FINE NEEDLE ASPIRATION CYTOLOGY & ULTRASOUND AS DIAGNOSTIC MODALITY IN CLINICOPATHOLOGICAL EVALUATION OF THYROID NODULES

By

DR. DEEPIKA PATIL

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DR. M. B. PATIL M.S.

PROFESSOR

DEPARTMENT OF SURGERY

B.L.D.E UNIVERSITY'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE, BIJAPUR, KARNATAKA.

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Date: **DR. DEEPIKA PATIL**

Place: Bijapur. Post Graduate Student,

Department of General Surgery,

B.L.D.E.U.'s Shri B. M. Patil Medical College,

Hospital &Research Centre, Bijapur.

B.L.D.E UNIVERSITY'S
SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL &
RESEARCH CENTRE, BIJAPUR.

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Date: **DR. M. B. PATIL**$_{\text{M.S.}}$

Place: Bijapur. Professor,

Department of General Surgery,

B.L.D.E.U.'s Shri B. M. Patil Medical College,

Hospital &Research Centre, Bijapur.

B.L.D.E UNIVERSITY'S
SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL &
RESEARCH CENTRE, BIJAPUR.

ENDORSEMENT BY THE HEAD OF DEPARTMENT

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Date: **DR.TEJASWINI UDACHAN$_{M.S.}$**

Place: Bijapur. Professor & Head of Department,

Department of General Surgery,

B.L.D.E.U.'s Shri B. M. Patil Medical College,

Hospital &Research Centre, Bijapur.

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Date**:** **DR. M. S. BIRADAR$_{M.D.}$**

Place: Bijapur. Principal,

B.L.D.E.U.'s Shri B. M. Patil Medical College,

Hospital &Research Centre, Bijapur.

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Date:

Place: Bijapur

DR. DEEPIKA PATIL

Post Graduate Student,

Department of General Surgery,

B.L.D.E.U.'s Shri B. M. Patil Medical College,

Hospital &Research Centre, Bijapur.

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Date: **DR. DEEPIKA PATIL**

Place: Bijapur. Post Graduate Student,

Department of General Surgery,

B.L.D.E.U.'s Shri B. M. Patil Medical College,

Hospital &Research Centre, Bijapur.

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Introduction

INTRODUCTION

The thyroid gland is unique among endocrine glands, in that it is the first endocrine gland to appear in the fetus. It is the largest of all endocrine glands (weighing about 25 gm) and is the only one which is amenable to direct physical examination because of its superficial location. Autopsy studies have demonstrated that the thyroid nodularity is present in approximately 37% of the general population of which 12% form the group with solitary thyroid nodules. The incidence of clinically apparent thyroid nodules in general population is 4-5%. The overall incidence of malignancy in solitary thyroid nodules ranges between 10% - 30% depending on the selectivity of surgical indications.

Diseases of thyroid gland, especially multinodular goiter due to deficiency of iodine is prevalent in India. India has the world's biggest goiter belt in the sub Himalayan region with nearly 55 million cases are estimated to be suffering from endemic goiter. Currently, no less than 140 million people are estimated to be living in goiter endemic regions of the country.[1]

Few subjects in surgery have generated as much controversy as the management of solitary thyroid nodule, the two major issues being the diagnostic work up and the extent of thyroidectomy. The goal of diagnostic workup is to select those patients for surgery who have a high likelihood of harboring malignancy in the nodule.

At one extreme, the diagnosis of malignancy may be strongly suspected on clinical grounds. On the other hand, one finds many patients in whom the history and clinical findings are not so conclusive.

FNAC and USG are used in association with clinical features but there are drawbacks of each technique and the final answer to the problem is still elusive. The present study is undertaken to evaluate usefulness of clinical features, FNAC and USG in managing thyroid nodules.

Aims & Objectives

AIMS AND OBJECTIVES

The objectives of the study were to evaluate the patients with thyroid nodules in terms of efficacy of Fine Needle Aspiration Cytology and Ultrasonography in comparison to Histopathology in diagnosis of thyroid nodules.

Review of Literature

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

The name thyroid is derived from the Greek description of a shield shaped gland in the anterior aspect of neck ("thyreoeides").[2] Goiters (from the Latin, Gutter, meaning throat) were known in China in 2700 B.C, but it was the Italians of the renaissance period who first recognized the normal thyroid gland.[3] In 1619, Fabricus ab Aquapendente (1537- 1634) recognized that goiters arouse from the thyroid.

The first credible account of thyroid surgery was given in 1170 by Roger Frugardi of Salerno in the Bamberg manuscript. Goiters that failed to respond to medical treatment were removed by finger dissection, insertion of setons, ligation enmasse and the application of Caustic powder. All such procedures were liable to major complications.[4] The first well documented partial thyroidectomy was undertaken in Paris, in 1791, by Pierre Joseph de Sault (1744-1795) during the era of French revolution.

In the late 19th century, two surgeons- physiologists revolutionized the treatment of thyroid diseases- Theodor Billroth and Emil Theodor Kocher. As a result of pioneering developments in the understanding of thyroid physiology, pathology and surgery , Kocher received the Noble prize in 1909. The collar incision,, introduced by Jules Boeckel (1848-1927) of Strasbourg, was adopted widely.[5] Payer recorded the first transplantation of thyroid in 1906. He transplanted a portion of the thyroid from a woman into the spleen of her myxedemic daughter.

ANATOMY

The thyroid gland occupies an important position in the centre of the visceral compartment of the neck, lying astride the trachea just above the thoracic inlet. It weighs about 25 gm. The gland has 2 lobes, shaped roughly like slender pears, hugging the anterolateral aspect of the cervical trachea from the level of the thyroid cartilage to the 5^{th} or 6^{th} tracheal ring. The right lobe is often larger than the left and the lobes are joined together across the midline by a thin isthmus plastered quite firmly to the anterior surface of the trachea, at the level of the 2^{nd} and 3^{rd} tracheal rings. A variable sized but usually small, pyramidal lobe arises from the isthmus or the adjacent part of either lobe (more often the left). The thyroid gland is covered by fascia and the strap muscles and more laterally, it is tucked under diverging anterior borders of the sternomastoid muscles.[6]

MUSCULO-FASCIAL COVERINGS

The strap muscles are ensheathed by the general investing layer of cervical fascia and this unites them in the midline. These muscles are applied to the anterior surface of the gland, but separated from it by a loose condensation of fascia derived from the pretracheal fascia. This false capsule covers the gland which is enclosed by its diaphanous true capsule with its very rich blood supply, clearly visible just beneath its surface.

In the surgical approach to the thyroid gland the musculo-fascial envelope is incised down in the midline which is relatively avascular and the ‘space’ between the two capsules of the gland is entered. This loose plane is easily developed and the gland exposed by retracting the strap muscles. The other important implication of the musculo-fascial covering of the gland is that, at the

end of thyroid operations the divided fascial envelop is resutured in the midline and this again closes the visceral space. If there is post-operative hemorrhage into this closed space, respiratory embarrassment from tracheal compression results and requires immediate release of the sutures to restore the airway.

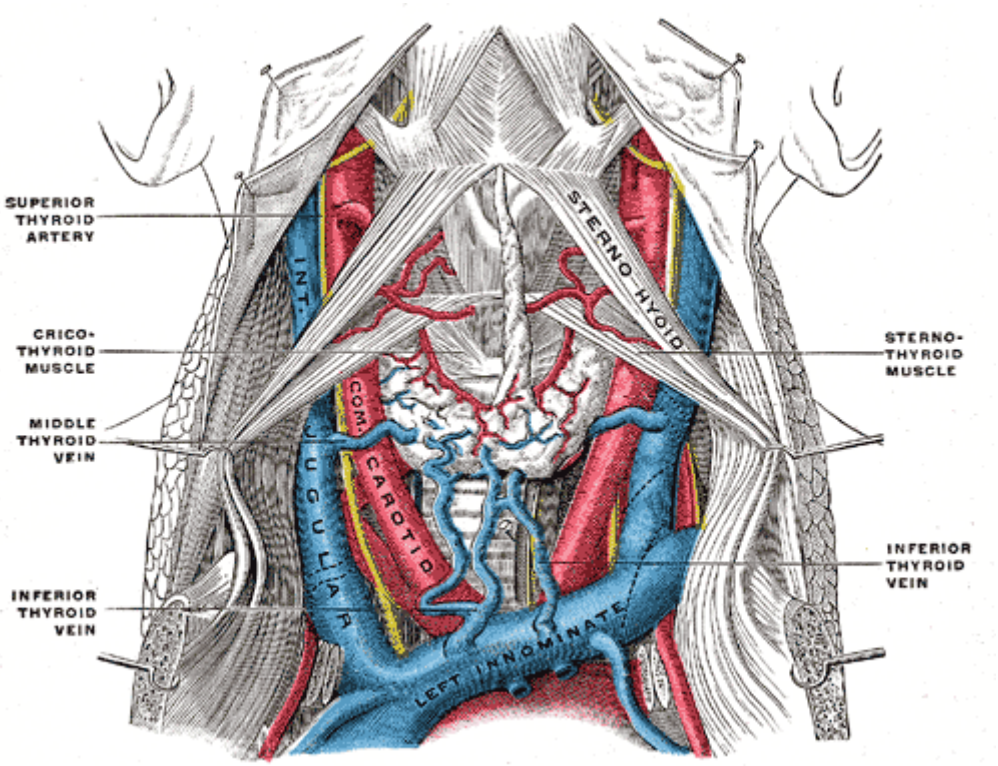


Figure 1: Anatomy of Thyroid Gland

BLOOD SUPPLY

The thyroid is a highly vascular organ with a normal flow rate of 5ml/gm/min. Perfect knowledge of its blood supply will facilitate any surgical procedure on it and make possible the minimization of hemorrhage. Two pairs of arteries (superior and inferior thyroid artery), two pairs of veins (superior and inferior thyroid veins) and an inconstant artery (thyroidea ima artery) and vein (middle thyroid vein) serve the thyroid gland.

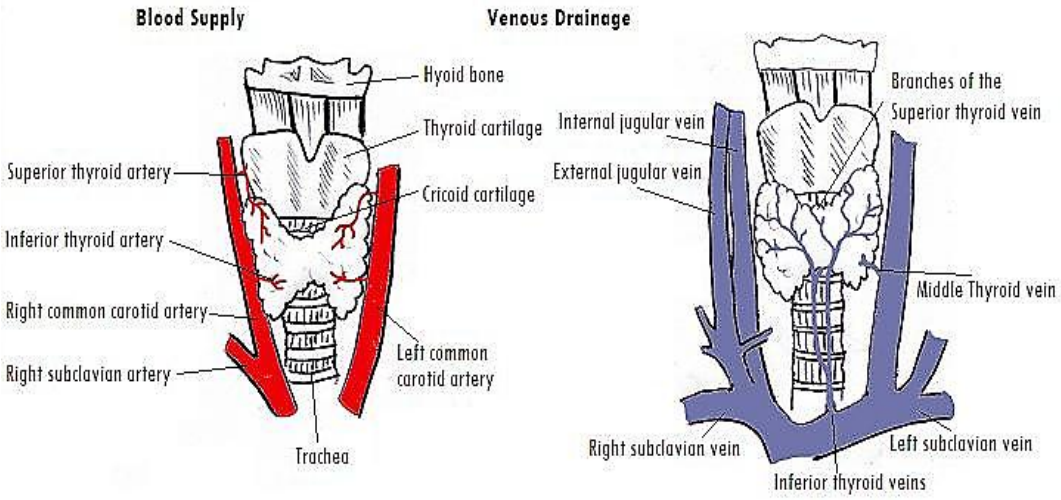


Figure 2: Blood Supply of Thyroid Gland

The **superior thyroid artery** is the first branch of the external carotid artery arising from its lower anterior part, turning caudal and ending at the apex of the corresponding lobe of the thyroid by dividing into glandular branches.

The **superior thyroid vein** accompanies the superior thyroid artery and ends in the internal jugular vein. At the anterior surface of the thyroid gland are prominent connections between superior and inferior thyroid veins.

A **middle thyroid vein** which has no accompanying artery is often present, leaving the gland in its mid position to follow the outer border of the omohyoid muscle, cross the common carotid artery and terminate into the internal jugular vein. Applied anatomy is important because it is a short, thin walled vessel.

The **inferior thyroid artery** is a branch of the thyrocervical trunk, which arises from the subclavian artery. As it passes behind the gland, the inferior thyroid artery crosses the recurrent laryngeal nerve in front, behind or on both sides of it. It is covered anteriorly by carotid sheath and usually closely approximates the middle cervical sympathetic ganglion.

The **inferior thyroid veins** originate on the anterior surface of the gland and descends in front of the trachea. Both may terminate in the left innominate vein, or the left ends in the left and the right in the right internal jugular or brachiocephalic veins.

The **thyroidea ima artery** present in 10%, arising from aortic arch or innominate artery or lower common carotid artery and reaches the inferior border of the isthmus after running upward on the anterior surface of the trachea.

THE IMPORTANT CLOSE SURGICAL RELATIONS

These are recurrent laryngeal nerves, the external laryngeal nerves and the parathyroid glands. Like all important relations, they should be recognized immediately and cared for respectfully.

1. Recurrent Laryngeal Nerve

Innervates the intrinsic laryngeal musculature and provide sensory innervations to the glottic larynx. The RLN arises from the Vagus nerve at the level of the subclavian artery on the right and at the level of the aortic arch on the left. The nerves then turn superior- medial to run towards the tracheo-esophageal (TE) groove, giving off esophageal and tracheal branches. The RLN ascends in close association with the trachea and esophagus but not necessarily in the true TE groove.

Weisberg et al[7] stated that the right RLN is at a higher risk for stretch injuries during cervical spine surgeries because of its lateral position relative to TE groove. Typically the nerves may pass superficial or deep or between branches of the inferior thyroid artery (ITA).[8] This variable branching pattern (of the nerves

and the arterial system) limits the ability of the surgeon to rely solely on the ITA as a landmark to identify the nerve. The position of the nerve can be further influenced by the formation of the suspensory ligament of the thyroid gland (Berry's ligament).[9] It is the pretracheal fascia that covers the thyroid gland, condenses and attaches the thyroid to the upper two to three tracheal rings. RLN often passes through this layer on its way to enter the larynx.

