malignant potential
  - Hyalinizing trabecular tumour
- Malignant
  - Papillary carcinoma
  - Follicular carcinoma
    - Conventional type
    - Oncocytic type
  - Poorly differentiated carcinoma
  - Anaplastic (undifferentiated) carcinoma
- C-cell origin
  - Medullary carcinoma
- Mixed follicular and C-cell origin
  - Mixed medullary and follicular carcinoma
  - Mixed medullary and papillary carcinoma
- Epithelial tumours of different or uncertain cell origin
  - Mucoepidermoid carcinoma
  - Sclerosing mucoepidermoid carcinoma with eosinophilia
  - Squamous cell carcinoma
  - Mucinous carcinoma
  - Spindle cell tumour with thymus-like differentiation (SETTLE)
  - Carcinoma showing thymus-like differentiation (CASTLE)
  - Ectopic thymoma

– Nonepithelial

- Primary lymphoma and plasmacytoma
  - Angiosarcoma
  - Teratoma
  - Smooth muscle tumours
  - Peripheral nerve sheath tumours
  - Paraganglioma
  - Solitary fibrous tumour
  - Follicular dendritic cell tumour
  - Langerhans cell histiocytosis
  - Rosai-Dorfman disease
  - Granular cell tumour
- Secondary (metastatic).

### What are the characteristics of thyroid tumours?

Thyroid tumours are differentiated from benign lesions by the following features:

1. The new nodule in tumours is hard
2. Thyroid tumours are associated with nodes in the neck
3. They grow rapidly
4. They are associated with secondary changes like hoarseness of voice
5. They have restricted mobility
6. They may involve the surrounding structures like the carotid artery.

### What is the etiology behind development of thyroid tumours?

The risk factors for development of thyroid carcinoma include:

- *Ionizing radiation*: Thyroid gland is sensitive to medical or accidental exposure to ionizing radiation. Latency period after medical radiation exposure for treatment of various conditions is about 30 years or more. Papillary carcinoma is common in such situations.
- Genetic syndromes like Gardner's syndrome, familial adenomatous polyposis and Cowden's disease may be associated with papillary carcinoma. MEN syndrome is associated with medullary carcinoma where the tumour is bilateral and multicentric.
- In patients of long standing goiter follicular carcinoma may develop due to overstimulation by TSH or prolonged stimulation.
- Thyroid may be involved in lymphomas or lymphoma may arise *de novo* in cases of Hashimoto's or autoimmune thyroiditis.

### What is the common differential of thyroid tumours?

The common differential diagnosis includes:

1. Calcified nodular goiter
2. Thyroid carcinoma
3. Thyroiditis
4. Neurofibroma
5. Malignant involvement of lymph nodes

### What is the classification of thyroid malignancy?

Thyroid malignancy may be divided into the following types:

- Papillary carcinoma of thyroid
- Medullary carcinoma of thyroid
- Follicular carcinoma of thyroid
- Lymphoma
- Secondary metastases to thyroid
- Anaplastic carcinoma
- Hurthle cell variant

Carcinoma of the thyroid is the most common endocrine malignancy. Most of these tumours are well differentiated. The most common thyroid malignancy is papillary carcinoma thyroid. It accounts for more than 50% of all thyroid cancers. Follicular carcinoma is the next most common malignancy.

Hurthle cell variant is a form of follicular thyroid cancer that arises from the oxyphyllic cells of the thyroid which secrete thyroglobulin. Compared to the follicular carcinoma only a small percentage of these tumours (15–20%) are malignant but they have a propensity to be multifocal, bilateral and associated with positive lymph nodes. This tumour does not take up radioiodine but is detected using sestamibi scan.

Papillary, follicular and Hurthle cell variant are classified together as differentiated thyroid cancers.

### Describe the TNM staging of thyroid tumours.

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour is found
T1 Tumour size ≤2 cm in greatest dimension and is limited to the thyroid
T1a Tumour ≤1 cm, limited to the thyroid
T1b Tumour >1 cm but ≤2 cm in greatest dimension, limited to the thyroid
T2 Tumour size >2 cm but ≤4 cm, limited to the thyroid
T3 Tumour size >4 cm, limited to the thyroid or any tumour with minimal extrathyroidal extension (e.g. extension to sternothyroid muscle or perithyroid soft tissues)
T4a Moderately advanced disease; tumour of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve
T4b Very advanced disease; tumour invades prevertebral fascia or encases carotid artery or mediastinal vessel

*All anaplastic carcinomas are considered as stage IV:*

T4a Intrathyroidal anaplastic carcinoma
T4b Anaplastic carcinoma with gross extrathyroid extension

*Regional Lymph Nodes (N)*

Regional lymph nodes are the central compartment, lateral cervical, and upper mediastinal lymph nodes:

NX Regional nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis
N1a Metastases to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)
N1b Metastases 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 is found
M1 Distant metastasis is present

### What is the difference between follicular and papillary thyroid carcinoma?

- Papillary carcinoma is the most common thyroid malignancy accounting for 60% of the cases of thyroid carcinoma that spreads mainly by lymphatics. Follicular carcinoma spreads by blood-borne route, therefore, involvement of lymph nodes is a rare.
- Papillary carcinoma does not invade the capsule or vessels, whereas follicular carcinoma commonly involves both.
- Papillary carcinoma has a good prognosis compared to follicular carcinoma of the thyroid.
- Histopathological examination reveals presence of orphan Annie eyed nuclei and papillary distribution of cells along with psammoma body in more than half of the cases.

### How is a case of suspected thyroid carcinoma worked up?

Fine needle aspiration cytology can be used to confirm the diagnosis of thyroid carcinoma. However, this test cannot differentiate between follicular carcinoma and follicular adenoma. The only reliable way of differentiating these two lesions is by demonstration of capsular invasion or vascular invasion.

In papillary carcinoma of thyroid orphan Annie eyed nuclei will be seen. The nuclear membrane is irregular and there is grooving around the cells. There may be inclusions within the nucleus or cytoplasm.

An ultrasound scan is also needed as that can tell about the number of foci, status of surrounding structures and assessment of lymph nodes. In all cases, a thyroid profile must also be done which includes T3, T4 and TSH.

On the radioiodine scanning these lesions appear cold as there is no update due to loss of function in most cases. Technetium-99m sestamibi scan may be helpful in cases of suspected Hurthle cell cancer. These investigations are not routinely required.

An indirect laryngoscopy should also be done to assess the vocal cords prior to surgery. In a number of cases the vocal cord may be affected without change in the voice. Also in about 1% of patients there may be congenital paresis of the vocal cord.

### What is lateral aberrant thyroid?

In a papillary carcinoma of the thyroid the primary tumour may not be palpable, instead of lymph node may be palpable. This represents metastasis from the occult primate tumours and is often wrongly called lateral aberrant thyroid.

Papillary microcarcinoma was initially regarded as an occult thyroid carcinoma presenting as lateral aberrant thyroid. It is now classified separately as any papillary tumour ≤1 cm in size.