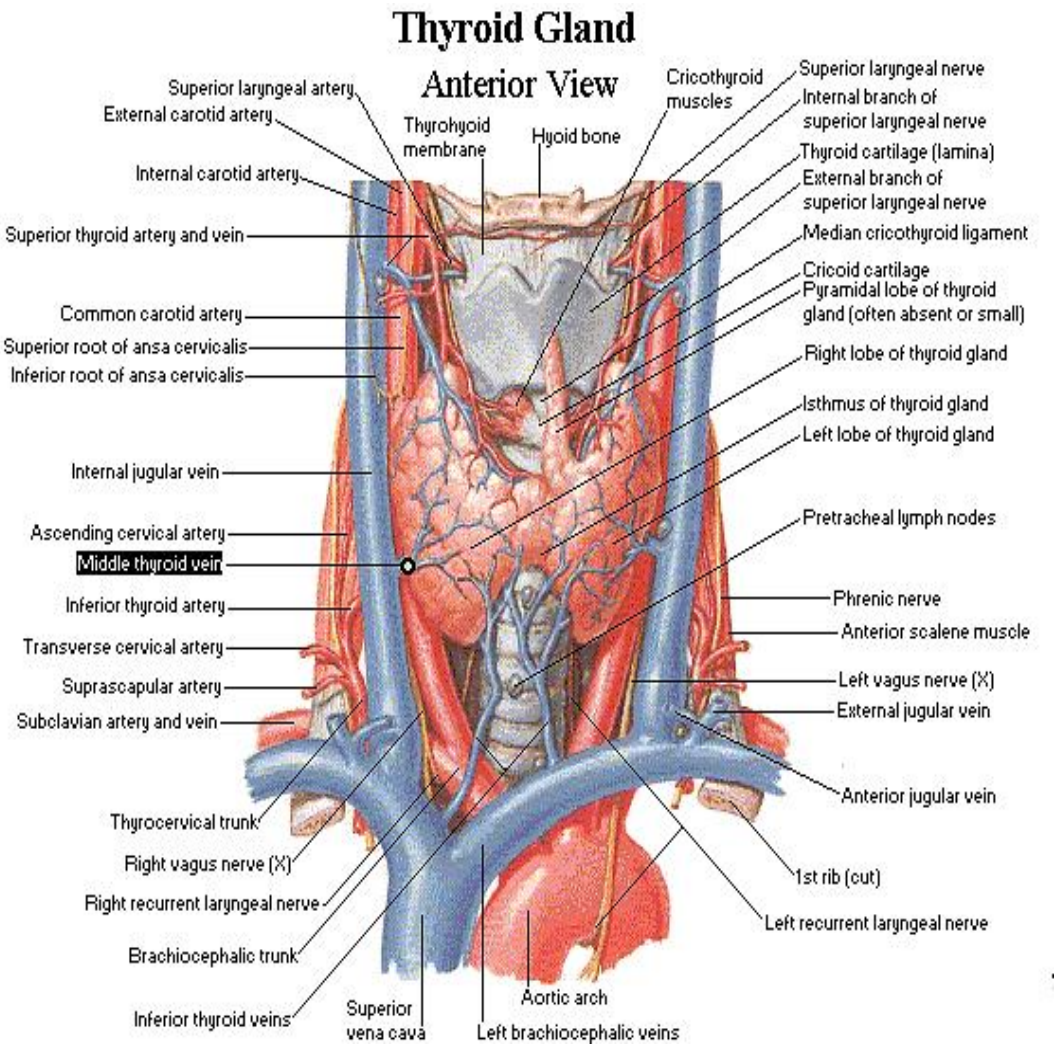


Figure 3: Anatomic relationships of the thyroid gland and recurrent laryngeal nerve

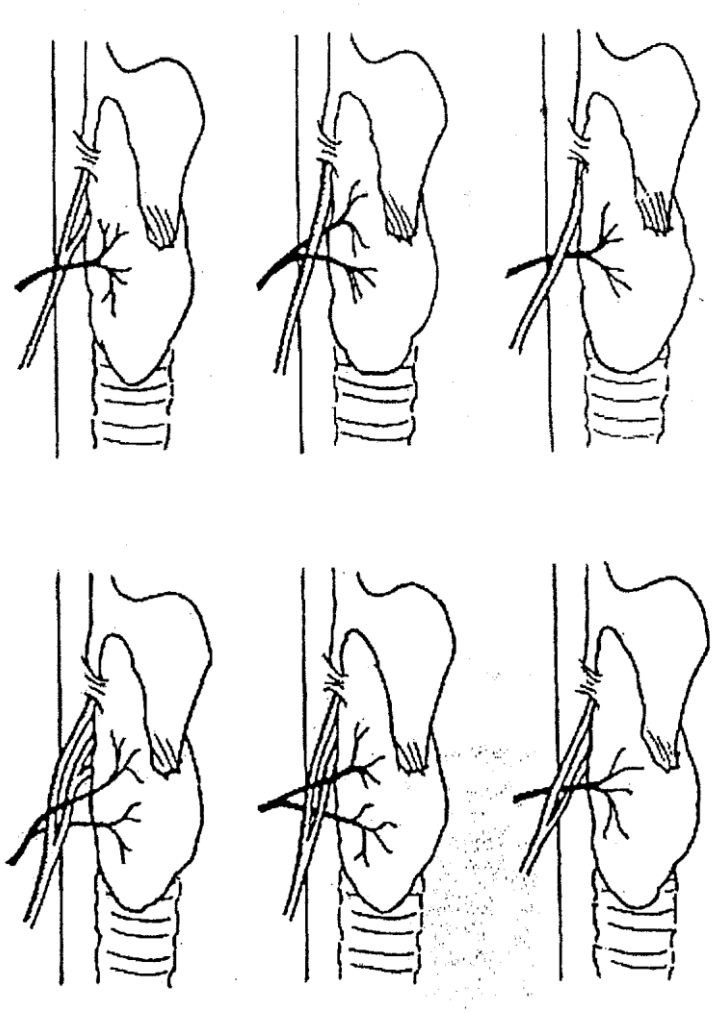


Figure 4: Anatomic variations of RLN and the ITA.

RLN may divide extralaryngeally in 35 -80% of anatomic dissections.[8] The typical division includes an anterior (motor division) and a posterior (sensory division) but patterns with two to eight branches were described. The RLN will then enter the larynx posterior to the cricothyroid joint.

An anomalous or non-recurrent nerve was reported in 0.3% to 0.8% of cases. It arises directly from the cervical portion of the vagus at about the level of the larynx or the thyroid gland and enters the larynx posterior to the crico-thyroid joint without looping low in the neck. It commonly occurs on the right side but rare cases from left side also reported.

2. Superior laryngeal nerves

The superior laryngeal nerves (SLN) arise from the inferior (nodose) vagal ganglion and descend inferiorly deep to carotid system. Posterior to the internal carotid artery the SLN branches into an external branch (SLNE) and an internal branch.[10] Cerna et al[11] described a classification system with 37% of nerves crossing the superior thyroid pedicle within 1 cm of superior thyroid pole (type 2). Regardless of the classification system, it is clear that the SLNE travels in close proximity to the STA (approximately 20%-60% within one cm of STA and superior thyroid pole) and must be protected by the surgeon.

Unilateral damage of the external laryngeal nerve may result in variable hoarseness or weakness of the voice and bilateral injury may add easy fatiguability in speaking or decrease of range volume or pitch.

Another vulnerable structure, the cervical sympathetic chain is in close relation to the inferior thyroid artery, where the latter arches medially in front of the thyrocervical trunk. Damage to the chain may result in “Horner’s syndrome”. Damage usually occurs during the attempts to ligate the inferior thyroid as far laterally as possible to avoid damage to the recurrent laryngeal nerve.

3. Parathyroid glands

Most commonly 4 in number, arise from the third branchial pouch (inferior parathyroids) and fourth branchial pouch (superior parathyroids).The superior parathyroids are most consistently located (~ 80%) within 1 cm superior to the intersection of the RLN and ITA (near the cricothyroid joint). The inferior parathyroids are more variable in their location because of the longer migration with inferior thyroid and thymus. Approximately 45% - 61% are located inferior,

lateral, or posterior to the inferior thyroid pole below the level of the ITA. 26-35% is positioned immediately inferior to the inferior thyroid pole in association with the cervical thymus and less than 1% are in the anterior mediastinum. The blood supply to the parathyroids is predominantly by way of the ITA system with some variable component from the STA. From a surgical view point, they are seen as small bean shaped structures with a yellow tan to caramel color. A medial to lateral dissection is utilized with the plane of dissection along thyroid capsule, which allows identification and mobilization away from the thyroid while preserving the blood supply.

LYMPHATIC DRAINAGE[2]

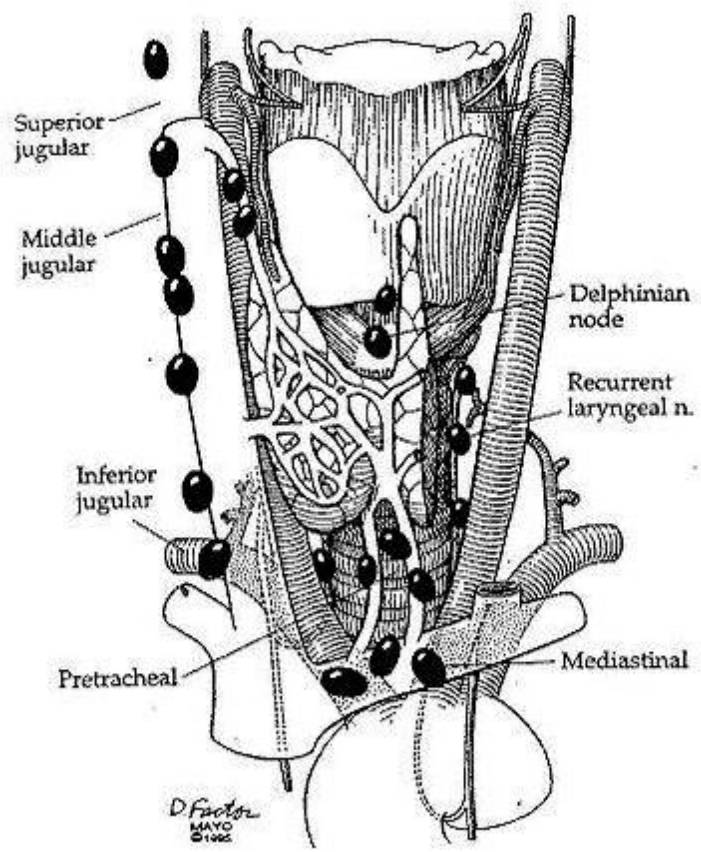


Figure 5: Lymphatic drainage

Thyroid is drained in almost every direction. Within the gland, lymphatic channels occur immediately beneath the capsule and communicate between lobes through the isthmus. Regional lymph nodes exist in a pretracheal position immediately superior to isthmus; paratracheal nodes; tracheoesophageal groove nodes; mediastinal nodes in the anterior and superior position; jugular lymph nodes in the upper, middle, and lower distribution; and retropharyngeal and esophageal lymph nodes. Laterally, cervical lymph nodes within posterior triangle may be involved in patients with widespread thyroid cancers. Submaxillary triangle lymph nodes may be involved with metastatic activity.

Papillary carcinoma is commonly associated with adjacent nodal metastasis and medullary carcinoma has a strong predilection for metastatic lymphatic involvement, usually within central compartment (the space between the internal jugular veins).

HISTOLOGY OF THE THYROID GLAND

The essential unit of thyroid gland is the follicle which varies considerably in size with an average diameter of 200 microns. The follicle is a closed sac lined by epithelium, the height of epithelial cells range from 3-20 microns and is directly related to their secretory activity. The lumen contains viscus colloid material in which thyroglobulin is present in concentrated solution. Each follicle is enclosed by a basement membrane and closely enmeshed by a rich network of capillaries. Groups of 20-40 follicles, bound together by connective tissue and supplied by a single arterial twig, constitute a thyroid lobule.[12]

The functional state of thyroid is reflected by the histological indicators. Columnar cells means hyperactivity, low and flat cells means inactivity. The

height of the cells is the index of TSH activity, since the epithelium is stimulated by TSH. Concerning the size of the follicles, large follicle suggests inactivity and storage of hormone. Small follicles and scanty colloid with scalloped margins suggests increased activity.

'C' cells or the para follicular cells are dispersed with the follicles, especially in the posterior lateral parts of the lateral lobe: They make up about 0.1% of the epithelial mass.

PHYSIOLOGY

The thyroid gland is responsible for the production of two families of metabolic hormones: the thyroid hormones- thyroxine (T4) and triiodothyronine (T3) and hormone calcitonin. The thyroid follicle is the major production unit, as well as storage space for thyroid hormones. The effect of T3 and T4 is qualitatively very similar but differs dramatically in their time and course of action. They play an important role in the regulation of growth, heat production and cellular metabolism.[13] The thyroid function is closely related to the iodine metabolism. The C cells or parafollicular cells secrete a polypeptide hormone called calcitonin, which has a hypocalcemic effect.

Iodine deficiency can result in nodular goiter, hypothyroidism and cretinism, and possibly, the development of follicular thyroid carcinoma. In iodine excess, Grave's disease and Hashimoto's thyroiditis can occur.[2]

Thyroid hormone synthesis

Both MIT and DIT are biologically inert.[14] Two molecules of DIT are then coupled to form one molecule of thyroxine (T4- tetraiodothyronine) or one molecule of MIT couples with one molecule of DIT to form triiodothyronine (T3).

Thyroxine forms approximately 90% and triiodothyronine 10% of hormones formed.

The physiologically active thyroid hormone is T3 which is formed by the removal of a 5` iodine from T4. 80% of T3 is formed in peripheral tissues from the deiodinization of T4, whereas 20% released directly from the thyroid gland. T4 is not considered to be biologically active but is the main storage form. 99.97% of T4 is bound where as 99.7% of T3 is bound to the proteins. Only unbound form is biologically active.[15]

Regulation of thyroid secretion

The main factors that determine the amount of hormone secreted by the thyroid gland are the thyrotrophic hormone (TSH) secreted by the anterior pituitary and availability of iodine to the gland.

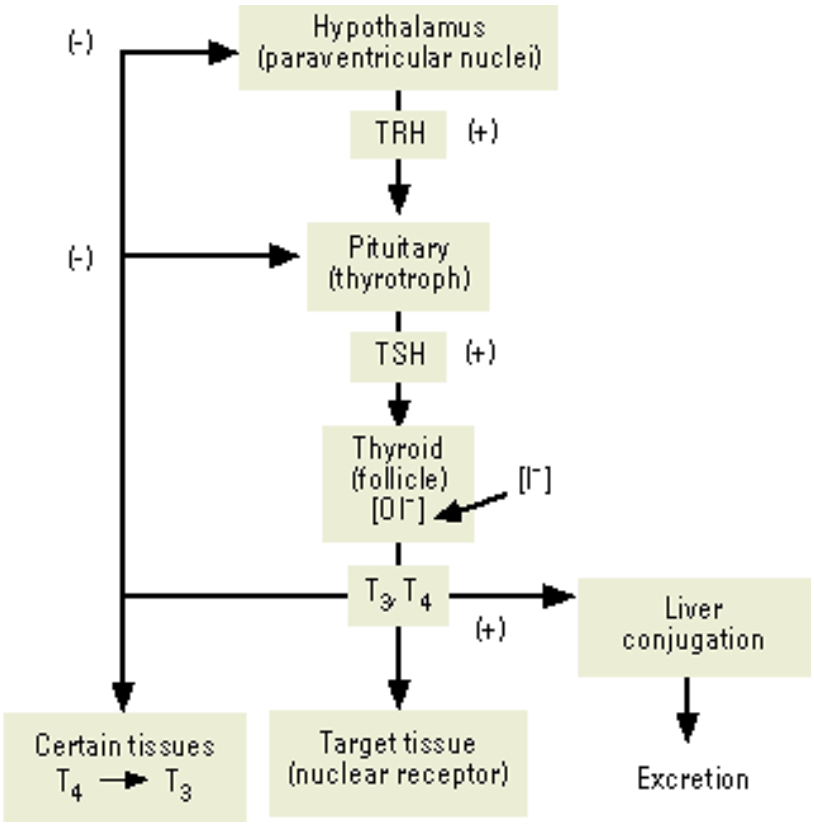


Figure 6: Hypothalamic-pituitary-thyroid axis

Control of Thyrotropin (TSH) secretion:

1) **Hypothalamic control:** Thyrotrophic releasing hormone (TRH) from the hypothalamus stimulates production and release of TSH.
1) **Thyroid hormone:** The thyroid hormones, in turn, inhibit the secretion of TSH at the level of pituitary and antagonize the effects of TRH by down regulating TRH receptors at the thyrotrophic cells.

Each change in the T4 levels by 2 units causes an inverse change in TSH secretion by 100 units. Thus, TSH is sensitive to minute and subclinical changes in T4 levels. This delicate relationship is the basis of obtaining thyrotropin levels as first line testing for thyroid dysfunction.

Other factors that affect are, somatostatin and dopamine which are physiologic inhibitors of TRH secretion, glucocorticoids decrease responsiveness to TRH and estrogens enhance responsiveness to TRH.

Functions of thyroid hormones

1. Stimulates metabolism by increasing the ATP synthesis in cells, relative increase in the heat production and raises cardiac output.
2. Participates in co-enzyme reactions of the metabolic processes, so that normal development, growth and maturation are attained.
3. Adenohypophysis requires thyroxine for adequate synthesis of growth hormone.
4. Increase glycogen synthesis and peripheral utilization of glucose and thus potentiates insulin in this respect. Also increase, glycogenolysis, gluconeogenesis and enhance rate of intestinal absorption of glucose and galactose. Overall in thyrotoxic patients, there is hyperglycemia and

diminished sensitivity to exogenous insulin and converse changes occur in hypothyroidism. Thyroxine plays a vital role in glucose metabolism in RBC by influencing the synthesis of 2, 3- diphosphoglycerate.

5. In physiological amounts it increases the synthesis of protein from accelerated synthesis of specific enzymes.
6. Increase the synthesis and degradation of lipids.
7. Required for synthesis of vitamin A from carotene. In hypothyroidism, the requirements of water soluble vitamins and vitamin D and E are increased.
8. Calcitonin regulates the calcium homeostasis.

EVALUATION OF THYROID NODULES

History[16]

The usual presentation is an asymptomatic mass that is discovered by either the patient or the clinician. Factors that increase the risk of malignancy include: previous head and neck irradiation, rapid growth, symptoms of compression or invasion such as dysphagia, dysphonia and hemoptysis, male sex, pain, age younger than 20 or older than 60, family history of thyroid cancer or multiple endocrine neoplasia. Compression symptoms of globus sensation, dysphagia or recumbent dyspnoea may develop. Tracheal deviation or narrowing may cause respiratory symptoms and hoarseness may develop as a result of recurrent laryngeal nerve pressure, although vocal cord paralysis is unlikely and should raise suspicion of malignancy. Goiters result in cosmetic deformity of the neck that may be the reason for presentation in a number of individuals, with a long history of MNG.

Physical Examination[16]

Examination of neck begins by inspection of the seated patient from front and side and noting any surgical scars, obvious masses or distended veins. The thyroid can be palpated with both the hands from behind or while facing the patient, using the thumbs to palpate each lobe. It is best to use a combination of these methods, especially when the nodules are small. The patient's neck should be slightly flexed to relax the neck muscles. After locating the cricoid cartilage, the isthmus can be identified and followed laterally to locate either lobe (normally the right lobe is slightly larger than the left). By asking the patient to swallow sips

of water, thyroid consistency can be better appreciated as the gland moves beneath the examiner's fingers.

Features to be noted include thyroid size, consistency, nodularity and any tenderness or fixation. An estimate of thyroid size (normally 12-20g) should be made and a drawing is often the best way to record findings. However, ultrasound is the method of choice when it is important to determine thyroid size accurately. The size, location and consistency of any nodules should also be defined. A bruit over the gland indicates increased vascularity, as occurs in hyperthyroidism. If the lower borders of thyroid lobes are not clearly felt, a goiter may be retrosternal. Large retrosternal goiter can cause venous distension over the neck and difficulty in breathing especially when the arms are raised (Pembertson's sign). With any central mass above the thyroid, the tongue should be extended, as thyroglossal cysts then move upwards. The thyroid examination is not complete without assessment of lymphadenopathy in the supraclavicular and cervical regions of the neck.

Laboratory Tests[17,18]

1. Total Thyroid Hormones

Total T4 and total T3 are designated as T4 and T3 respectively. These are measured by specific radioimmunoassay. Since they are highly protein bound, their values depend on the levels of the binding proteins in serum. Most patients with hyperthyroidism with normal levels of protein have high T4 and T3. Less commonly only T3 is high (T3 toxicosis) and this is more characteristic of hyperthyroidism due to a functioning autonomous nodule, early Grave's disease or those relapsing after stopping antithyroid drugs.

2. Tests of Thyroid Binding Proteins

There are specific radioimmunoassays for TBG and TBPA. Since TBG is a most important binding protein carrying 70-80% of hormones, it is usually measured alone. Thyroid binding capacity (TBC) can be measured indirectly by quantitating the capacity of binding sites in serum, which are not carrying hormones. This is done using the T3 resin uptake test (T3 RU) and usually it is in the range of 25-35%. If there are a lot of unoccupied binding sites on the proteins, the tracer will bind there and the T3RU is low and vice versa. Knowledge of T4, T3 and T3RU values makes it possible to determine if the problem is due to thyroid disease, or to a binding protein abnormality. If both the tests are abnormal in the same direction, the thyroid is at fault, e.g. if T3 and T3RU are both high, hyperthyroidism is diagnosed. In contrast, if one test is high and the other low, the defect is due to a carrier protein.

3. Free Thyroid Hormone Measurement

Two methods: equilibrium dialysis or radioimmunoassay can measure FT4. It is generally accepted that the dialysis method is gold standard, however it is restricted to research laboratories. FT4 obtained by two step radioimmunoassay are sensitive and specific. FT4 measurements provide excellent index of thyroid status in almost any clinical situation with the few exceptions, which are very rare, e.g. heparinized patients, and in acute psychiatric illness. This test is not influenced by abnormalities in the thyroid binding proteins.

4. Pituitary thyroid axis- TSH

TSH radioimmunoassay became available in 1965. When TSH is above normal range and T4 and T3 are normal, it is called subclinical hypothyroidism. But older assays could only differentiate TSH levels of 1 to 2 mU / L and since many euthyroid individuals have TSH levels of 0.5 — 2.0 mIU/L, the assay could not separate suppressed values from normal. But with the introduction of immunoradiometric assay (IRMA) and amplified enzyme linked immunoassays (ELISA), TSH levels of 0.lmU/L can be detected. The addition of chemiluminescent techniques allowed this ultrasensitive thyrotropin assay to detect thyrotropin levels at 0.01mU/L. Most screening and initial evaluations now are based upon the results of a single sensitive TSH. Thyrotropin levels rise logarithmically in response to small decreases in T4 levels, even if these decreases keep T4 levels within normal levels.

5. Hypothalamic pituitary thyroid axis (TRH test)

Thyrotropin releasing hormone was isolated, characterized and synthesized in 1968. The test involves injecting TRH intravenously and evaluating the response of the pituitary to secrete TSH. A normal response is a raise in TSH which is maximal at 20-30min with return to normal by 60-90 min. In hyperthyroidism the pituitary is suppressed by thyroid hormone and there is no raise in TSH after injection of TRH.[13]

This test was of great value in understanding the physiology and pathophysiology of hypothalamic-pituitary- thyroid interactions and it was valuable clinically in the diagnosis of borderline hyperthyroidism. Because of the

development of sensitive TSH measurement, which shows suppressed levels in hyperthyroidism, the TRH test is superfluous in this role.

FINE NEEDLE ASPIRATION CYTOLOGY

Scandinavian workers introduced fine needle aspiration. It eventually gained wide acceptance and was endorsed by the American Thyroid Association.[19] This technique is one of the standard methods in the evaluation of thyroid nodule. There are many reasons for this: 1) Most nodules are benign, and surgical excision is not required in most cases. With the wide acceptance of FNA, there has been a decrease in the number of thyroidectomies performed and an increase in the yield of malignancies in the excised glands. 2) FNA is a safe and quick procedure with few complications and it does not involve radiation exposure. 3) FNA decreases the overall cost of care by approximately 25%, mainly by eliminating unnecessary surgeries and limiting the use of frozen section intra operatively.[20] It should be correlated with clinical findings and other investigations. The advantage being it is a simple office procedure, done without any anesthesia, and is cost effective. The technique is relatively painless and produces a speedy result. Its better efficacy avoids the need for frozen section study.

FNA is performed with a 10 cc or 20 cc pistol syringe coupled with a fine 22, 23, or 25 gauge needle. Use of 10-20 ml syringe producing a good negative pressure, and a syringe holder for the conventional aspiration technique is recommended. The holder leaves one hand free, to immobilize and to feel the target lesion and this allows more precision in placing the needle. Cameco syringe pistol (Cameco AB, Taby, Sweden), made to fit 10 cc plastic syringes are usually

used. The nodule is secured firmly between fingers, and while suction is applied, 2-6 passes are made into the nodule. Suction is released before exiting the nodule or as soon as the material appears at the hub of the needle. If the sample enters the syringe, part or the entire specimen may be lost in the syringe.

Technique

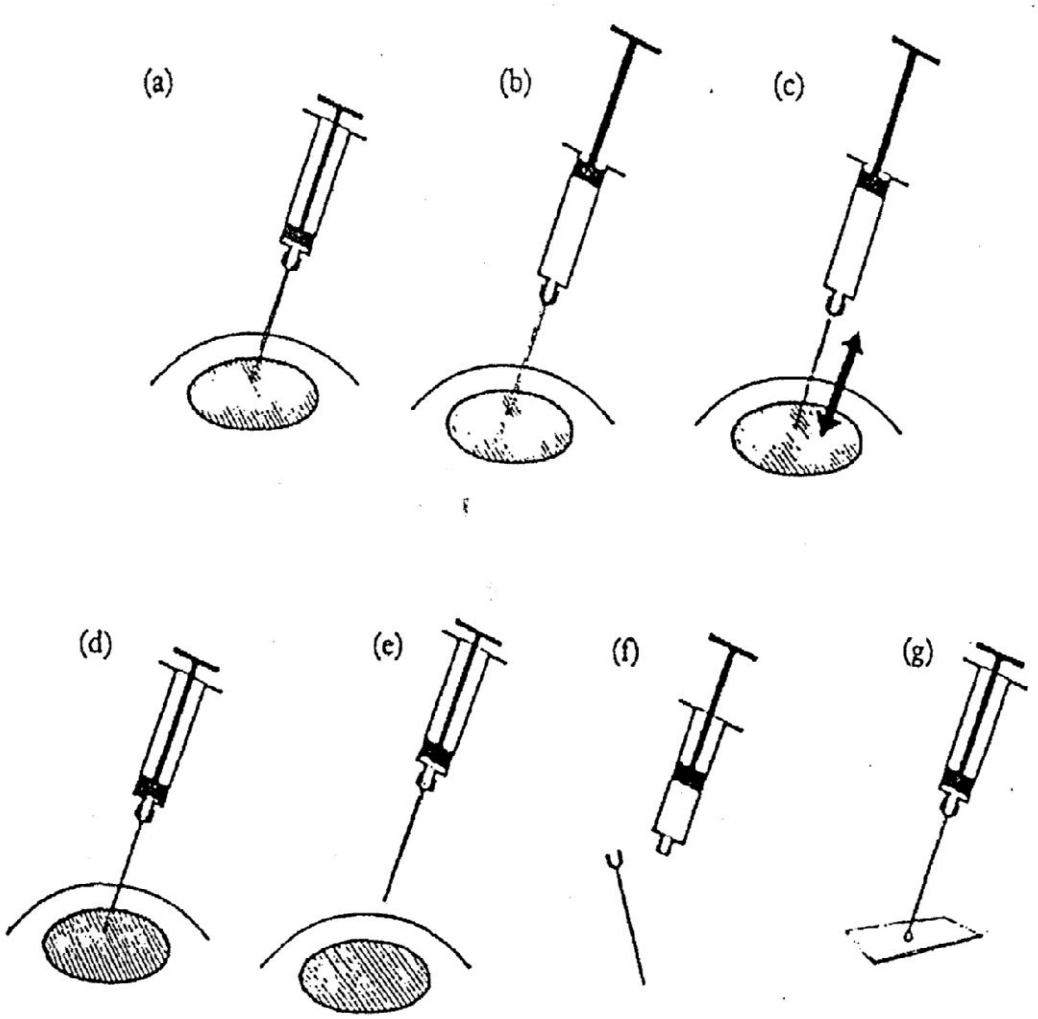


Figure 7: FNAC Procedure: a) Needle positioned within target tissue, b) Plunger pulled to apply negative pressure, c) Needle moved back and forth within target tissue, d) Negative pressure released while needle remains in target tissue, e) Needle withdrawn, f) Needle detached, air drawn into syringe, g) Aspirate blown on to slide.

This technique, although simple to perform, is subject to the operator's experience. It is dependent on the placement of the needle, the sensitivity of fingertips, and the amount of suction applied.

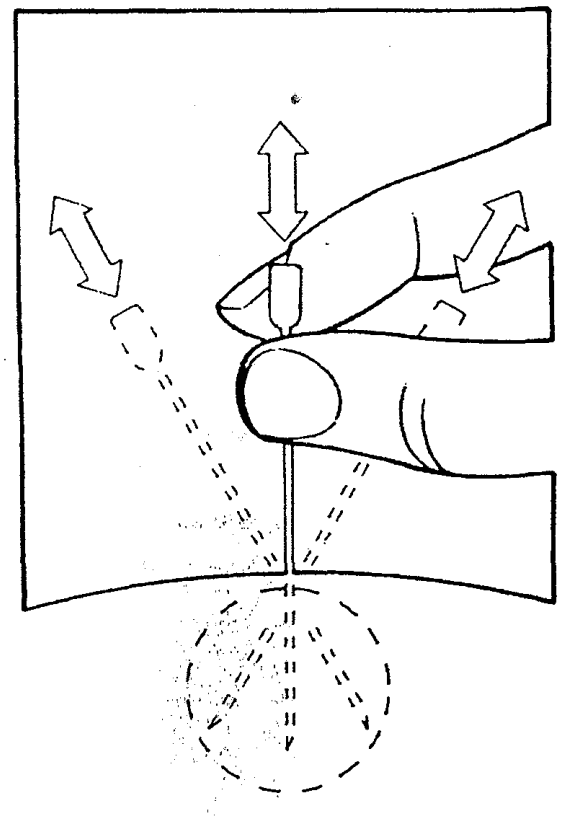


Figure 8: Needle biopsy without aspiration.

To maximize the yield of FNA, this technique is probably best by experienced cytopathologist. Recently, a technique of needle biopsy without suction was advocated to reduce traumatic blood aspiration and has been particularly useful in smaller nodules. This technique uses the needle for cutting and capillary pressure of tissue for sampling.[21] Air dried and wet smears can be obtained concurrently, as they are complementary. Air dried smears include the Diff-Quick and the May-Grunwald-Giemsa methods. This method is best for

immediate reading by a cytopathologist. The air dried smears highlight the background colloid, the cell architecture and the cytoplasmic details. This technique is helpful for the diagnosis of medullary and lymphoid tumors. The Papanicolaou stain is a wet smear that requires immediate fixation with 95% alcohol. This method enhances nuclear morphology such as grooving and inclusions, and is better suited for detecting papillary cancers.[22]

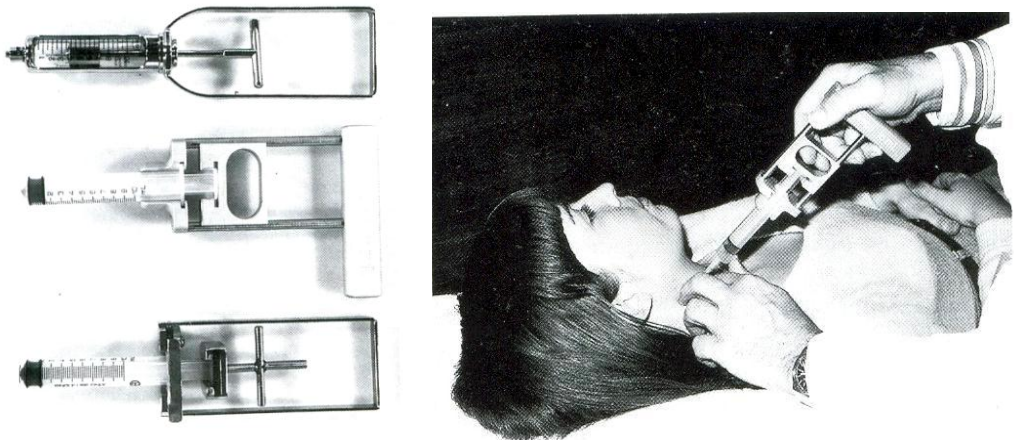


Figure 9: (**Cameco syringe** Pistol with disposable 10 cc syringe) FNA of thyroid. Needle and syringe operated with one hand, leaving the other hand free to feel and fix the target lesion.

Cell block processing has potential of increasing the accuracy of FNA, particularly for FNA that are labeled as "suspicious".[22] The aspirate can also be processed by ThinPrep (Cyte Corporation, Boxborough, MA), which is an automated preparation method that results in a concentrated, thin layer of cells with improved nuclear details.[21] This technique requires added experience and is more expensive.

Ancillary tests to improve the accuracy of FNA include immunohistochemistry, ploidy studies, molecular markers, and more recently,

Reverse Transcription-Polymerase Chain Reaction (RT-PCR) to detect thyroglobulin mRNA and thyrotropin receptor mRNA.[21,22,23] This RT-PCR technique is most useful when an FNA is obtained from an adjacent lymph node. Arturi et a1[24] reported that if the lymph node biopsied was positive for thyroglobulin mRNA and thyrotropin receptor mRNA, then there was a 100% concordance with metastatic cancer originating from the thyroid gland.