### What are the prognostic markers for thyroid carcinoma?

As per AGES criteria the favorable prognostic factors are:

- *A*: Age <40 years in female and <50 in males
- *Grade of tumour*: Well-differentiated tumour
- *Extent*: Intrathyroidal
- *Size*: <1 cm for papillary and <4 cm for follicular

*Other prognostic systems that have been used include*:

- *AMES system*: Includes age, metastases, extent of spread and size of tumour.
- *MACIS system*: Includes metastases, age, completeness of resection, invasion of surrounding structures and size of tumour.
- *Sloan Kettering system*:
  - *High risk*: Age >45 years, size >4 cm, presence of unfavorable factors.
  - *Intermediate risk*: High risk patients with low risk tumours or vice versa.
  - *Low risk*: Age <45 years, size <4 cm, presence of favorable factors.

### What are the indications of performing Tru-cut biopsy of the thyroid?

Tru-cut biopsy is a method to obtain tissue for histopathology and can more precisely define the type of tumour. It is indicated when one is suspecting lymphoma (in presence of organomegaly or multiple lymph nodes), anaplastic tumour (history of rapid growth) or other lesions like tuberculosis. It is not preferred over FNAC because it is associated with complications like pain, hematoma formation and injury to surrounding structures like trachea, or the nerves.

### What is the management of papillary and follicular carcinoma of the thyroid?

Differentiated thyroid cancers which include papillary and follicular carcinoma of the thyroid are best managed by total or near total thyroidectomy. Total thyroidectomy includes removal of all of the thyroid tissue eliminating any chance of residual thyroid cancer in any of the lobes. In near total thyroidectomy, a small amount of thyroid tissue (≈1–2 grams on either side) that lies within the trachea-esophageal groove is removed. This preserves the parathyroids and their vascular supply and lessens chances of damage to the recurrent laryngeal nerve. In the event that vascular supply (superior and inferior parathyroid artery) to parathyroid glands are accidentally damaged, parathyroid glands can be divided into small fragments and implanted over the sternocleidomastoid muscle or the forearm muscles.

### What is the difference in management of Hurthle cell tumour and differentiated thyroid cancers?

Hurthle cell tumours have fewer propensities to be malignant. If they are limited to one lobe only, hemithyroidectomy can be performed and subjected to frozen section analysis. Only if carcinoma is present that a completion thyroidectomy with removal of lymph nodes (central neck dissection) is indicated. If a pre-operative diagnosis of Hurthle cell carcinoma has been made already by core biopsy, then one may proceed straightaway to surgery. If lymph nodes are palpable, modified radical neck dissection is also needed.

### How are lymph nodes managed in patients with differentiated thyroid cancers?

Modified radical neck dissection is performed when lymph nodes are involved. Alternatively, functional neck dissection can also be performed. In this procedure structures like the internal jugular vein, spinal accessory nerve and sternocleidomastoid are preserved.

When lymph nodes are not involved but tumour is T3 or T4 central compartment, dissection can be done which involves removal of thymus, paratracheal, pretracheal and prelaryngeal nodes along with trachea-esophageal nodes and thyroid gland. The boundaries of dissection include hyoid bone superiorly, innominate artery inferiorly and carotid arteries laterally on each side. However, majority of surgeons do not remove thymus gland.

Up to 50% of the patients with thyroid cancers may have positive nodes in the central compartment which may be difficult to manage later on and lead to recurrence and difficulties in follow-up.

### What is radio remnant ablation and when is it indicated?

Radio remnant ablation is administered when any remnant tumour is detected on radioiodine scan. In this Iodine 131 is administered which is taken up by the remnant tissue and destroys it. Usual dose is 30 mCi. RRA is indicated in tumours >4 cm, gross extension of tumour beyond thyroid capsule, involvement of lymph nodes and distant metastasis. If there is evidence of distant metastasis, a higher dose of 100–200 mCi radioiodine can be given. For ablation of skeletal metastasis an even higher dosage of 300 mCi is administered.

### How are patients followed up after thyroidectomy?

Patients are followed up after thyroidectomy by radionuclide whole body scan ($I^{131}$ in a dose of 3 mCi) to look for any evidence of residual disease usually one week after surgery. The patient is given suppressive doses of L-thyroxine. Alongside, serum thyroglobulin is also used as a marker for metastatic, residual or recurrent disease. Its levels should ideally be undetectable after total thyroidectomy and suppressive therapy but level <2 ng/mL is considered normal.

Whole body radioiodine scanning can be repeated after 6 months to one year along with yearly thyroglobulin for follow-up.

### What are the clinical features of anaplastic carcinoma of the thyroid?

Anaplastic carcinoma thyroid is an aggressive form of thyroid cancer with a dismal outcome. It can be clinically differentiated from other thyroid tumours by presence of:

- Rapidly growing swelling in the neck
- Hard and irregular swelling that appears to be fixed to underlying structures and often engulfs surrounding structures
- Associated with compressive symptoms arising from involvement of the nearby structures like difficulty in breathing, stridor and hoarseness of voice and difficulty in swallowing.
- Usually involves the elderly patients. F>M

### How is anaplastic thyroid cancer managed?

When detected at an early stage by FNAC, anaplastic thyroid cancer can be managed by total thyroidectomy along with radical lymph node dissection. Adjuvant chemotherapy can be given after surgery. However, most patients present in the advanced stage and management is essentially palliative. Radiotherapy and chemotherapy may be given and to relieve pressure on the trachea an isthumusectomy can be performed.

### What are the systemic agents used in management of anaplastic carcinoma of thyroid?

The various systemic chemotherapy agents used are:

- Paclitaxel or carboplatin
- Cisplatin
- Doxorubicin

### What are the common syndromes associated with thyroid carcinoma?

Although a number of syndromes are associated with thyroid carcinoma, Cowden syndrome and multiple endocrine neoplasia (MEN) syndrome are frequently associated with thyroid cancer.

**Cowden syndrome:** Cowden syndrome or disease is an autosomal dominant condition caused by mutation in the PTEN gene. This gene is located on the long arm of chromosome 10. This syndrome is also well known by the name of multiple hamartoma syndrome as it is associated with hamartomatous lesions on the mucosa, bones, eyes, gastrointestinal and genitourinary tract. This syndrome involves the thyroid in 60–70% of the cases. There is increased incidence of differentiated thyroid cancers in this syndrome along with breast cancer. Colon cancer and renal cancer may also be associated.

**MEN syndrome:** MEN syndrome has been summarized in the table given as follows:

| | *Men 1* | *Men 2A* | *Men 2B* |
|---|---|---|---|
| Name | Werner syndrome | Sipple syndrome | Mucosal neuronal syndrome |
| Associated tumours | Pituitary adenoma, pancreatic tumours (M/C gastrinoma, followed by insulinoma, VIPoma, glucagonoma) and parathyroid hyperplasia | Parathyroid hyperplasia, pheochromocytoma and medullary thyroid carcinoma (occurs in up to 100% patients) | Medullary carcinoma of thyroid, pheochromocytomas, multiple mucosal neuromas in a patient with marfanoid habitus |

Familial medullary thyroid cancer is another type of MEN2 syndrome where medullary thyroid cancer may present in isolation.

### What are the different forms of medullary thyroid carcinoma?

Medullary carcinoma of the thyroid can occur as a sporadic tumour which usually represents as a solitary nodule in the elderly patient. Most cases of MTC are sporadic (up to 75%).

Up to 20% of the tumours are familial and such tumours are bilateral, multifocal and aggressive in nature. There tumours are poorly responsive to radiotherapy and associated with higher rate of recurrence and mortality. They occur at a younger age usually in the 2nd or 3rd decade. History of other family members having such tumours, presence of diarrhea, abdominal pain and hypertension should be taken in suspected cases.