Complications of FNA

Pain is localized but can also radiate to the ipsilateral ear and may persist for weeks. When a thyroglobulin level is a part of the evaluation, it should be obtained prior to the FNA since a transient but substantial thyroglobulin elevation can be noted after an FNA. Seeding along the tract is extremely rare and only one case has been reported.[25] Hemorrhage or hematoma formation may complicate the procedure.

Reporting

Reports of cytology need to be standardized, and the current guidelines were discussed and reported by the Papanicolaou Society in 1997.[26] The four recognized categories of FNA are malignant (3.4-5%), benign (60-75%), suspicious (7.2-30%) and insufficient (7-29.5%).[21,27,28] The "malignant" category includes papillary, medullary, poorly differentiated or undifferentiated thyroid cancers, lymphomas and metastatic nonthyroid cancers.[21] "Benign" reports include hyperplastic colloid nodules in 90% of the cases and chronic inflammatory lesions (Hashimoto's thyroiditis, subacute lymphocytic thyroiditis, De Quervain's thyroiditis) in the other 10%.[21,27] The category of "suspicious"

lesions on FNA is due to the inability to unequivocally detect cytological features of either benign or malignant neoplasm. The most common cause of categorizing an FNA aspirate as "suspicious" is the inability to differentiate a follicular adenoma from a well-differentiated follicular carcinoma. Some of the other possible causes of a "suspicious' report are as follows [21]:

- Hürthle cell neoplasm
- Follicular variant of papillary carcinoma
- Low-grade papillary carcinoma
- Hyalinising trabecular adenoma
- Hashimoto's thyroiditis with metaplasia
- Any cancer with sub-optimal sampling
- Adenomatous goiter with micro follicular structure predominance

Efficacy

An adequate smear consists of at least 5-6 groups of follicular cells, with each group containing at least 10 cells.[29] The main goal of FNA is to accurately predict which nodule is cancerous. Numerous studies cited the following data. Sensitivity is 65-100% and specificity is 70-100%.[21,30,31] Overall accuracy is estimated at 92-95%.[28,32] One of the most recent and largest series was conducted by Amrikachi et al,[27] who retrospectively reviewed 6226 consecutive FNA from 1982-1998. They reported a sensitivity and specificity of 93% and 96% respectively. The overall sensitivity of FNAC in Kamaljit Kaur et a1[33] series was 83.3%, while the overall specificity was 100% as all malignancies reported on FNAC were correctly confirmed by final HPE. The sensitivity and specificity of FNAC were 71.43% and 100% respectively according to Altavilla et al. (1990),[34]

98% and 99% according to Goellner et al (1987),[29] 93.5% and 75% according to Bouvet et al (1992).[35]

In most series, the false positive rate is approximately 0.8% - 9%, and the false negative rate is 0-16%.[27,28,31,32] Most experts agree that the actual false negative ratio is less than 5%.[36] One of the most common causes of a false negative reading are cystic nodules, especially when larger than 3 cm, because they carry a rate of inadequate sampling of 20% and a false negative reading upto 30%.[21,37] It was previously believed that cystic nodules were benign, but purely cystic nodules were demonstrated to be uncommon. The presence of colloid is not always a reassuring finding and it is imperative that a few clusters of normal cells be found to minimize nondiagnostic and false negative FNAs.[22] Pseudocysts are believed to occur in cancerous and benign nodules at a rate of 23% to 33%, and 27% to 35%, respectively; cystic nodules should be considered to have the same cancerous potential as more solid nodules.[21] Papillary cancer is the most likely culprit in cystic degeneration of cancerous lesions. Repeat FNA, ultrasound-guided FNA, or excision is recommended in patients with cystic nodules.

Pitfalls in FNAC of thyroid as mentioned by Shaha (2000)[38]

- Adequacy of specimen (quantitative and qualitative)
- Accuracy of specimen (nonhomogeneity of needle placement)
- Accuracy of cytopathologic interpretation
    - Cysts (difficulties with degenerative nodules)
    - Follicular lesions (benign vs. malignant)
    - Hürthle cell lesions (benign vs. malignant)
    - Lymphocytic lesions (lymphocytic thyroiditis vs. lymphoma)

ULTRASOUND

Ultrasonography is most widely used imaging technique for the evaluation of thyroid nodules. Thyroid ultrasound is performed with high frequency transducers (7-13 MHz) and **can detect solid nodules of 3mm to 4mm and cystic nodules of 2mm in diameter.** When routinely used for solitary nodules, it can discover coexisting nodules in approximately 50% of patients. The routine use of ultrasound for solitary nodules was investigated by Marqusee et al[39] at the Thyroid Nodule Clinic of Brigham and Women's hospital. Ultrasonography changed the clinical management of 44% of patients who were referred for solitary nodule. The findings that altered management included the discovery of multiple nodules, no actual nodule identified, and very small solitary nodules (<1 cm). High frequency probe can detect vascular pattern and papillary projection inside the cyst, which can change the management.)

Purely cystic nodules are uncommon (~4%), with partially cystic lesions accounting for up to 20% of nodules. Cystic lesions were reported to carry a lower risk of malignancy (0.5% to 3%). Predominantly solid nodules carry a higher risk of malignancy (~10%). Many studies looked into the echogenic pattern of nodules to predict malignancy, but currently, none of them had discovered a definitive pattern.[40,41]

Ultrasound features suggesting malignancy

- Absent 'halo' sign
- Solid or hypoechogenicity
- Heterogeneous echo structure
- Irregular margin
- Fine calcification

- Extraglandular extension

Kakkos et al[40] reported a series of 82 solitary thyroid nodules that were imaged with ultrasound and managed by surgical excision. Ultrasound showed that 22 patients had calcification in their thyroid glands. They noted a malignancy incidence of 55% (12 out of 22) in patients with solitary nodules with calcifications versus 23% (14 out of 60) for patients with noncalcified nodules' In another study, Takashima et a1[42] reported a series of microcalcifications with a specificity of 93% and positive predictive value of 70% for cancer, albeit with a sensitivity of only 36%. Koike et al[41] applied multiple logistic regression analysis on five different findings (margin, shape, echo structure, echogenicity and calcification) in a retrospective series of 329 nodules (all >5mm) that were imaged with ultrasound. Patients then underwent thyroidectomies and USG findings were correlated with histopathology. Their sensitivity of preoperative diagnosis was 86.5% for patients with nonfollicular neoplasms, and 18.2% for patients with follicular neoplasms. The specificity was 92% and 89% respectively. In Kamaljit Kaur et al[33] study, they found sensitivity and specificity of USG to be 71.4% and 77.7% respectively for differentiating between the benign and malignant nodules Watters et al (1992)[43] found that the sensitivity and specificity of USG in suggesting a malignant lesion were 74% and 83% respectively. They interpreted an USG report as suggestive of malignancy if the nodule was solid or of a mixed solid-cystic variety and a hypo echoic and non-haloed lesion. They emphasized that the USG has added advantage of allowing the whole gland to be examined rather than the dominant nodule but was limited by the fact that no features were pathognomonic for malignancy so that it should be regarded as a complementary rather than alternative investigation to FNAC in the management of solitary

thyroid nodules. Jones et al (1990)[44] found the sensitivity and specificity of USG to be 75% and 61% respectively.

It has been a consistent observation, according to published literature, that **the risk of thyroid cancer is less with multiple nodules than with the solitary nodules. High resolution real-time USG is far better than clinical examination in detecting thyroid nodularity.** Walker et al (1985)[45] have shown that the prevalence of multinodularity in clinically solitary nodules is between 20% and 40% and it has been observed that for a thyroid nodule to be detected by palpation, it must be at least 1cm in diameter while USG detects nodules as small as 3 mm in diameter. Simeone et al (1982)[46] stated that the detection more than one lesion with USG reduces the probability of malignancy to 1-6%.

Thyroid ultrasound has become the first line imaging modality for evaluation of thyroid gland, and has largely supplanted scintigraphy for thyroid evaluation due to excellent visualization of thyroid parenchyma, its high sensitivity in detection of small nodules, calcification, septations, and cyst formation, as well as image guidance for needle-aspiration biopsies.[47] Measurement of thyroid lobe can be obtained: longitudinal (height), transverse (width), and anteroposterior dimensions (depth). On average normal values are less than 5, 2 and 2 cm respectively.[48] Anteroposterior diameter stands out as an important and relatively independent measurement that is remarkably constant among individuals. When it is greater than 2 cm, it is suggestive of underlying thyroid pathology that is not sonographically visible, and when it is above 2.5 cm it is considered grossly abnormal.[49] USG findings are nonspecific and play a very limited role in the diagnosis of diffuse thyroid diseases. The main application of USG in such circumstances is identification of co-existent nodular lesions and

monitoring structural changes and vascularity of the gland in response to medical treatment.[50]

An USG is a safe, non-invasive, non-radioactive test that should be ordered judiciously. Recommendations for ultrasound are:

- Non palpable or difficult to palpate nodules for USG guided FNA.
- Follow up imaging for solitary nodules that are managed medically or by observation.
- Non diagnostic fine needle aspirate (as an adjunct to repeat FNA).

RADIOISOTOPE IMAGING:

Nuclear scans of the thyroid, once the cornerstone of the thyroid nodule evaluation, have fallen out of favor in the past few decades. The most commonly used radioisotopes are technetium (99m Tc) and iodine (I^{123}). The choice of radioisotope is dependent on the preference of the clinician and radiologist, because they provide similar information. I^{123} is more physiological than Tc 99m. Tc 99m quickly washes out of the thyroid gland before being organified inside the gland. This property of Tc99m allows for a shorter scanning time (20-30 min) and the scanning can be performed immediately after the administration of Tc99m. I^{123} imaging needs to be performed 24 hours after administration of I^{123} and the scanning time can run 4-6 hours in length. Radiation exposure is comparable for both the agents, and is not significant. The whole body exposure from 1-123 and Tc99m scanning is 0.04cGy and 0.07cGy respectively.[51,52] Imaging resolution is better with Tc99m than radioiodine. Nodules that are smaller than 1cm cannot be detected reliably by either scan, as they are below the discriminating power of scintigraphic devices.

Approximately, 80-85% of nodules are 'cold' on scintigraphy, with 14-22% of them ultimately proven to be malignant. 5% of nodules are 'hot' with less than 1 % risk of malignancy. The remaining 10-15% are 'warm' or indeterminate nodules. It was suggested that these nodules harbor a higher risk of malignancy than hot nodules, with a reported range of <10% up to 36%.[53]

The following circumstances would be indications for nuclear scans.[51,53]

1. Identification of a functional solitary thyroid nodule when initial TSH is decreased.
2. If an FNA is reported as "follicular neoplasm" or "suspicious", the finding of a "hot" nodule may decrease a suspicion of a malignancy.
3. Detecting neck metastasis.

Recently, Thallium-201 scan was reported to be a useful diagnostic tool to differentiate between benign and malignant thyroid nodules.[54] Sinha et al[54] reported risks of malignancy for low uptake, intermediate uptake, and high uptake lesions to be 0%, 6% and 55%, respectively.

COMPUTED TOMOGRAPHY:

CT scan has very limited role in the initial management of thyroid nodules. CT scans are more useful in detecting thyroid tissue in retrotracheal and retroclavicular regions and allow the assessment of mediastinal involvement and cervical lymphadenopathy. The inherent high iodine content of the thyroid gland will increase the brightness of the gland on CT scan even without contrast material. It is preferable to obtain non-contrasted CT scan because the use of iodine based contrast will delay any nuclear scintigraphy for 4-8 weeks because of the saturation of iodine agents in the cellular components of the thyroid gland.

MAGNETIC RESONANCE IMAGING:

MRI also plays a minor role in the evaluation of thyroid nodules. MRI is more expensive than CT and USG but it demonstrates exquisite soft tissue details and vascular anatomy. This allows identification of extraglandular invasion and involvement of the great vessels. An advantage of the MRI scan over the CT scan is the possible use of contrast (gadolinium) without interfering with nuclear scintigraphy.

THYROID ENLARGEMENTS:

The normal thyroid is impalpable. The term goiter is used to describe generalized enlargement of the thyroid gland. A discrete swelling (nodule) in one lobe with no palpable abnormality elsewhere is termed an isolated (or solitary) swelling; discrete swellings with evidence of abnormality elsewhere in the gland is termed dominant.

Etiology of goitre

1. Iodine deficiency

The immediate cause of goiter is the failure of thyroid gland to obtain a supply of iodine sufficient to maintain its normal structure and function. Lack of iodine may be absolute or relative. Absolute lack occurs in regions where soil and water are poor in iodine and the goiter is known as endemic goiter. Relative lack is seen in girls at the time of puberty and in women during pregnancy and lactation. The goiter is therefore common in women than in man.[55]

The lack of iodine is the stimulus to hyperplasia and when this gives place to involution both the acini and the gland may remain enlarged, condition which constitutes goiter.

The changes produced by hyperplasia involution cycle are not uniform throughout the gland but patchy in distribution. As a result localized areas develop which gives the gland nodular appearance.

Probably in many instances the intake of iodine is adequate, but its utilization may be impaired owing to the defect in the alimentary systems of enzyme deficiencies in the synthesis of thyroxine.

2. Iodine excess goiter

It occurs in persons with certain predisposing conditions viz. familial predisposition, deranged thyroid parenchyma, no response of goiter to iodine withdrawl, unsuppressibility of exogenous thyroid hormone, increased sensitivity of the thyroid to iodine, or positive iodine perchlorate discharge and patients with chronic thyroiditis.

Its mechanism is not completely understood, but seems probable in iodine goiter. There is persistently a high concentration of intrathyroidal iodide that occurs for some reason and induces a failure to escape from the acute **Wolff Chaikoff effect.** Thus blockade of hormone is sustained.

It is also probable that iodide goiter is attributable to coincidental intake of goitrogens like lithium or antipyrium and sulfonamides.

3. Thyroid stimulating hormone stimulation (TSH stimulation)[56]

During puberty, pregnancy and physiological stress from any source, the gland increases in size and becomes more active functionally. This extreme functional liability is reflected in transient hyperplasia of the thyroid epithelium. At this time thyroglobulin is reabsorbed, and the follicular cells become tall and columnar sometimes forming small infolded buds.

When the stress abates, involution occurs. These changes are due to increased production of thyroid stimulating hormone. Failure of this normal balance between hyperplasia and involution may produce major and minor deviations from the usual physiological pattern.

Formation of goiter from hyperplasia is now sustained by the current increase of serum TSH levels, which stimulates thyroid hyperplasia and synthesis

of thyroglobulin and hence T3 and T4. The thyroid hormones in turn suppress the TSH.

4. Long acting thyroid antibody (LATS)

Originally the responsible antibody was thought to be long acting thyroid stimulating antibody (LATS) described by Adams and Purves in 1956. It is apparent now that a whole family of antibodies contributes to the development of the disease. Thyroid stimulating immunoglobulins (TSI) or antibodies (TSAb) attach to and stimulate the TSH receptor and TSH-binding inhibiting immunoglobulins (TSII) or antibodies (TBIA) block the TSH receptor. Current practice is to group all the antibodies together under the town thyroid receptor antibody (TRAb).

5. Dyshormonogenesis

Mr. Girr (1960) suggested this name as a genetic term for those conditions in which there was a failure of hormone biosynthesis as a result of inborn metabolic defects. If the defects are severe, goiter and hypothyroidism will result and if incomplete, goiter may compensate and the patients are euthyroid. If the defects are mild but the patients are exposed to an iodine deficiency environment or goitrogenic influence, the combination of factors may produce goiter where each alone would be inadequate.

These conditions have been classified by Stanbury et al (1960) according to the defect.

1. Iodine trapping defect.

2. Failure to convert iodine into, organic form. Group (a) similar to (b) but group (c) also has familial 8th nerve palsy. - Pendred's syndrome.
3. A heterogenous group charactetized by secretion of abnormal iodinated peptides into circulation.
4. Those who have deficiency of iodothyronine di-iodinase. This defect results in leakage of MIT and DIT in the urine, resulting in depletion of iodine stores.
5. Those who are unable to couple MIT and DIT to form T3 and T4.

All these conditions will respond to the administration of thyroid hormone. If the iodine intake is very high the enzyme deficiency may be overcome e.g. in Iceland where goiter is practically unknown, enzyme deficiency is often associated with low iodine intake of a dislike to sea fish.

An acute development of MNG gives rise to the suspicion of inflammatory thyroid disease which is painful in case of acute thyroiditis and the subacute thyroiditis of de Quervain, or painless in the case of granulomatous diseases such as sarcoidosis or tuberculosis.[57]

6. Genetic factors

Genetic factors play a part in the etiology of most types of thyroid diseases.

a) Single gene defects

1. Defects in thyroxine biosynthesis
2. Iodide transport defect
3. Organification defect
4. Pendred syndrome

5. Iodotyrosine coupling defects
6. Deiodinase deficiency
7. Thyroglobulin synthesis defect

b) Thyroid hormone resistance and receptor defects. These are very rare.

c) Variants of serum thyroid binding globulin.

7. Environmental aspects:

Iodine: Goiter prevalence rates of more than 50% are found in endemic areas with extreme iodine deficiency. In these areas goiters are usually multinodular and of very large size.

Other environmental agents: A large number of agents in the environment, both naturally occurring, manmade as well as some medications are known to induce goiter.

- Isothiocynates, Flavanoids, Lithium
- Resorcinol and Phenols
- DHBAS, Pyridine
- Iodide transport oxidation proteolysis
- Organic binding release and coupling dehalogenation thyroglobulin

8. Immunological factors:

Immunological disturbances occur in many thyroid diseases, including malignant conditions. The immune system may be primarily responsible for the disease process, the so called autoimmune thyroid disease (AITD), or the immunological changes may be secondary to some other disease process.

The major diseases included in AITD are Grave's disease, lymphocytic thyroiditis (including Hashimoto's thyroiditis and primary myxedema) and postpartum thyroid dysfunction.

PATHOGENESIS OF THYROID NODULE

Stages:

- Persistent growth stimulation causes diffuse hyperplasia; all lobules are composed of active follicles and iodine uptake is uniform. This is a diffuse hyperplastic goiter, which may persist for a long time but is reversible if stimulation ceases.
- Later, as a result of fluctuating stimulation, a mixed pattern develops with areas of active lobules and areas of inactive lobules.
- Active lobules become more vascular and hyperplastic until hemorrhage occurs, causing central necrosis and leaving only a surrounding rind of active follicles.
- Necrotic lobules coalesce to form nodules filled either with iodine-free colloid or a mass of new but inactive follicles.
- Continual repetition of this process results in a nodular goiter. Most nodules are inactive, and active follicles are present only in the internodular tissue.

Etiology and pathophysiology of MNG

In iodine deficient areas, hypothyroidism causes an increase in TSH, which stimulates growth of the thyroid gland. More recently, a gene located on chromosome 14q, dubbed 'MNG-1', has been associated with familial non-toxic MNG. In addition, polymorphism of codon 727 has been associated with toxic

MNG.[59] Individual follicular cells, furthermore, demonstrate variable activity, morphology, and growth potential, and, through an ill-defined mechanism, nodular formation occurs.[60] Increasing sizes begin to outgrow their blood supply, leading to localized hemorrhage and reparative fibrosis.

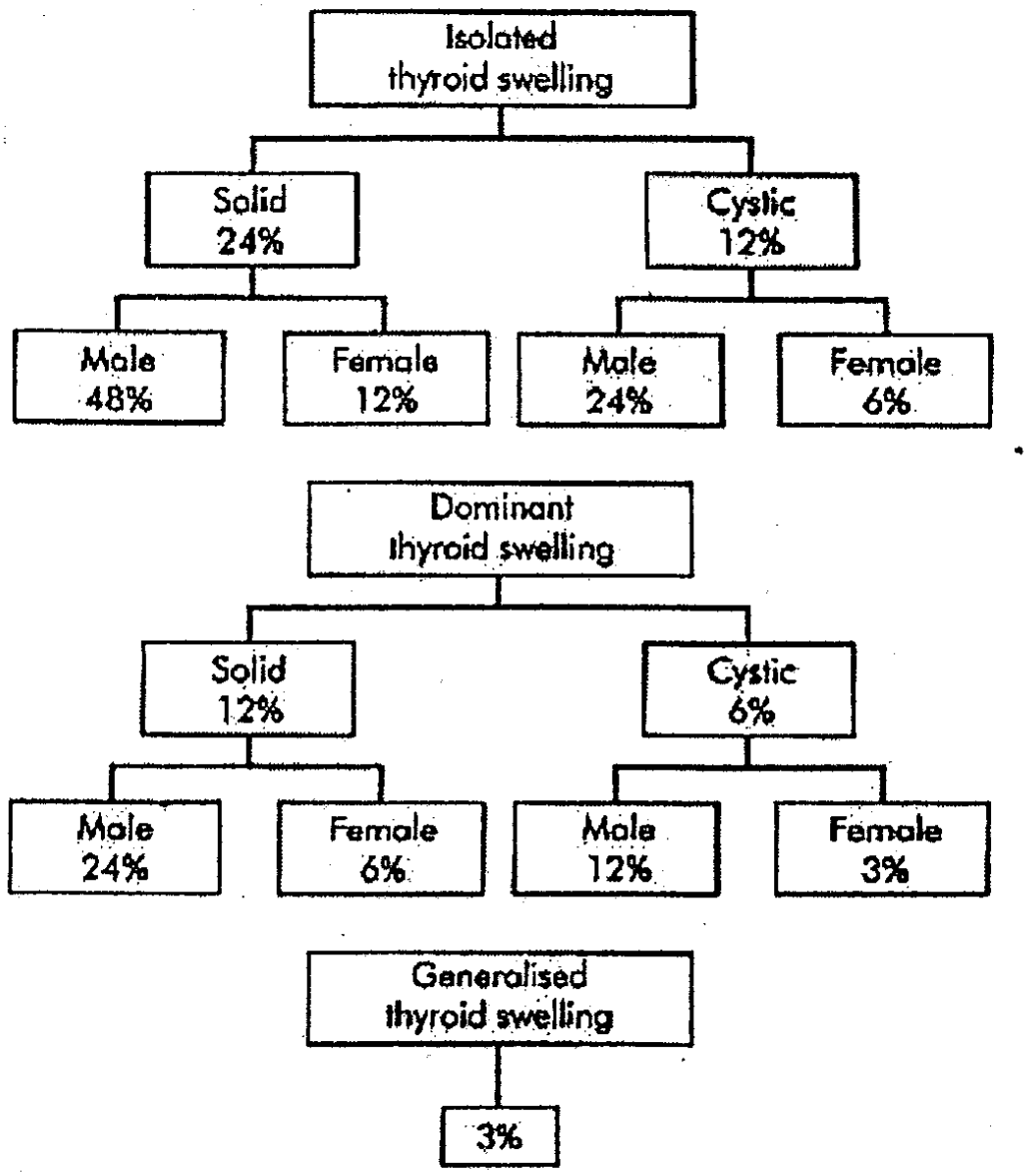
The natural history of MNG includes, increase in tissue with an annual growth potential up to 20%. Areas of increased functioning may progress to hyperthyroidism or toxic MNG (Plummer's disease), which occurs in 5-10% of MNG in a 5 year period. These conditions may occur slowly as autonomous adenomatous form may occur more acutely following an excessive source of iodine such as radiographic contrast material or medications such as amiodarone.

It is well established that MNG may harbor occult malignancy. Formerly, it was thought that solitary nodules had an increased risk of malignancy (7.5%-24%) compared with MNG (4%-12%). More recent studies have indicated, however, similar frequencies in solitary and multinodular conditions of approximately 4%.[61] Tan et al reported that half of the cases of palpable solitary nodules later were identified as multinodular goiter with USG evaluation.[62] The substernal extension of MNG may harbor a greater incidence of malignancy.[63]

Histology

Microscopically there are wide ranges of appearances. Some nodules are composed of huge follicles lined by flattened epithelium, others are extremely cellular and hyperplastic, and still others are composed predominantly by Hürthle cells. Some of the dilated follicles have a conglomerate of small active follicles at one pole (so called Sanderson's Polsters). Others have papilloid projections facing the lumen of cystic follicle, a feature that may lead to confusion with papillary carcinoma.

Risk of malignancy in thyroid swellings[56] (Rule of 12):



The risk of cancer in a thyroid swelling can be expressed as a factor of 12. The risk is greater in isolated vs. dominant swellings, solid vs. cystic swellings and men vs. women.

Complications of MNG

1. Pressure symptoms and signs:

   a. Scabbard trachea- trachea compressed from side to side.

b. Very rarely the cartilaginous rings are softened by the pressure chondromalacia.

c. The cervical sympathetic chain is sometimes affected by sudden hemorrhage into a nodule and results in Horner's syndrome. If hoarseness develops due to recurrent laryngeal nerve palsy, malignant change of goiter should be suspected.

d. Pressure on esophagus is rare in simple goiters.

2. Hemorrhage

Sudden hemorrhage may occur in one of the nodules and patient may come with acute dyspnea / pain.

3) Hyperthyroidism

4) Hypothyroidism: It is extremely rare for the overt symptoms of hypothyroidism to make themselves evident, and myxedema in this condition is even rarer.

5) Malignant transformation: The incidence of follicular carcinoma is high in endemic goiter areas. An incidence of 5-8% has been suggested.

6) Retrosternal goiter: A very few retrosternal goiters arise from the ectopic thyroid tissue, but most arise from the lower pole of a nodular goiter. The degree of descent varies accounting for-

- Substernal type: This extends into the superior mediastinum behind the sternum. Here the nodule is palpable.
- Plunging Goiter or Goiter Plongeant: Here the intra thoracic goiter, which is forced jerkily up into the neck by increased intrathoracic pressure, and recedes into the chest almost as quickly when the expulsive force, is spent.
- Intrathoracic Goiter: Here the goiter is placed fully in the thoracic cavity, which includes a group called mediastinal goiter.

Most intrathoracic or substernal goiters are labeled ‘secondary’ because they are enlargements or extensions of multinodular goiters, based on the inferior thyroid vasculature. They expand downward into anterior mediastinum. The extremely rare (~1%) ‘primary’ substernal goiter arises as aberrant thyroid tissue within the anterior or posterior mediastinum and is based on intrathoracic vasculature and not supplied by the inferior thyroid artery.

MANAGEMENT OF THYROID NODULES

Indications for operation in thyroid swellings[56]

1. Neoplasia (FNAC positive, clinical suspicion)
    - Age
    - Male sex
    - Hard texture
    - Fixity
    - Recurrent laryngeal nerve palsy
    - Lymphadenopathy
    - Recurrent cysts
2. Toxic adenoma
3. Pressure symptoms
4. Cosmetic grounds
5. Patient’s wishes

Surgery of thyroid

The types of thyroid operations can be assembled from 3 basic elements:

- Total lobectomy
- Isthmusectomy
- Subtotal lobectorny

Total thyroidectomy = 2x total lobectomy'+ isthmusectomy

Subtotal thyroidectomy = 2x subtotal lobectomy + isthmusectomy

Near total thyroidectomy = total lobectomy. + isthmusectomy + subtotal lobectomy

Lobectomy = total lobectomy + isthmusectomy

Role of different thyroid operations in relation to presenting condition[56]

Procedure	Multinodular goiter	Isolated or dominant swelling
Total thyroidectomy	Risk of hypoparathyroidism	Known to be PCT or FCT and in high risk group or MCT
Subtotal thyroidectomy	Best prospect of longterm euthyroidism Risk of regrowth and difficult Reoperation	No
Near total thyroidectomy	Risk of regrowth difficult reoperation	Known to be PCT or FCT and in high risk group Reduced risk of Hypoparathyroidism
Lobectomy	If confined to one lobe	Diagnosis benign or uncertain or if PCT or FCT in low risk Group.

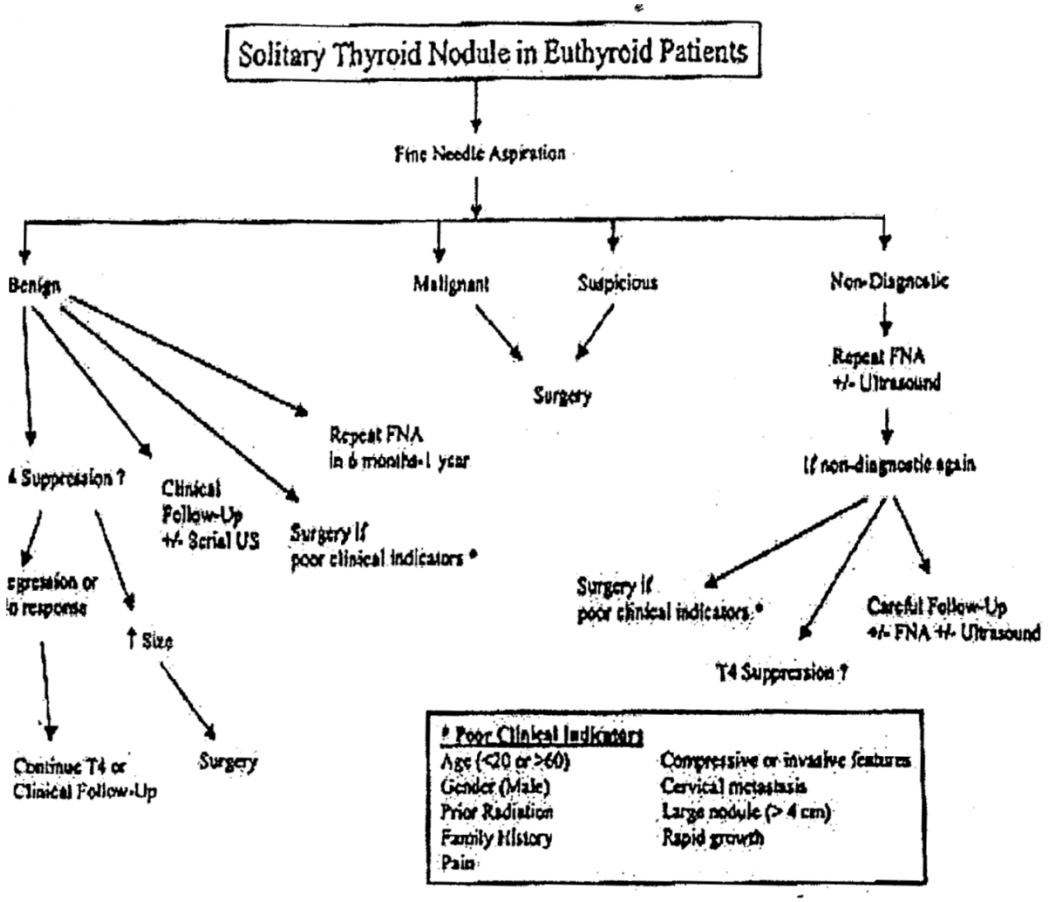
MANAGEMENT OF SOLITARY THYROID NODULES:

Surgical excision based on clinical indicators:

The following clinical factors may warrant surgery despite an FNA that is reported as 'benign' or 'non-diagnostic': 1) age extreme (younger than 20 or older than 45); 2) male sex; 3) nodules that occur in patients with Grave's disease or Hashimoto's thyroiditis; 4) previous radiation to the cervical region; 5) strong

family history of thyroid cancer; 6) pain; 7) compressive, infiltrative/invasive features; 8) cervical metastasis; 9) large nodule (>4cm); 10) rapid growth; and 11) growth despite thyroid suppression therapy.

Management algorithm of a thyroid nodule based on FNA results:



The natural history of FNA 'benign' nodules is unpredictable, and therefore, close observation is recommended. Although yearly follow up with or without USG is probably sufficient, some nodules may warrant further work up when poor clinical indicators are present.

Thyroid suppressive therapy: Several series were conducted to determine the benefits of T4 suppressive therapy of patients with benign solitary nodules. Gharib and Mazzaferri[69] reviewed the literature and concluded that because only

10%-20% of patients respond to suppressive therapy, benign solitary nodules are best followed without suppression, thus avoiding potential complications of long term therapy.