### What is the role of genetic screening and screening of family members?

When a diagnosis of medullary thyroid cancer is made, genetic screening is advocated for the RET proto-oncogene. All family members must be screened if the patient is positive for RET. Screening tests should include ultrasound of the neck, serum calcitonin, calcium and parathormone assay. Stimulated calcitonin test may uncover the defect when basal calcitonin levels are normal. For this test pentagastrin injection is given subcutaneously in a dose of 5 μg/kg and a rise in serum calcitonin is noted.

Prophylactic thyroidectomy should be considered in family members as early as 1 year of age.

### What are the additional tests required when medullary thyroid cancer is suspected?

Medullary thyroid cancer is associated with many other clinical disorders. Screening should be done additionally for:

- Ultrasound abdomen is required to screen for pheochromocytoma
- CEA may be raised up to 50% of the cases
- 24 hours urinary metanephrines
- Calcitonin levels unstimulated and stimulated.

### What are the special precautions and prognostic factors in medullary carcinoma of the thyroid?

Medullary thyroid cancers are managed with total thyroidectomy and central node dissection even in the absence of palpable nodes. If nodes are present modified radical neck dissection along with central neck dissection should be performed.

*Prognostic factors that must be looked to include*:

- Calcitonin level
- CEA level
- DNA ploidy
- Stage
- Type of MEN associated (MEN 2A is most favorable).

## THYROIDECTOMY

*Robert Udelsman, Sudhir Kumar Jain*

### DEFINITION

The term 'thyroidectomy' means a range of surgical operations on the thyroid, the precise intervention being tailored according to the existing pathology.

### HISTORY

The earliest account of thyroidectomy was probably given by Roger Frugardi of Salerno in 1170. Thyroid surgery remained a relatively rarely performed procedure till 1850 and William Halsted could find only 77 cases of thyroid surgery between 1596 and 1850. Even in the 19th century, thyroid surgery was considered barbaric, Samuel Gross described it as "horrid butchery". Thyroid surgery was condemned for years and French Academy of Medicine in 1850 proscribed any thyroid surgery. Jules Boeckel of Strasbourg introduced the collar

incision to thyroid surgery in 1880. In between 1870–1880 Theodor Billroth of Vienna began to improve the technique of thyroidectomy with reduced mortality and demonstrated importance of preserving recurrent laryngeal nerve. Von Eiselberg realized the importance of preserving parathyroid gland. Theodor Kocher from Berne emerged as leader in thyroid surgery. He performed 5000 cases by 1917 and was awarded Noble Prize in Medicine for his contributions to thyroid physiology, pathology and surgery 1909. He brought down mortality of thyroidectomy to less than 1 percent. William Halsted of Baltimore, Charles Mayo of Rochester, and George Crile of Cleveland refined the operative techniques of thyroid surgery. Prioleau wrote in 1933, "a nerve if seen is more likely to get injured."This philosophy of intentionally not seeing the recurrent layryngeal nerves, influenced an entire generation of surgeons and still practiced today by some of inexperienced surgeons. Lahey in 1938 results of more than 3000 thyroidectomy performed by his fellows and staff during a 3-year period. The recurrent laryngeal nerve was dissected in every case. He wrote that careful dissection would "not increase but definitely decrease the number of injuries to the recurrent laryngeal nerves," Lahey's emphasis on anatomy set the course and direction for modern thyroid surgery. Riddell in 1970 emphasized that when the nerve is identified and carefully followed throughout its course, a nerve injury may occur, but the paralysis is nearly always *transient*. When the nerve is not identified, permanent *injury to RLN leading to* paralysis of the vocal cord which can occur in one-third of cases leading to hoarseness of voice.

## Classification of Various Types of Thyroidectomy

Kebebew and Clark formulated classification of various types of thyroidectomy

a. *Hemithyroidectomy*: Hemithyroidectomy means that a lobe has been completely removed, along with the isthmus and any associated pyramidal lobe if present.

   It is performed for follicular adenoma, low risk papillary carcinoma, multinodular goiter confined to one lobe and toxic solitary nodular goiter which is autonomous.

b. *Total thyroidectomy*: It is complete removal of both lobes, isthmus and pyramidal lobe if present. It is procedure of choice for thyroid malignancy except low risk papillary carcinoma where many surgeons advocate hemithyroidectomy. In this procedure on the parathyroid gland is isolated and auto-transplanted.

c. It is similar to total thyroidectomy except one of the parathyroids is preserved and left *in situ*. In order to preserve one parathyroid gland part of posterior capsule of thyroid along with some tissue is left (around 1 gm). Such a remnant must be free from nodular and away from the cancer focus.

d. *Excision of isthmus*: This carried out in anaplastic carcinoma lymphoma or in Ridel's thyroiditis to have tissue diagnosis and to relieve tracheal obstruction. The isthmectomy may be performed for benign disease that is confined to the isthmus, such as the isthmus toxic nodule or follicular or Hurthle neoplasia.

e. *Subtotal thyroidectomy*: Subtotal thyroidectomy implies that a lobe and the isthmus have been completely removed and that the contralateral lobe has been partially removed, usually in its medial and ventral portion typically leaving a posterior element. Bilateral subtotal implies significant portion of both lobes is removed. It comprises subtotal removal of both lobes of thyroid and isthmus. Around 4 gm of thyroid tissue (thyroid remnant in tracheoesophageal groove) on each side is left. It is indicated for multinodular goiter (both toxic and non-toxic) and in Graves' disease. In toxic goiter experienced thyroid surgeon in high volume centre are carrying out total thyroidectomy but for an average general surgeon is advisable.

f. Partial lobectomy, performed in rare cases, implies that a portion of the lobe has been removed. Obectomy implies that an entire lobe has been completely removed with its capsule intact without isthmus resection.

## Indications

Thyroidectomy is commonly performed for the following conditions:

1. *Proven or potential malignancy*: All cases of papillary, follicular, and medullary carcinoma are treated by surgery.
2. *Hyperthyroidism*: Indications of doing thyroid surgery in hyperthyroidism are following:
   A. All patients with multinodular goiter with hyperthyroidism

B. Young patients with toxic solitary nodules.
C. Patients with Graves disease having one or more of the following factors:
   a. Desire for early pregnancy because if antithyroid drugs are started conception has to be delayed for at least 2 to 3 years from start of antithyroid drugs to prevent recurrence.
   b. Very young children below 15 years.
   c. Socioeconomic reasons when patients cannot afford long-term drug therapy.
   d. Severe ophthalmopathy as eye signs can deteriorate after starting antithyroid drugs.
   e. Large goiter as thyrotoxicosis is more likely to recur after antithyroid drug therapy.
   f. First trimester of pregnancy.
   g. Poor drug compliance
   h. Cold nodule in Graves' disease as chances of malignancy is very high in these patients.
   i. Patients of Graves disease who relapse on or after antithyroid drug therapy.
   j. Patients who exhibit drug allergy or resistance.
D. Patients with significant tracheal compression.
E. Patients presenting with thyroid storm require semi-surgery emergency.
F. Thyrotoxic patients with retrosternal extension associated with obstructive symptoms should be treated by surgery primarily because antithyroid drugs or radioactive iodine treatment may enlarge the goiter.
G. Amidarone-induced thyrotoxicosis.
H. The toxic nodule retaining activity 6 months after $^{131}$I therapy. Toxic solitary nodule treated by $^{131}$I should become nonfunctional on isotope scan by about 6 months.