The management of FNA 'malignant' nodules is more straight-forward because the predictive value of malignancy in FNA is close to 100% with specificity also close to 100%. Surgical excision is warranted for 'malignant' nodules.

For the FNA 'suspicious' lesions, literature strongly suggests the need for surgical management. The last category of a FNA result is the 'non-diagnostic' or 'insufficient' for diagnosis reading, a repeat FNA is performed, possibly with ultrasound guidance to increase the yield. The clinical follow up, with surgical intervention only when poor prognostic indicators were present was acceptable.

Extent of surgery

With the exception of lesion that is limited to the isthmus, the least extensive procedure recommended is a hemithyroidectomy. When limited to the isthmus, simple excision of the nodule can be done, leaving the 2 lobes intact. In cases where a definitive diagnosis was not made before surgery or in cases of suspected benign lesions where a malignancy still needs to be ruled out, the specimen is often examined on frozen section. There is consensus that a total thyroidectorny should be performed for patients in the high risk group.

TREATMENT OF TOXIC NODULE[56]

Surgery or radioiodine treatment is appropriate. Resection is easy, certain and without morbidity. Radioiodine is a good alternative over the age of 45 years

because the suppressed thyroid tissue does not take up iodine and there is thus no risk of delayed thyroid insufficiency.

TREATMENT OF MULTINODULAR GOITRE

In general, surgery is necessary in extremely large MNG, suspicion of malignancy, tracheal or esophageal symptomatology, substernal extension, vocal cord paralysis, and rapid growth. Otherwise, consideration should be given to medical or radioiodine - treatment.

Medical Treatment

Suppression therapy, commonly used in nontoxic MNG, is accomplished when a supplemental thyroid hormone is given to suppress TSH. Side effects of cardiac arrhythmias and osteopenia from prolonged suppressive therapy are a greater risk. The goal TSH is commonly 0.1 mU/L to 0.3 mU/L (normal - 0.3 to 4.0 mU/L). Controversy exists as to its efficacy and indications. Once hormone supplements are stopped, however, regrowth of the goiter commonly occurs. Antithyroid drugs such as thionamides, propylthiouracil, and methimazole can normalize hormone concentrations in patients with toxic MNG. Recurrence, however, occurs in greater than 95% after therapy stops.[64]

Radioiodine (I^{131}) is also used to treat toxic and nontoxic MNG. It reduces size by approximately 40-60% in 2 years.[65] Dosage varies from 5mCi - 150mCi. Although the MNGs were reduced in size and hyperthyroidism had resolved, the MNGs were shown to remain.

a. **Toxic MNG:** RAI is known to provide a return to a euthyroid state in toxic MNG and provide a reduction in size of MNG, although the overall

incidence of hypothyroidism is a potential disadvantage. There is evidence that higher calculated doses of RAI may provide a higher percentage return to a euthyroid state in a shorter period of time than low dose treatment. Toxic MNGs are often pretreated with antithyroid drugs to limit complications of a thyroid storm, although they may affect the outcome of treatment negatively with RAI.

b. **Nontoxic MNG:** These are treated successfully with RAI. When comparing subtotal thyroidectomy with RAI for nontoxic MNG, the response to surgery was better at 1 year than with RAI. The use of recombinant human thyrotropin potentially may reduce the dosage of RAT necessary to achieve the desired result in nontoxic MNG.[66] Treatment is not without potential complications and includes hypothyroidism, radiation thyroiditis in 2-3% of patients, and autoimmune hyperthyroidism in 3-4%. Hypothyroidism is reported to have a 20-40% incidence at 4-5 years following treatment. In addition, the risk of subsequent thyroid cancer, leukemia and congenital abnormalities in offspring is unknown but of concern. There is an estimated 0.5% age adjusted lifetime risk for extrathyroidal cancer compared with a 20% lifetime risk of fatal cancer for an unexposed population. TM It is considered particularly in those unable to tolerate surgical treatment.

Surgical Treatment

The typical nontoxic MNG without evidence of dominant nodules, toxic nodules, or other associated conditions can be treated with total thyroidectomy or subtotal thyroidectomy with reasonable success and provides pathologic

confirmation, avoidance of radiation, one- stage treatment and low risk for recurrence. The use of potassium iodide is not recommended in patients with nontoxic MNG at any time during their treatment. Toxic MNG is commonly treated surgically with subtotal or total thyroidectomy. As in preparation for treatment with RAI, patients with toxic MNG need preoperative cardiac evaluation and medical management including antithyroidal medications, beta-blocker and potassium iodide.

Controversy remains regarding the extent of thyroid requiring removal to prevent recurrent MNG, although most surgeons now recommend total thyroidectomy. The surgical techniques utilized by the surgeon should allow for the best chance for removal of the abnormal thyroid tissue with the least morbidity, and they remain surgeon dependent and controversial.[67]

Postoperatively, it is important to monitor TSH levels and most clinicians treat with thyroid hormone theoretically to decrease the potential for recurrence or growth of any residual thyroid tissue present and to provide thyroid replacement. Scientific evidence, however, has not proven a benefit in outcome following treatment with suppressive therapy.[68]

Percutaneous ultrasound guided ethanol injection, a more common technique used in Europe is an alternative for toxic, autonomous or dominant cystic nodules- especially in the nonsurgical candidate. Hyperthyroidism resolves in 42% of the lesions at 3 months and 66% at 1 year. An increased likelihood of success is seen in nodules smaller than 3 cm. Treatment is given weekly with 2 cc to 4 cc of 95% ethanol injected to induce cellular necrosis, until normalized hormone serum values are achieved.

POSTOPERATIVE COMPLICATIONS

In a well-managed thyroid patient, the postoperative complications are uncommon. But when they occur, they may prove to be quite dangerous. They are

1. Hemorrhage
2. Respiratory obstruction
3. Recurrent laryngeal nerve injury
4. Parathyroid insufficiency
5. Thyroid storm (thyroid crisis)
6. Wound infection
7. External laryngeal nerve injury
8. Homer's syndrome
9. Thyroid insufficiency
10. Keloid of the scar
11. Stitch granuloma
12. Recurrence of the tumor

NEOPLASMS OF THE THYROID

Classification of Thyroid Neoplasms:[56]

A. Benign

- Follicular adenoma

B. Malignant

• Primary: 1) Follicular epithelium-differentiated

- Papillary
- Follicular
- Hürthle cell

2) Follicular epithelium-undifferentiated

- Anaplastic

3) Parafollicular cells

- Medullary

4) Lymphoid cells

- Lymphoma

• Secondary: Metastatic

Benign Tumors

Follicular Adenoma[56]

They present as clinically solitary nodules and the distinction between a follicular carcinoma and an adenoma can only be made by histological examination; in the adenoma, there is no invasion of the capsule or of pericapsular blood vessels. Treatment is, therefore by wide excision, i.e. lobectomy. The remaining thyroid tissue is normal so that prolonged follow up is unnecessary. It is

doubtful if there is such an entity as a papillary adenoma and all papillary tumors should be considered as malignant even if encapsulated.

Malignant tumors

Relative incidence of primary malignant tumors of the thyroid gland:[56]

Relative incidence	Percentage
1. Papillary carcinoma	60%
2. Follicular carcinoma	20%
3. Anaplastic carcinoma	10%
4. Medullary carcinoma	5%
5. Malignant lymphoma	5%

Etiology[56]

The single most important etiological factor in differentiated thyroid carcinoma, particularly papillary, is irradiation of the thyroid under 5 years of age. Short latency, aggressive papillary cancer is associated with the RET/PTC_3 oncogene and later developing, possibly less aggressive, cancer with ret/PTC1. The incidence of follicular carcinoma is high in endemic goitrous areas, possibly due to TSH stimulation. Malignant lymphomas sometimes develop in autoimmune thyroiditis and the lymphocytic infiltration in the autoimmune process may be an etiological factor.

TNM staging for papillary and follicular carcinoma[70,71]

(AJCC 2010)

Primary Tumor (T)

TX Primary tumor cannot be assessed

T0 No evidence of primary tumor

T1 Tumor 2 cm or less in greatest diameter, limited to the thyroid

T1a Tumor 1 cm or less, limited to thyroid

T1b Tumor more than 1 cm but not more than 2 cm in greatest dimension, limited to the thyroid

T2 Tumor> 2 cm and <4 cm in greatest diameter, limited to the thyroid

T3 Tumor> 4 cm in greatest diameter and limited to the thyroid or any tumor with minimal extrathyroidal extension (e.g., extension to sternothyroid muscle or perithyroidal soft tissues)

T4a Moderately advanced disease

Tumor of any size extending outside the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve

T4b Very advanced disease

Tumor invading prevertebral fascia or encases carotid artery or mediastinal vessels

All anaplastic carcinomas are considered T4 Tumors

T4a Intrathyroid anaplastic carcinoma

T4b Anaplastic carcinoma with gross extrathyroid extension

Regional Lymph Nodes (N):

NX	Regional nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
N1a	Metastasis to level VI (pretracheal, paratracheal, and prelaryngeal nodes)
N1b	Metastasis to unilateral, bilateral, or contralateral cervical (levels I, II, III, IV or V) or retropharyngeal or superior mediastinal lymph nodes (Level VII)

Distant Metastasis (M)

MX	Distant metastasis cannot be assessed
MO	No distant metastasis
M1	Distant metastasis

Clinical Stage Grouping

Papillary or Follicular (Defferentiated)

	<45 years	45 years & above
Stage I	Any T, any N, MO	T1, NO, MO
Stage II	Any T, any N, M1	T2, NO, MO
Stage III		T3, NO, MO
		T1-3, N1a, MO
Stage IV a		T1-3, N1b, MO
		T4a, NO-1b, MO
Stage IV b		T4b, Any N, MO
Stage IV c		Any T, Any N, M1

Medullary Carcinoma (All age groups)

Stage I	T1, N0, M0
Stage II	T2-3, N0, M0
Stage III	T1-3, N1a, M0
Stage VIA	T1-3, N1b, M0
	T4a, N0-1b, M0
Stage VIB	T4b, any N, M0
Stage VIC	Any T, Any N, M1

Anaplastic Carcinoma

All anaplastic carcinomas are considered Stage IV

Stage IVA	T4a, Any T, M0
Stage IVB	T4b, Any T, M0
Stage IVC	Any T, Any N, M1

Stage unknown

Prognostic Risk Classification for Patients, with Well Differentiated Thyroid Cancer (AMES or AGES)[2]

	Low Risk	High Risk
Age	< 40 years	> 40 years
Sex	Female	Male
Extent	No local extension, Intrathyroidal, no capsular invasion	Capsular invasion, Extrathyroidal extension
Metastasis	None	Regional or distant
Size	< 2 cm	> 4 cm
Grade	Well differentiated	Poorly differentiated

Other Risk Group Classification[72]

Memorial Hospital GAMES	**Mayo clinic 1987 AGES**	**Mayo clinic 1993 MACIS**	**Lahey clinic AMES**	**Karolinska Institute DAMES**
Grade	Age	Distant Metastasis	Age	DNA
Age	Grade	Age	Metastasis	Age
Metastasis	Extension	Completeness of resection	Extension	Metastasis
Extension	Size	Invasion	Size	Extension
Size		Size		Size

DIFFERENTIATED CARCINOMA

Papillary Carcinoma

It is most common of thyroid malignancies. The size of the tumor ranges from microscopic to huge. Grossly most cases are solid, whitish, firm, and clearly invasive. Marked cystic changes are seen in 10 % of cases, most of them are bilateral and multifocal (30- 87.5 %).

Microscopically the diagnosis of papillary carcinoma depends on the presence of certain architectural features and / or characteristic nuclear changes. The papillae are usually complex, branching and randomly oriented with a central fibrovascular core and a single or stratified lining of cuboidal cells. Tumors with a combination of papillary and follicular structures have the biologic behavior of papillary carcinoma and should therefore be classified as such.

Nuclear features consist of: 1) ground glass nuclei, 2) nuclear pseudo inclusions, 3) nuclear grooves. A characteristic fibrovascular stroma with calcium deposits (Psammoma bodies) may be present.[74] Most, if not all, anaplastic carcinomas arise as a result of anaplastic transformation of a pre-existing well differentiated carcinoma, usually papillary carcinoma. Coarse calcification is common and can be prominent enough to be detectable radiologically. Recurrence is not very uncommon in these patients after surgery.

Follicular Carcinoma

More common in women (female:male ratio is 3:1). Usually presents as a solitary nodule. These appear to be macroscopically encapsulated but microscopically there is invasion of the capsule and of the vascular spaces in the

capsular region. Multiple foci are seldom seen and lymph node involvement is much less common than in papillary carcinoma. Blood borne metastasis is almost twice as common and the eventual mortality rate is twice as high.

Hürthle Cell Tumor

These tumors are a variant of follicular cell neoplasms in which oxyphil (Hürthle, Askanazy) cells predominate histologically,

They are more often multifocal and bilateral, are more likely to metastasize to local nodes and usually do not take up I^{131}.

MANAGEMENT[70]

Operative Treatment

Surgical therapy for the majority of well differentiated thyroid carcinomas should be tailored to the eradication of macroscopic disease while preserving the patient's capacity for functional speech and swallowing and parathyroid preservation. For patients considered at high risk, total thyroidectomy is the procedure of choice. Controversy over the extent of thyroid surgery in low risk patients is well documented. The benefits offered in local control and survival with the use of postoperative RAI and thyroid hormone suppression are compelling evidence favoring total thyroidectomy (for tumors more than 1.5 cm) to give patients access to these adjunctive therapies.

Use of intra operative frozen section histopathology examination of tissue is also a controversial topic. Its use is reasonable in a patient with the cytological diagnosis of follicular neoplasm or findings suspicious for papillary carcinoma but not diagnostic for carcinoma.

For patients undergoing a second procedure in a previously operated bed, the laryngeal electromyogram can be helpful to monitor the recurrent laryngeal nerve.

The locally invasive presentation of well differentiated thyroid carcinoma occurs in less than 5 % of all cases. The most common pathology is papillary carcinoma.

Regional Metastasis

Cross communication of lymphatics may occur with the contralateral lobe and isthmus. First-echelon nodal drainage is to the paralaryngeal, paratracheal, and the prelaryngeal (Delphian) nodes generally considered to be level VI. The second level of drainage includes the upper, mid, and lower jugular nodal groups (level II, III and IV) in addition to the inferior spinal accessory nodes (level V). Bilateral spread is common. Regional spread to levels Ia and Ib submental and submandibular nodal groups is uncommon.

Occult nodal metastasis may occur in upto 90% of cases. Bilateral spread is seen in 30% of cases. Mediastinal spread may occur in about 15% of patients. Level I spread accounts for fewer than 5%. Although elective neck dissection in the setting of papillary carcinoma will detect occult spread in approximately 50% of patients, the performance of the neck dissection is reported to have no impact on survival.

Routine performance of radical and modified radical neck dissections is not necessary in the setting of limited, well defined regional disease. Functional (level II-V) and selective (anterolateral level II - IV) neck dissections allow the

removal of macroscopic disease while minimizing the risk of associated complications.

Anaplastic carcinoma

It is uncommon and represents less than 2% of all thyroid cancers; it is marked by an aggressive course of rapid growth and local tissue invasion. The malignancy is typically fatal with a mean survival of 6 months after diagnosis. Anaplastic carcinoma does not concentrate iodine or express thyroglobulin. It is seen most commonly in elderly as a rapidly enlarging thyroid mass marked by pain, dysphagia, hoarseness and occasionally dyspnea with extensive local invasion of surrounding tissue.

Treatment[72]

The role of surgeon in the management of patients with anaplastic thyroid carcinoma is clearly to establish tissue diagnosis and to provide management of the airway. Surgical resection is generally not recommended, the only exception being a very small primary tumor contained within the capsule of the thyroid gland which happens to be histologically an anaplastic tumor. Tracheostomy is seldom indicated since it may prove to be a frustrating technical challenge and indeed may be quite hazardous. On the other hand, establishment of a safe airway can be accomplished with endotracheal intubation until further definitive is undertaken.