3. Patients of mutinodular goiter (MNG)
   Indications of thyroidectomy in MNG are:
   a. On cosmetic grounds
   b. For pressure symptoms or discomforts
   c. Patients anxiety to get the swelling removed
   d. Retrosternal extension with actual or incipient tracheal compression assessed by CT scanning of thoracic inlet and functional obstruction assessed by volume air loop studies and peak flow measurements.
   e. Presence of dominant area of enlargement which may be neoplastic.
   f. Recurrent bleeds into degenerative areas.

### Various Types of Thyroid Procedures Are

1. **Hemithyroidectomy:** This involves removal of whole of involved lobe plus isthmus of thyroid. Hemithyroidectomy is indicated in the following conditions:
   - Solitary nodule with follicular cytology.
   - Dominant nodule in a multinodular goiter with follicular cytology
   - If multinodular changes are confined to one lobe.
   - Hyperthyroidism caused by hyperfunctioning nodule in a unilateral goiter.
     - Locoregional symptoms caused by unilateral goiter or a single large nodule.
     - Patients of papillary thyroid cancer (PTC) localized to one lobe and less than 1.0 cm in diameter without metastatic involvement of ipsilateral lymph nodes or distant metastasis without any history of head and neck irradiation or family history of PTC.
     - Follicular thyroid carcinoma which are minimally invasive with only capsular invasion, well encapsulated and unifocal. These subgroups of patients have a little risk of subsequent recurrence.
2. **Total thyroidectomy:** This involves en bloc removal of both lobes of thyroid gland along with isthmus. Alternatively, near total thyroidectomy is performed in which less than 1gm of thyroid tissue (about 1 cm) is left on one side to preserve at least one parathyroid gland. Total thyroidectomy is being performed increasingly for majority of papillary and follicular malignancy. Rationale for total thyroidectomy in papillary malignancy is presence of multifocal disease in many cases until they fall in subgroup described in section of hemithyroidectomy. In follicular cancer rationale for total thyroidectomy is complete eradication of thyroid tissue so that any metastasis can be identified and treated by uptake of radioactive iodine. It is also performed prophylactically in patients who are genetically at high-risk of familial medullary thyroid cancer. Other indications of total thyroidectomy are some cases of extensive multinodular goiter or severe thyrotoxicosis associated with small goiter.
3. **Subtotal thyroidectomy:** Classically it involves leaving 2 gm of thyroid tissue on both sides if

performed for thyrotoxicosis or up to 4 gm of thyroid tissue on each side if performed for non-toxic multinodular goiter. This procedure is being performed less commonly these days as majority of patients with hyperthyroidism are treated by near total thyroidectomy. In multinodular goiter alternatively Hartley-Dunhill procedure can be performed which involves total lobectomy and isthmectomy on most diseased side and subtotal resection on leaving 4 gm of tissue on the contra-lateral side.

4. **Excision of isthmus:** Excision of isthmus is indicated in anaplastic carcinoma or lymphoma of thyroid gland to free the airway. In cases of suspected Riedel's thyroiditis, isthmus is removed to differentiate it from anaplastic carcinoma and to free the trachea.

## Minimally Invasive Thyroidectomy (MIT)

The goals of MIT are:

a. To treat the disease effectively
b. To minimize long-term side effects of surgery and to reduce complications
c. To minimize postoperative discomfort and pain.

MIT can be defined procedures through a short (less than 3 cm) and discrete incision that allow direct access to the thyroid resulting in a focused dissection.

MIT may be broadly classified in two groups:

a. The open approach (mini incision) performed under direct vision via a small cervical incision. The 3 cm incision with no flap creation and minimal dissection to deliver the thyroid into wound and in the end perform pretracheal and paratracheal dissection. The short incision open techniques can be carried out as day-case surgery under local or cervical block anesthesia.
b. The various endoscopic approaches
    1. The endoscopic midline approach employs constant gas insufflations and four trocars.
    2. The gasless video-assisted technique is carried out through a 15 mm midline incision with small conventional retractors to maintain the operative space; an additional assistant is needed.
    3. Endoscopic lateral approach technique which includes developing the plane between the carotid sheath laterally and the strap muscles medially although this 'rear gate route provides excellent exposure for identification of the recurrent laryngeal nerve and parathyroid glands, it does not permit a bilateral exploration.
    4. Non-cervical incision approaches like trans axillary, incision in anterior chest wall, breast approach and supraclavicular approach.
    5. Robotic assisted thyroidectomy.

Indications for MIT are

a. Solitary nodules smaller than or equal to 3 cm,
b. The thyroid volume less than 25 ml,
c. Absence of thyroiditis,
d. Absence of previous neck irradiation,
e. Absence of previous neck surgery
f. Benign disease, low risk papillary carcinoma or Graves' if thyroid volume is less than 25 ml or nodule less than 3 ml.

Contraindications for MIT are:

a. Recurrent disease
b. Locally advanced or metastatic disease
c. Short neck in obese patients

## Axillary Approach

1. 3 cm skin incision in the axilla.
2. 12 mm and 5 mm trocar inserted through incision.
3. An additional 5 mm trocar inserted by the size of skin incision.
4. Carbon dioxide is insufflated up to pressure of 4 mm of Hg to create a working space.
5. The anterior border of sternocleidomastoid muscle is identified and separated from sternohyoid muscle to expose the sternothyroid muscle.
6. The sternothyroid muscle is split to expose thyroid gland.
7. The lower pole of thyroid gland is identified and mobilized to expose recurrent laryngeal nerves.
8. Berry's ligament is dissected and divided by harmonic shear
9. The upper pole of thyroid is separated from cricothyroid muscle and external branch of superior laryngeal nerve is safeguarded.
10. The upper pole of thyroid is dissected free.

### Anterior Chest Approach

a. 12 mm skin incision is given 3–5 cm below the lower border of ipsilateral clavicle.
b. Two extra 5 mm ports are inserted under endoscopic guidance.
c. Rest of the procedure is same as described in axillary approach.

### Preoperative Preparation

Preoperatively thyroid function should be brought to normal by administration of antithyroid drugs to reduce the risk of thyroid storm postoperatively in patient with hyperthyroidism. Both Carbimazole or Propylthiouracil can be used for preoperative preparation but propylthiouracil has additional advantage that it reduces the peripheral conversion of T4 to T3. Carbimazole is given in doses of 30–40 mg daily divided equally in 6–8 hourly interval. When patient becomes euthyroid dose is reduced to maintenance level and drug is continued till the evening before surgery.

If there is less time to prepare the patient can be made clinically euthyroid by giving nonselective beta blockers, e.g Propranolol 40–60 mg every 8 hourly or long acting Nadolol 320 mg once a day. Beta blockers rapidly control hypersympathomimetic manifestations, reduces elevated oxygen consumption by 50 percent and inhibit peripheral conversion of T4 to T3. As beta blockers do not inhibit synthesis of thyroid hormones and serum hormones remain high during treatment and during some days after surgery, beta blockers should be continued for 7 days after surgery.

Lugol's iodine is started 7 days before surgery which decreases thyroid blood flow and friability and hence reduces intraoperative blood loss.

### Preoperative Investigations

1. Thyroid function tests are done in every case
2. Indirect laryngoscopy is done to record that both vocal cords are functional preoperatively. In 3–5 percent of cases there may be asymptomatic paresis of unilateral vocal cord due to previous exanthematous infections.
3. Thyroid antibodies are done in case of thyrotoxicosis. If thyroid antibodies are positive, these patients are more likely to develop hypothyroidism.
4. Baseline serum calcium levels are done
5. Isotope scan is performed in case if surgery is performed for toxic nodules to know which nodule is hyperactive.
6. Ultrasound-guided fine needle aspiration cytology is performed in every case of solitary nodular goiter or dominant nodule.
7. X-ray cervical is done in every case to rule out pathology in cervical spine and to know any tracheal deviation. If there is any pathology in cervical spine, hyperextension of spine should be avoided.

### Anesthesia

The procedure is carried out in general anesthesia with endotracheal tube.

### Operation

***Position of patient***
***Incision***
***Raising of flaps***
***Exposure of thyroid***
***Mobilization of thyroid lobe and ligation of middle thyroid vein***
***Mobilization of superior pole and ligation of superior thyroid vessels***
***Identification of recurrent laryngeal nerve and inferior thyroid artery***
***Identification of parathyroid glands***
***Removal of thyroid lobe***
***Closure***

### Subtotal Thyroidectomy

Subtotal thyroidectomy is performed for multinodular disease or Graves' disease. 4–5 gm of remnant of thyroid tissue is left on each side. Hemostasis is secured by ligation of individual vessels and by suturing the thyroid remnant to tracheal fascia. These days this procedure is performed less commonly because of high incidence of recurrence in thyrotoxicosis.

Drains of both closed and open types have been employed by many surgeons but are not necessary in most patients as a dry operative field is the expectation and not the exception at the end of procedure. However, if a drain is used, it can be placed through a separate stab incision or brought out through the lateral aspect of the wound. Closure of the strap muscles is performed in the midline using a continuous suture of 3/0 polyglactin (Vicarly). It is very important to avoid injury to the anterior jugular veins which are in close proximity.

Patients are routinely extubated in the operating room and transported with their heads elevated at approximately 30° to the recovery room. After approximately 1 hr they are transported to a routine floor where the head of the bed is kept elevated at approximately 30°. They are offered clear liquids the evening of surgery and a regular diet the next morning. Patients are routinely discharged on the first postoperative day.

### Risks to the Patients

The most important complications of thyroidectomy are:

- Recurrent laryngeal nerve injury
- External branch of superior laryngeal nerve injury
- Hypo-parathyroidism
- Laryngeal edema-airway obstruction
- Bleeding hematoma
- Hypothyroidism
- Hyperthyroidism
- Wound infection
- Keloid scar
- Suture granuloma.

Meticulous operative technique is the mainstay for injury prevention.

Complication rates of less than 1% are routinely reported by experienced surgeons.

Neck hematoma and recurrent nerve injury are potential life-threatening problems in the immediate postoperative day.

The serum calcium level is measured in the postoperative period. Asymptomatic hypocalcemia will almost always normalize without calcium supplementation. Symptomatic postoperative hypoparathyroidism requires treatment with calcium and occasionally vitamin D. In emergency situations, calcium can be administered intravenously.

The position of the patient in the operating room is critical in order to gain adequate exposure and to minimize injury to the patient. The operation is performed in the reverse Trendelenburg position with the patient in the supine position and the head extended on the head ring. Table is tilted up to 15 degrees to reduce venous engorgement. Neck is extended by placing a sang bag transversely under the shoulders so that thyroid becomes more prominent and skin, platysma and strap muscles get tense, thus to make dissection easier. Both arms are tucked at the patient's sides after padding, especially of the elbow region to prevent injury to the ulnar nerves. Intravenous access is obtained by a peripheral intravenous line in one or both arms. The neck and chest from the level of the mandible to the nipples are included in the operative field (Figs 15.3A and B).

Skin crease can be identified which is ideally suited for a cosmetic result. If no skin crease is available, a stretched silk suture is pressed against the skin, which results in a symmetrical and gentle curve. The incision extends in between the lateral borders of the two sternocleidomastoid muscles

Skin retractors are pulled superiorly, and subplatysmal flaps are raised, preserving the anterior jugular veins. The plane of dissection is directly superficial to these veins (Figs 15.5A to C).

The counter traction is applied with the left hand on a gauze pad and, using the right thumb, the superior flap is raised utilizing blunt dissection in the subplatysmal plane.

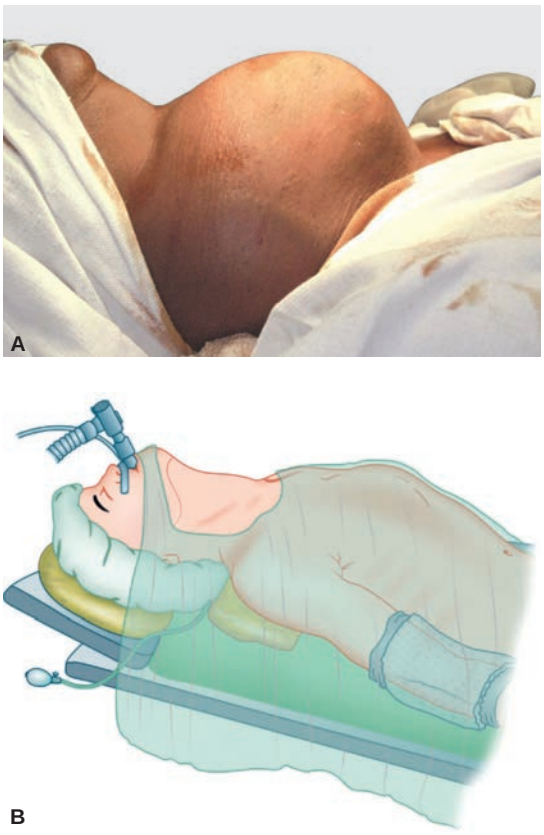



**Fig. 15.3A and B:** Position of patient for thyroid surgery

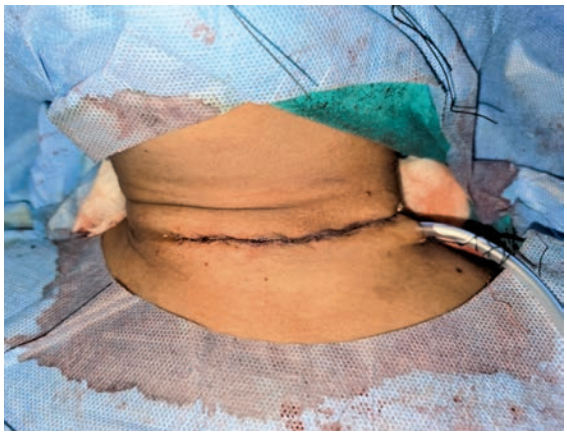


**Fig. 15.4:** Skin crease incision in between the lateral borders of two sternocleidomastoid muscles

The superior extent of the dissection extends up to the notch on the thyroid cartilage.

The inferior dissection is performed in a similar manner up to suprasternal notch. This flap, although short, allows access to the anterior mediastinum.