Medullary carcinoma

These are tumors of the parafollicular C - cells derived from the neural crest. There is a characteristic amyloid stroma. High levels of serum calcitonin (>0.08 mg/ml) which is also a valuable tumor marker, is produced by many medullary tumors. Its level falls after resection and will rise again if the tumor recurs. Diarrhea is a feature in 30% of patients. Medullary carcinoma may occur in combination with adrenal pheochromocytoma and hyperparathyroidism (due to hyperplasia) - MEN IIa (Sipple's Syndrome). When familial form is associated with mucosal neuromas, marfanoid habitus, the syndrome is referred to as MEN IIb.

Lymph node involvement is seen in 50-60% of cases and blood borne metastasis is common. Histologically characteristic features are cell bells and amyloid.

Treatment[75]

Total thyroidectomy with central compartment neck dissection has become a standard therapy for sporadic and hereditary types. Radiation therapy is used as an adjuvant for patients with extensive soft tissue or significant extracapsular extension in positive nodes after removal of all gross disease. It may also be considered for palliative control of inoperable disease. Calcitonin and CEA levels should usually be assessed for baseline levels approximately 4 weeks after surgery.

Metastatic Carcinoma

Thyroid gland is a rare site of metastasis from other cancers, e.g. kidney, breast, lung and melanoma; most common among them is hypernephroma. Approximately 3 % of bronchogenic carcinoma metastasizes to thyroid and these account for 20 % of secondary metastasis to thyroid. Clinical examination and history often suggests the source of the metastatic disease and FNAC usually provides definitive diagnosis. Resection of the thyroid, usually lobectomy, may alleviate symptoms in symptomatic cases.[3]

Lymphomas

Thyroid lymphomas are usually B cell in type and are regarded as being related to mucosa associated lymphoid tissue (MALT). Response to irradiation is good and radical surgery is unnecessary once the diagnosis is established by biopsy. In patients with tracheal compression, isthmusectomy is the most appropriate form of biopsy although the response to therapy is so rapid that this should rarely be necessary unless there has been difficulty in making a histological diagnosis. The prognosis is good if there is no involvement of cervical lymph nodes. Rarely, the tumor is part of widespread malignant lymphoma disease, and the prognosis in these cases is worse.

Sarcomas

Malignant hemangioendothelioma, though rare is the most common thyroid sarcoma. Other sarcoma like fibrosarcoma, leiomyosarcoma, liposarcoma and osteogenic sarcoma can occur very rarely.

Material & Methods

MATERIALS AND METHODS

A prospective study was carried out on 58 patients of nodular thyroid swelling between 11-70 year age group, attending the Surgery OPD of Sri B. M. Patil Medical College, Hospital and Research Centre, Bijapur, during the period of October 2010 to May 2012.

INCLUSION CRITERIA:

Patients of all age groups & both sexes with complaint of thyroid swelling.

EXCLUSION CRITERIA:

1) Patients of thyroid nodules not fit for surgery.

2) Patients of thyroid nodules who refused for surgery.

3) Patients with non-nodular swelling of thyroid.

4) Patients of thyroid nodules who did not gave consent.

All patients were examined clinically after taking a detailed history. Then, they were investigated with FNAC and USG of the thyroid. High resolution 7.3 MHz probe was used. The results of FNAC were interpreted as benign, malignant, suspicious and inadequate aspirate. Sonographically, the nodules were evaluated for size, location, echotexture, margins, presence of halo, calcification, accessory nodules, associated cervical lymphadenopathy and consistency (solid, cystic or mixed) in order to differentiate between benign and malignant nodules. Then, all the patients were subjected to surgery and histopathological examination (HPE) of the specimen obtained. Finally, the histopathology reports were correlated with

the findings of FNAC and USG in order to evaluate their sensitivity and specificity by statistical methods.

SAMPELLING:

Study period: from October 2010 to May 2012.

All the patients admitted during this period, who fulfilled the inclusion criteria, were included in this study.

The incidences of thyroid nodules in patients with thyroid swelling are as follows:-

- uninodular → 39.52%
- multinodular → 47.31%

So, the cumulative incidence → 86.83%

Allowable error is considered as 10%.

Formula used to calculate the sample size is

$$n = [(1.96)^2 \times p \times (1-p)]/L^2$$

Using this formula, the minimum sample size is n= 57.

Following statistical tests were used to compare the results:

i) Mean ± S.D.

ii) X^2 Test

iii) Diagrammatic presentation

RESEARCH HYPOTHESIS:

Diagnosis & management of thyroid nodule is done more accurately by combination of clinical examination, Fine Needle Aspiration Cytology and Ultrasonography than individual techniques alone.

INVESTIGATIONS

1) Blood – Hemoglobin, Total Count, Differential Count, Erythrocyte Sedimentation Rate
2) Random Blood Sugar, Blood Urea, Serum Creatinine,
3) Blood grouping and Rhesus typing, Bleeding Time & Clotting Time.
4) Urine - Sugar, Albumin & Microscopy.
5) T3, T4 & Thyroid Stimulating Hormone.
6) Ultrasonography of Neck.
7) Fine Needle Aspiration Cytology of thyroid nodule.
8) X-ray of neck & indirect laryngoscopy.
9) Electro-cardio-gram and Chest X-ray (when age of patient is >35yrs, or if necessary).
10) Histopathology of thyroid specimen.

Observations & Results

OBSERVATION AND RESULTS

The present study deals with the clinical evaluation, FNAC, and USG of the thyroid nodules and determination of diagnostic accuracy of FNAC and USG with histopathology findings.

I. Age

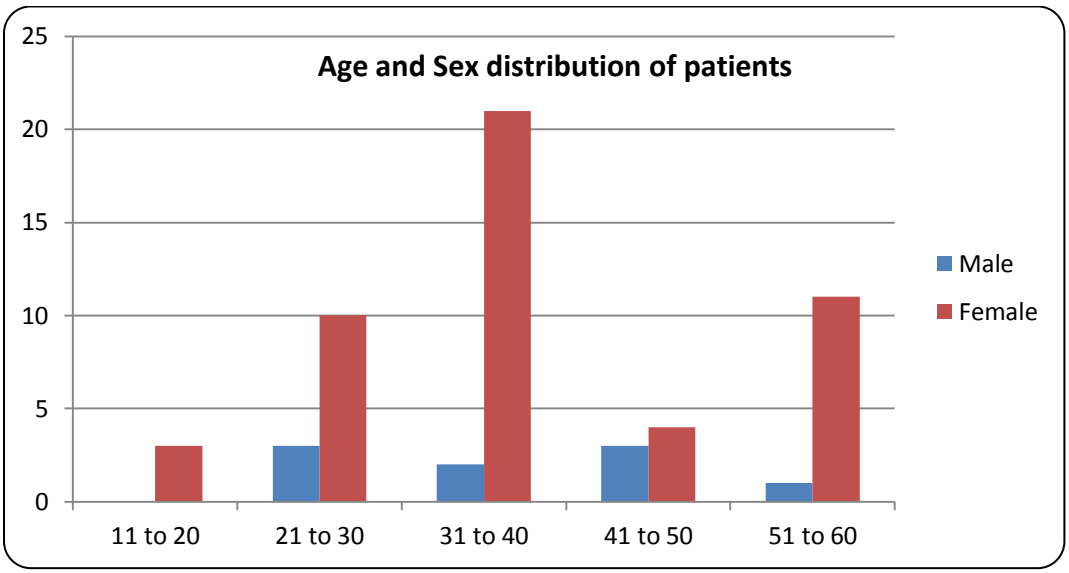
The age of the patients ranges from 11-60 years. The commonest age group with thyroid pathology is between 31-40 years.

Table 1: Age and Sex distribution of patients

Age	Male	Female	Total
11 – 20	0	3	3
21 – 30	3	10	13
31 – 40	2	21	23
41 – 50	3	4	7
51 – 60	1	11	12

II. Sex

Majority of the patients were females. Females accounted for 49 (84.48 %) of the total 58 patients and male to female ratio is 1:5.44.



III. Presenting Complaints

The commonest mode of presentation is swelling in the region of the thyroid in anterior neck. All 58 (100%) patients presented with the swelling. Six patients presented with pain in the swelling, one with difficulty in breathing and 3 with difficulty in swallowing. Among 6 patients with thyroiditis, 4 presented with associated history of recent onset of pain. Three of the patients who presented with thyroid swelling had cervical lymphadenopathy on clinical examination. No patient complained of swelling on other parts of the body. No patient had any change in voice or history suggestive of hypo/hyperthyroidism features. Two patients of papillary carcinoma of thyroid presented with associated history of pain and 2 patients of nodular goiter with cystic change presented with pain.

Table 2: Presenting Complaints

SI.No.	Presenting Complaint	No. of Patients
1	Swelling in front of neck	58
2	Pain in the swelling	06
3	Difficulty in breathing	01
4	Difficulty in swallowing	03
5	Change of voice	01
6	Hypo / hyperthyroidism features	--

IV. Duration of complaints

The duration of complaints ranged from 1 week to 8 years. Eight patients presented with history of recent onset of pain. Four (8%) patients had sudden onset of symptoms. Twelve percent patients presented within 1 month of onset of symptoms. Majority of the patients, i.e. 28 (56%), presented between 6 months to 3 years.

V. Family History and Past History

None of the patients had any significant history.

VI. Clinical Diagnosis

The most common clinical diagnosis was multinodular goiter, i.e. 37 (63.79%) patients. Solitary nodule of the thyroid was found in 21 (36.20%) patients.

Table 3: Distribution of cases on clinical diagnosis

SI. No	Clinical Diagnosis	No. of Patients
1	Solitary nodule	21
2	Multinodular goiter	37

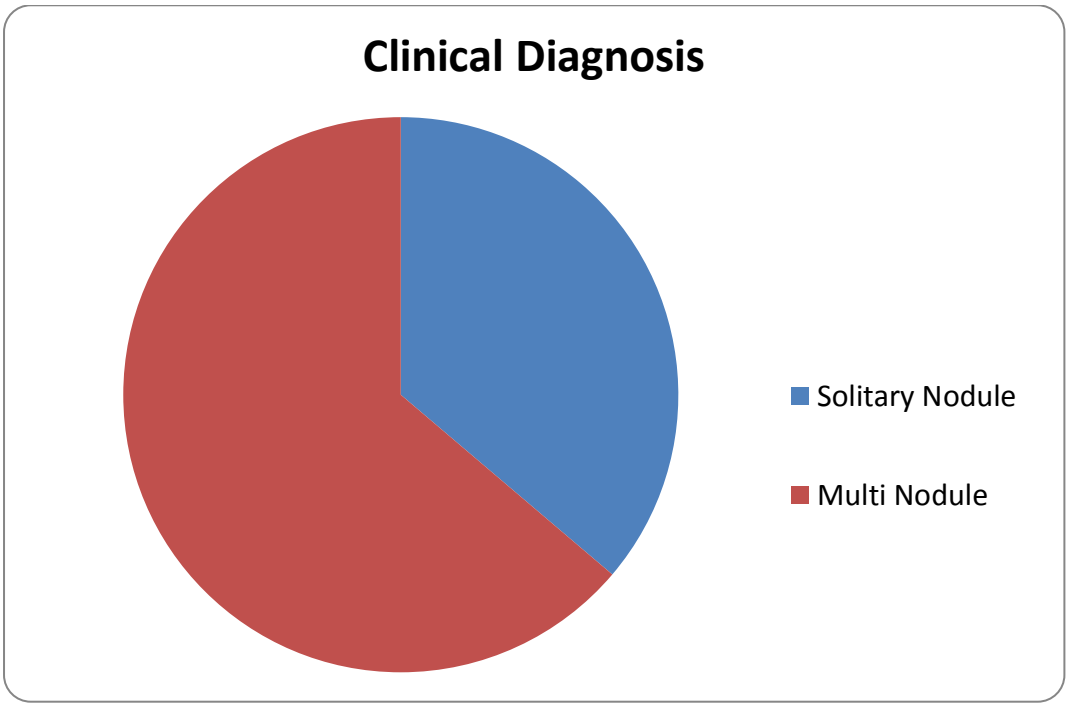


Table 4: Comparison of clinical diagnosis with histopathology

Clinical Diagnosis	No. of Patients	Histopathological diagnosis	No. of patients
Solitary nodule of thyroid	21	Benign cystic lesion	4
		Multinodular goiter	6
		Hashimoto's thyroiditis	2
		Follicular adenoma	2
		Follicular carcinoma	2
		Papillary carcinoma	5
Multinodular goiter	37	Multinodular goiter	29
		Hashimoto's thyroiditis	4
		Follicular adenoma	1
		Follicular carcinoma	3

Among 21 patients with solitary nodule of thyroid, 7 (33.33 %) were malignant. In 37 patients with multinodular goiter, 3 (8.10 %) were malignant.

VII. Fine Needle Aspiration Cytology

In the present study, non-neoplastic lesions were more commonly encountered than the neoplastic lesions.

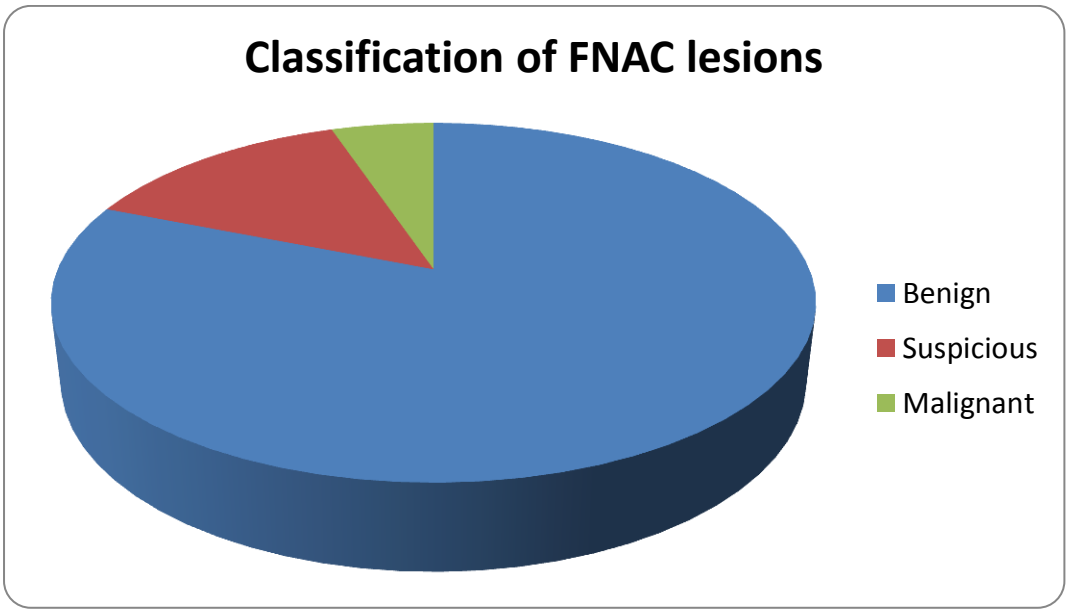
1. Classification of FNA lesions

Cytological evaluation of the smears was performed based on standard criteria reported in the literature. The 4 recognized categories are malignant (3.4 % to ~5 %), benign (60 % to ~75 %), suspicious (7.2 % to ~30 %) and insufficient or inadequate (7% to ~29.5%).[21,27,28] The 'malignant' category includes nodules that have unequivocal typical cytological characteristics of a malignant neoplasm. This category includes papillary, medullary, poorly differentiated or

undifferentiated thyroid cancers, lymphomas, and metastatic non thyroid cancer.[21] 'Benign' reports include hyperplastic colloid nodule and chronic inflammatory lesions.[21,27] The category of 'suspicious' lesions of FNA is due to the inability to unequivocally detect cytological features of either benign or malignant neoplasms. The most common cause is the inability to differentiate a follicular adenoma from a well differentiated follicular carcinoma. 'Non-diagnostic' reports are caused by the lack of cellular components in the aspirate or because of improper handling of the specimen.

Table 5: Classification of FNAC lesions

Sl. No	Category	No. of Cases	Percentage
1	Benign	47	81.03
2	Suspicious	8	13.79
3	Malignant	3	5.17
4	Inadequate	0	0



In comparison to all literature, the benign category occupies the major group with 47 (81.03%) cases, followed by suspicious, 8 (13.79%) cases and malignant 3 (5.17%) cases.