### Surgical Insight

Deep cervical fascia is identified by anterior jugular veins running on it. Midline raphe is identified between the sternohyoid muscles and this raphe is divided in blood less plane from thyroid cartilage superiorly to sternal notch inferiorly. Sternohyoid muscles which meet in the midline are separated to expose the isthmus of thyroid gland and tracheal rings. Sternothyroid muscles which do not meet in the midline and lie in a deeper and lateral position are separated of the thyroid gland to expose lateral aspect of thyroid gland (Figs 15.4 to 15.8).

Division of the strap muscles is rarely required, but can be performed for an unusually large gland. A self-retaining thyroid retractor is inserted to hold the skin, subcutaneous tissue and platysma muscle. This self-retaining retractor is extremely useful as it allows the assistant to participate actively. Both the sternohyoid and sternothyroid muscles are retracted bilaterally, preserving the anterior jugular veins. The extent of contralateral dissection is dependent upon the operative indication, but in all cases the contralateral thyroid lobe is palpated to rule out nodular disease. In cases of bilateral resection mobilization of the strap muscles is performed bilaterally.

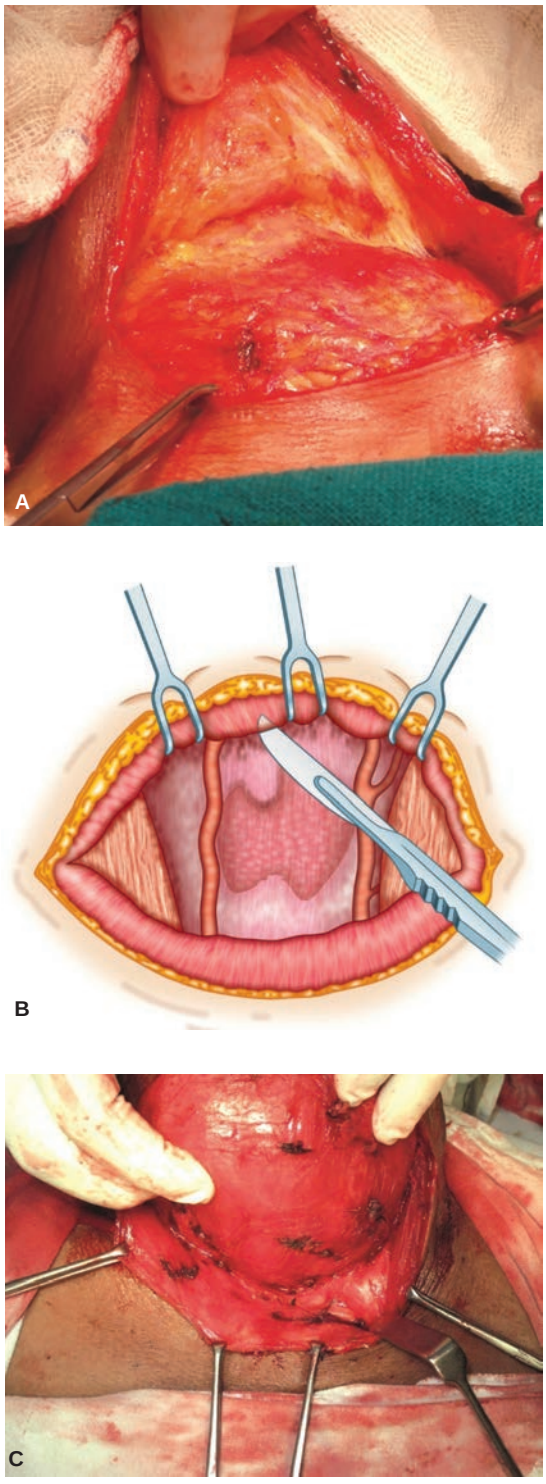



**Fig. 15.5A to C:** (A) Superior flap raised up to thyroid cartilage notch; (B) Plane of dissection is superficial to anterior jugular veins; (C) Lower flap raised up to sternal notch

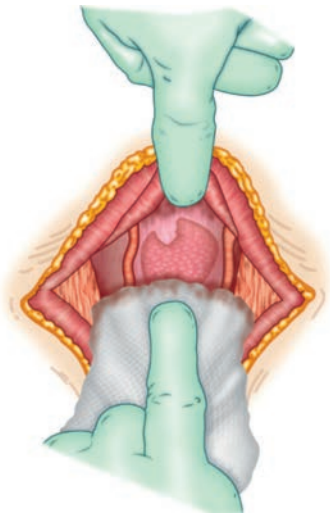


Fig. 15.6: Deep cervical fascia by anterior jugular veins

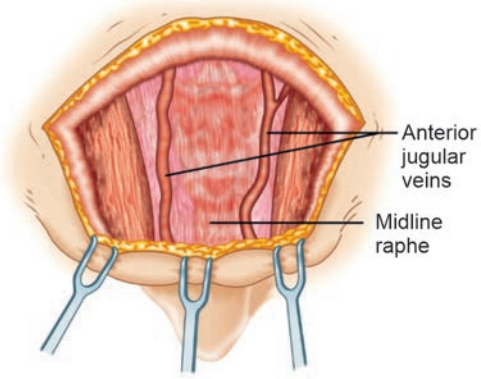



Fig. 15.7: Exposure of deep cervical fascia

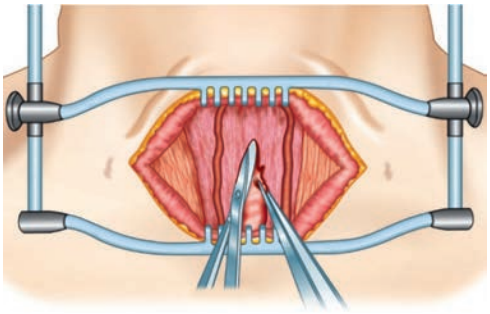


Fig. 15.8: Deep cervical fascia divided in midline raphe

The surgeon utilizes a gauze sponge to retract the thyroid gland medially which brings the middle thyroid vein into view. The thyroid lobe is rotated by applying traction on a gauze pad and pulling

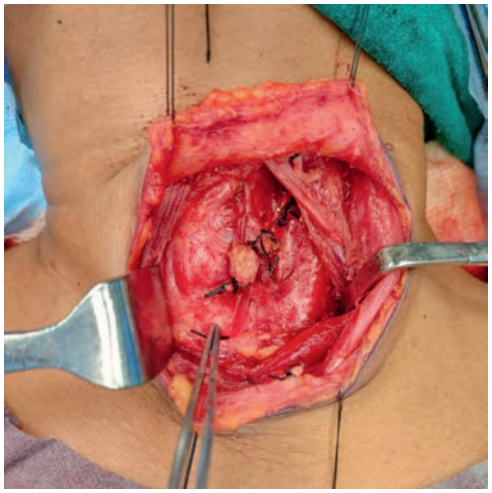


Fig. 15.9: Strap muscles retracted laterally forceps pointing on tracheal ring

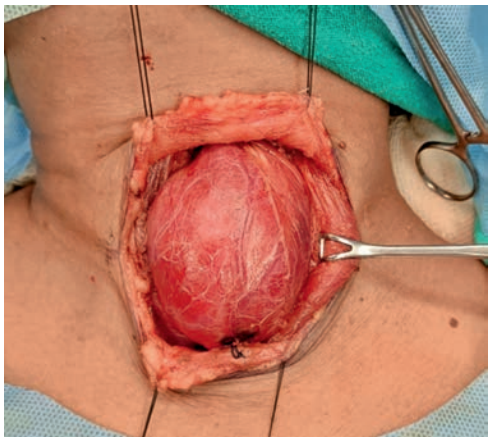
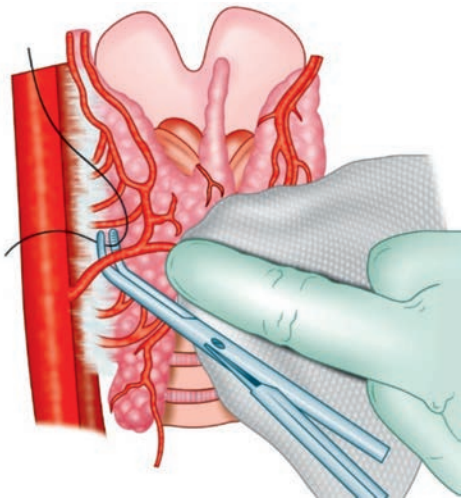


Fig. 15.10: Thyroid exposed

the gland in a medial direction. A fine-tipped right angled clamp is used to pass 3/0 silk ties around the middle thyroid vein.

The plane between the medial aspect of upper pole and the cricothyroid muscle is developed by keeping close to thyroid to avoid injury to the external branch of superior laryngeal nerve. A right angled forceps is then passed under the vascular pedicle to lift the vessels forward. The branches of the superior thyroid artery and vein must be individually tied with absorbable ligatures close to the thyroid gland in order to avoid damage to the external branch of superior laryngeal nerve. In approximately 20% of cases, this nerve may pass between the branches of the vessels and is



A

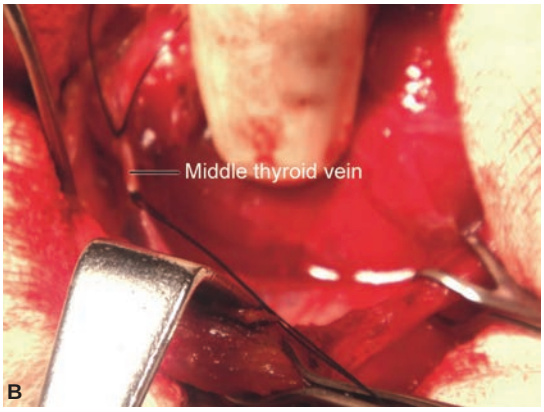



**Fig. 15.11A and B:** (A) Middle thyroid vein isolated and ligated; (B) Middle thyroid vein has been ligated

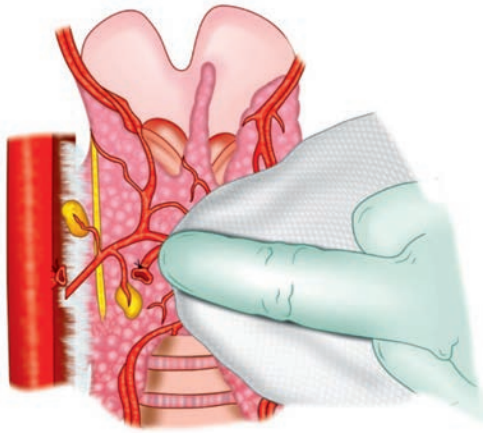
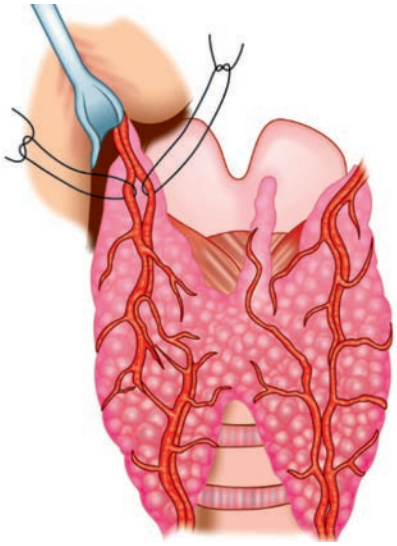


**Fig. 15.12:** Mobilization of superior pole of thyroid



in great danger if mass ligation is carried out. In a further 10% of cases, the nerve runs its distal course through the inferior pharyngeal constrictor muscle, is not visible at surgery and indeed is at no risk of damage. After ligation superior thyroid vessels lobe is rotated medially out of its bed.

After the middle thyroid vein and superior thyroid vessels have been ligated medial rotation of lobe is achieved, thus exposing the inferior thyroid artery which usually runs anterior to the recurrent laryngeal nerve. The parathyroid glands are supplied by end arteries which usually arise from the inferior thyroid artery. Recurrent laryngeal nerve is first sought below the level of inferior thyroid artery during its oblique course forward and upwards to the trachea and esophagus. The nerve may run close to tracheoesophageal groove and can be palpated as

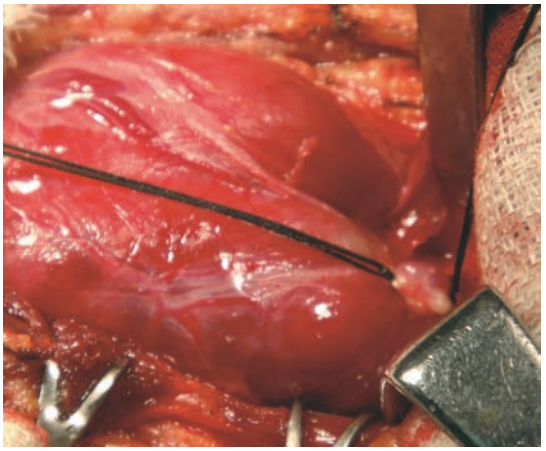
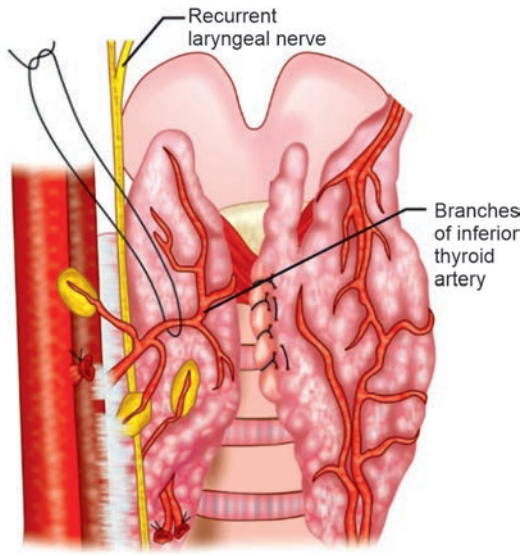


**Fig. 15.13:** Ligation of superior thyroid vessels



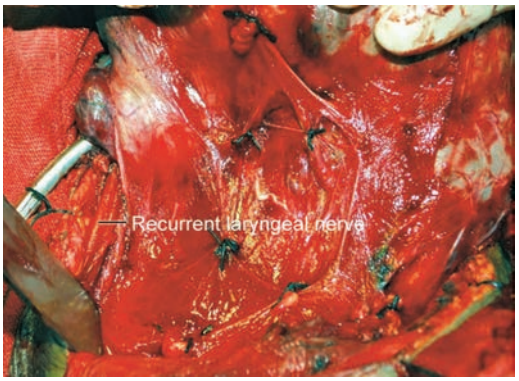




**Fig. 15.14:** Identification of recurrent laryngeal nerve

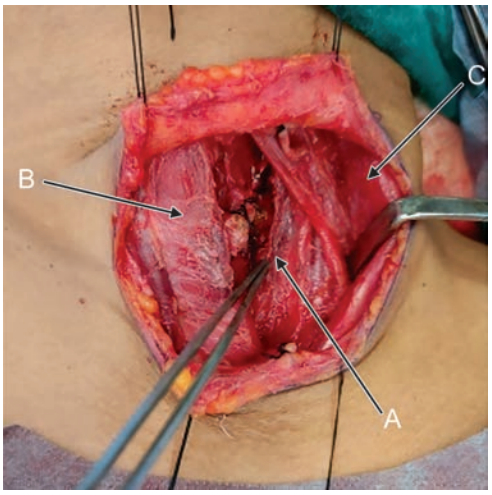



**Fig. 15.15:** Identification of recurrent laryngeal nerve in between branches of inferior thyroid artery

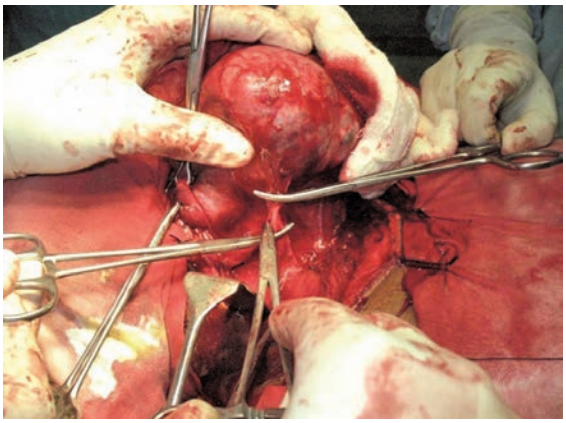


**Fig. 15.16:** Mobilization of thyroid lobe and division of ligament of Berry

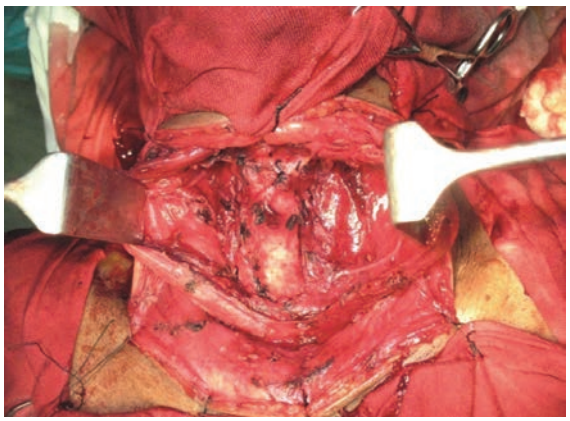


**Fig. 15.17:** Hemostasis secured after lobe removal by over-running sutures

cord-like structure against trachea. The nerve can then be exposed by gentle dissection of the overlying fascial layers with a small artery clip. It is noted that the structure often has a small blood vessel running on its surface. At higher level nerve lie between branches of inferior thyroid artery.

Inferior parathyroid gland is located close to inferior pole of thyroid gland anterior to recurrent laryngeal nerve. The superior gland is usually seen just above the inferior thyroid artery and in more than 90% of cases being within a 1 cm radius of the junction of the inferior thyroid artery and the recurrent laryngeal nerve.

The dissection of the thyroid should continue close to the capsule of the gland with ligation and division of the individual branches of the inferior

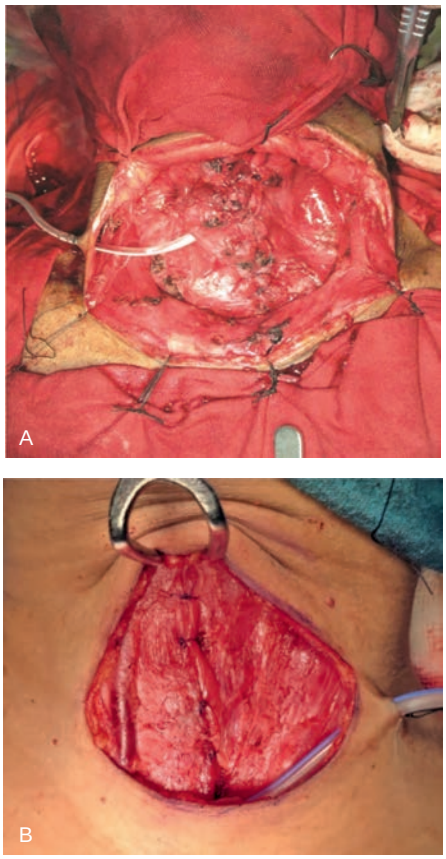



**Fig. 15.18A and B:** (A) Drain is inserted before closure; (B) Closure of strap muscles

thyroid artery, preserving those branches which supply the parathyroid glands.

The main inferior thyroid artery trunk is not ligated. It is possible to tease the parathyroid glands away from the thyroid with their blood supply intact, leaving them free but perfectly viable.

The diathermy usage is kept to a minimum as heat conduction may damage the recurrent laryngeal nerve, the blood supply of the parathyroids or the delicate joints within the larynx.

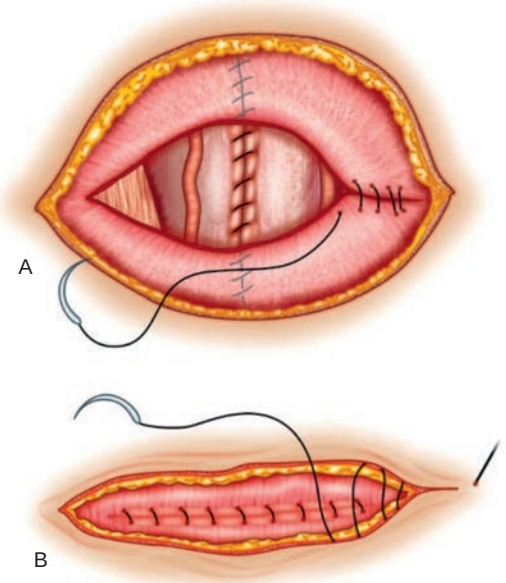



**Fig. 15.19A and B:** (A) Closure of platysma muscle; (B) Wound closure by subcuticular suture

At this stage thyroid lobe is totally free except at a point where it is attached to trachea by a vascular fascia known as ligament of Berry. Berry's ligament is divided but care is taken to re-identify the nerve at this stage. Mobilized thyroid lobe is removed along with isthmus and pyramidal lobe. The cut surface of the contralateral thyroid lobe is usually sutured to the trachea with Vicryl 3/0 absorbable sutures in order to obtain hemostasis.

Sand bag is removed from under the patient's shoulder and wound is re-examined for bleeding. A suction drain is placed deep to the strap muscles to drain any postoperative collection.

The midline is closed with continuous catgut, any bleeding points on the deep surface of the wound flaps are diathermized and the wound closed with subcutaneous catgut to platysma and a continuous subcuticular prolene suture.