There was no inadequate or insufficient cytological smear.

2. Benign lesions

In the present study, among 58 patients, colloid nodule was most common lesions, accounting for 39 (67.24%), followed by adenomatous goitre, i.e. 6 (10.34%).

Table 6: Distribution of benign lesion on FNAC

Sl. No.	Lesions	No. of Cases
1	Colloid goiter	39
2	Adenomatous goitre	6
3	Cystic lesion	2

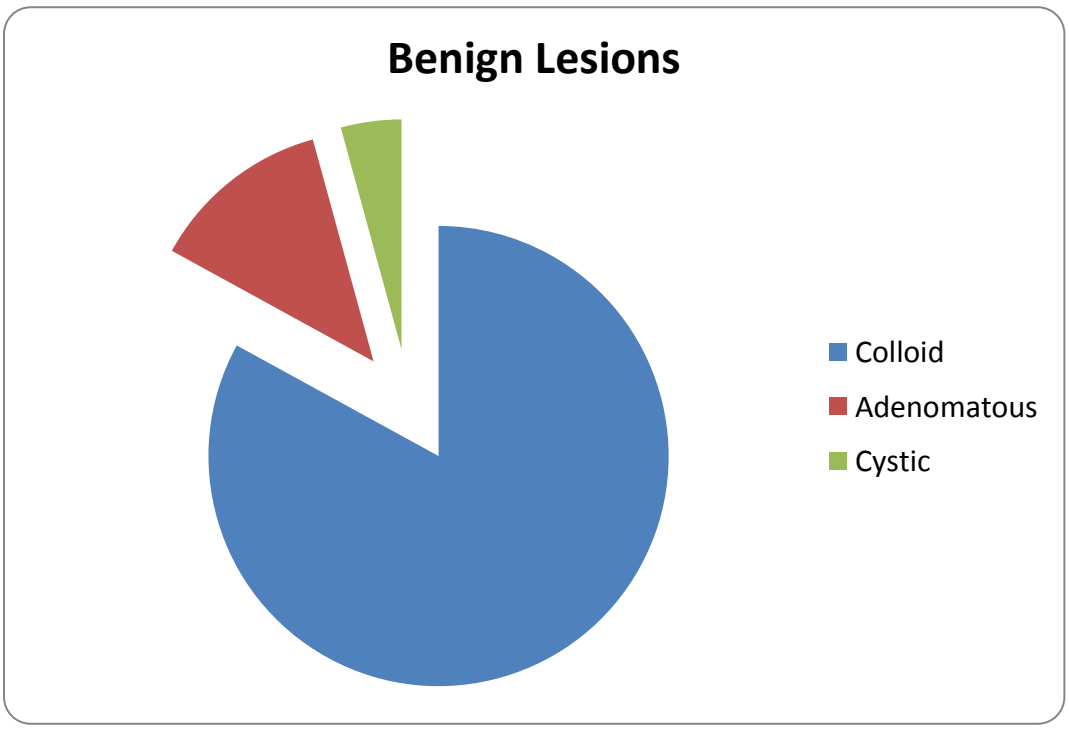


Table 7: Histopathological correlation of benign FNAC lesions

SI. No	FNAC lesions	No. of cases	Histopathological diagnosis	
1	Colloid goiter	39	Benign cystic lesion	03
			Multinodular goitre	34
			Hashimoto's thyroiditis	01
			Papillary carcinoma	01
2	Adenomatous goitre	6	Hashimoto's thyroiditis	05
			Multinodular goitre	01
3	Cystic lesion	2	Benign cystic lesion	01
			Papillary carcinoma	01

Of 39 cases of colloid goiter, 38 cases proved to be benign but one case was diagnosed as papillary carcinoma. In the category of benign cystic lesion, one case proved to be benign and one was papillary carcinoma. In 47 cytologically diagnosed benign cases, 2 case was found to be malignant by histopathology.

2. Malignant lesions on FNAC

In the present study, among 58 cases, only malignant lesion found was papillary carcinoma, in 3 (5.1%) cases.

Table 8: Histopathological correlation of malignant FNAC lesions

SI. No	Cytological diagnosis	No. of cases	Histopathological diagnosis	No. of cases
1	Papillary carcinoma	3	Papillary carcinoma thyroid	03

All cases of papillary carcinoma on FNAC diagnosis were confirmed by histopathology.

3. Suspicious lesion on FNAC

Eight cases were diagnosed as 'suspicious' lesions on FNAC, due to the inability to unequivocally detect cytological features of either benign or malignant neoplasms. All cases were of follicular neoplasia.

Table 9: Comparison of suspicious lesions with histopathology

FNAC diagnosis	No. of Cases	Histopathology diagnosis	No. of cases
Follicular neoplasia	8	Follicular adenoma	3
		Follicular carcinoma	5

All the 8 cases of follicular neoplasia were subjected to surgery and correlated with histopathology. Five cases were found to be malignant and 3 cases to be benign.

Table 10: Malignant histopathological diagnosis – correlation with FNAC diagnosis

Histopathological diagnosis	No. of Cases	FNAC diagnosis	No. of Cases
Papillary carcinoma	05	Cystic nodule	01
		Colloid goitre	01
		Papillary carcinoma	03
Follicular carcinoma	05	Follicular neoplasm	05

Of the 5 cases of papillary carcinoma of thyroid, FNAC revealed papillary carcinoma in 3 cases with a concordance rate of 60% and benign in 2 (40%) case.

VIII. Histopathological diagnosis

Table 11: Results of histopathological diagnosis

Sl. No.	Histopathological diagnosis	Number (%)
1	Benign cystic lesion	4 (6.89)
2	Follicular adenoma	3 (5.17)
3	Follicular carcinoma	5 (8.62)
4	Hashimoto's thyoriditis	6 (10.34)
5	Multinodular goitre	35 (60.34)
6	Papillary carcinoma	5 (8.62)

The most common lesion is multinodular goitre 35 (60.34%) and the least common is follicular carcinoma 3 (5.17%).

Table 12: Correlation of FNAC with histopathology

Histopathological diagnosis	FNAC diagnosis				Total
	Benign	Suspicious	Malignant	Inadequate	Total
Benign	45	03	00	00	48
Malignant	02	05	03	00	10
Total	47	08	03	00	58

The cytological diagnosis of benign nodule was confirmed in 45 (95.75%) of the 47 patients and was disputed in 2 (4.25%) which was shown to be malignant. In 8 cytologically suspicious cases, histopathology revealed benign lesion in 3 cases and malignant in 5 cases. All 3 malignant interpretations on cytology were confirmed by histopathology.

Hence, the sensitivity and specificity of FNAC in thyroid nodule in the study is 80% and 93.75%, respectively.

IX. Ultrasonography

Taking into consideration of the various ultrasonographical features, cases were classified in to benign, suspicious and malignant.

Table 13: Distribution of lesions on USG

Category	No. of Cases	Lesion	No. of Cases
Benign	43	Cystic	04
		Hyperechoic nodule	08
		Multinodular goitre	31
Suspicious	08	Suspicious multinodular goitre	08
Malignant	07	Mixed echogenic nodule	07

Table 14: Correlation of USG with histopathological diagnosis

Histopathology diagnosis	USG Diagnosis			Total
	Benign	Suspicious	Malignant	
Benign	40	04	04	48
Malignant	03	04	03	10
Total	43	08	07	58

The USG diagnosis of benign lesion was confirmed in 40 (93.02%) out of 43 cases and was disputed in 3 (6.97%) cases by histopathology which turned out to be malignant. In the eight USG suspicious lesions, histopathology revealed benign in four cases and malignant lesion in four cases. Among seven USG

diagnoses of malignant lesions, three were confirmed by histopathology, and four were diagnosed to be benign.

Hence, the sensitivity and specificity of USG in thyroid nodule in the study is 70% and 83.33%, respectively.

Also, among total 58 cases, 37 cases had multiple thyroid nodules on clinical examination, but USG revealed multiple nodules in 42 cases. Thus USG is more sensitive diagnostic modality to detect nodualarity.

Table 15: Assessment of nodularity by various methods

Modality	Nodularity	
	Solitary	Multiple
Clinical examination	21	37
USG	16	42

X. Types of Surgeries performed

The least procedure, but most commonly done for thyroid, was hemithyroidectomy. Among 2 near total thyroidectomies, one was done for papillary carcinoma and the other for Hashimoto's thyroiditis. Subtotal thryoidectomy was mainly done for MNG.

Table 16: Types of surgeries performed

SI. No	Type of Surgery	No. of Cases
1	Hemithyroidectomy	18
2	Subtotal thyroidectomy	17
3	Near total thyroidectomy	2
4	Total thyroidectomy	9
5	Functional neck dissection	3

The commonest performed surgery in our series is hemithyroidectmoy, which accounts to 18 (31.03%) cases. Functional neck dissection was done in all 3 cases of papillary carcinoma of thyroid as lymph nodes were palpable.

XI. Post-Operative Complications

Among 58 cases, the commonest and the only postoperative complication was transient hypocalcaemia in 4 (6.89%) of cases found in total thyroidectomy cases, which was subsided at the end of 1 week. There was no evidence of recurrent laryngeal nerve injury.

Analysis & Discussion

ANALYSIS AND DISCUSSION

In the present study age of the patient ranged from 11-60 years with a median age of 35 years. Age distribution of the present study is comparable to Jose to RJ et al.

Table 17: Age range and median' age of different studies[76, 77, 78,79,80,81]

Authors	Range of age	Median age
Tabaqchali et al (2000)	8.5-85	48
Sekhri et al (2001)	9-70	33.9+11
Jose R. J et al (2002)	17-65	35.5
Afroze N et al (2002)	16-78	40.2
Mitra R. B et al (2002)	16-70	39.6
Present study	11-60	35

The number of males in the present study was 9 (15.51%) and the females were 49 (84.48%) with a male to female ratio of 1:5.44. Sex distribution was similar when compared to Jose et al.

Table 18: Sex distribution and male to female ratio in different studies

Series	Total cases	Male	Female	M:F Ratio
Burch HB et al (1996)	422	91	331	1:3.6
Sekhri T et al (2001)	300	44	256	1:6
Tabaqchali et al (2000)	239	26	213	1:8.2
Popivanov et al (2000)	175	10	165	1:16.5
Jose RM et al (2002)	98	16	82	1:5.1
Afroze et al (2002)	170	48	122	1:2.54
Present study	58	9	49	1:5.44

The commonest clinical presentation is the presence of swelling in front of the neck and majority presented between 6 months to 3 years.

Aspiration was done from 2-3 sites. Afroze et al. suggests repeated aspiration 2-3 times from different areas of the gland in case of larger nodules. Gharib et al. suggests upto six aspirations and an average of 2-4 aspirations.

When FNAC reports of 8 patients with thyroid carcinoma was checked, it was found that 3 out of 8 cases had a correct preoperative diagnosis and 3 cases were reported as suspicious and 2 case as benign. A 37.5% concordance between the histological and cytological diagnosis was found which rose to 75% on inclusion of the suspect cases as positive cases. Altavilla and Pascale et al. reported in their series a 45.83% concordance between the histological and cytological diagnosis which on including the suspect cases as cytologically positive rose to 70%.

The overall sensitivity in our series was 80%, while the specificity was 93.75% as all malignancies reported on FNAC were correctly confirmed by final histopathology.

Table 19: Comparison of FNAC results

Study	Sensitivity (%)	Specificity (%)
Altavilla et al	71.43	100
Goellner et al	98	99
Bouvet al	93.5	75
Present study	80	93.75

FNAC has certain limitations because of suspicious diagnosis. In present series, 8 (13.79%) cases were found to be suspicious, out, of which 5 were found to be malignant on final histopathology examination. Thus, an overall malignant

rate of about 62.5% for the suspicious group was found. Because of this high incidence of malignancy in suspicious lesions, surgical removal of these nodules should be strongly considered in these cases.

The overall incidence of malignancy in solitary thyroid nodules varies from 10-30% according to various studies. In our study, the overall incidence of malignancy in solitary nodule was 33.33%. Complication due to aspiration cytology is rare. However, a few unusual complications have been reported in literature. In the present study, no complications were observed following aspiration procedure and all the patients tolerated the procedure well.

The thyroid nodules on USG were subdivided in to 3 groups-benign, suspicious and malignant on the basis of various sonographic features. Features suggestive of malignancy on USG are – hypoechoic pattern, incomplete peripheral halo, irregular margins, internal micro calcification, presence of cervical Lymphadenopathy and peripheral degeneration in mixed nodules. Features suggestive of benign diseases on USG are – halo sign (transonic uniform rim surrounding the mass), variable echogenicity, multi nodularity, large cystic lesion, diffusely nodular inhomogeneous gland and peripheral calcification.

USG correctly diagnosed malignancy in 2 patients when FNAC failed to achieve the correct diagnosis. In our study, out of 7 cases diagnosed to be malignant on USG, 4 cases were confirmed on histopathology and remaining 2 cases were differed to be benign. In 3 cases in whom USG gave false negative diagnosis of benign disease, histopathology revealed papillary carcinoma in one and follicular carcinoma in two cases.

In present study, we found the sensitivity and specificity of USG in detecting malignancy to be 70% and 83.33% respectively.

Table 20: Comparison of USG results

Series	Sensitivity (%)	Specificity (%)
Watters et al	74	83
Jones et al	75	61
Present study	70	83.33

Watter et al. interpreted an USG report as suggestive of malignancy if the nodule was solid or of a mixed solid-cystic variety and a hypoechoic and nonhaloed lesion. They emphasized that the USG has added advantage of allowing the whole gland to be examined rather than the dominant nodule but was limited by the fact that no features were pathognomic for malignancy, so that it should be regarded as complementary rather than an alternative investigation to FNAC in the management of solitary thyroid nodules.

It has been a consistent observation according to published literature, that the risk of thyroid cancer is less with multiple nodules than with the solitary nodules, as was also seen in this study (8.1% vs. 33.33%, respectively). High resolution real-time USG is far better than clinical examination in detecting thyroid nodularity. Walker et al. have shown that the prevalence of multinodularity in clinically solitary thyroid nodules is between 20% and 40%, and it has been observed that for a thyroid nodule to be detected by palpation, it must be at least 1cm in diameter, while USG detects nodules as small as 3mm in diameter. Simeone et al. stated that the detection of more than one lesion with USG reduces the probability of malignancy to 1-6%.

Summary

SUMMARY

Total 58 cases of nodular thyroid were evaluated in Sri B. M. Patil Medical College, Hospital and Research Centre, Bijapur, from October 2010 to May 2012. The results of FNAC and USG were compared with histology.

- Nodular goiter is more common in females (M: F ratio 1:5.44)
- Majority of the patients are in the age group of 31-40 years.
- Swelling in the anterior neck was the commonest mode of presentation.
- In majority of the patients, duration of swelling prior to presentation was between 6 months to 3 years.
- On clinical evaluation of 58 patients, majority had multiple thyroid nodules (63.79%).
- The incidence of malignancy in solitary nodule of thyroid was 33.33% and 8.10% in multinodular goiter.
- On FNAC majority of the lesions were benign, with nodular goiter being the largest group (60.35%).
- Two cases proved to be papillary carcinoma of thyroid, which were diagnosed as benign on FNAC.
- All the lesions diagnosed malignant on FNAC, were proved by histopathology.
- Among suspicious lesions on FNAC, 62.50% proved to be malignant, indicating the need for surgery.
- FNAC is the diagnostic modality of choice for the initial workup of thyroid nodule with sensitivity of 80% and specificity of 93.75%.

- USG with a sensitivity of 70% and specificity of 83.33% helps in diagnosing doubtful cases.
- USG proved to be a more sensitive modality to evaluate the nodularity of the thyroid than clinical evaluation.
- Extent of the surgery depends on the nature of the lesion and the risk group classification.
- Hemithyroidectomy is the most commonly performed surgery for the thyroid (31.03%).
- Except transient post-operative hypocalcaemia, there were no complications of the surgery when meticulously done.

Conclusion

CONCLUSION

The present study was undertaken to evaluate the usefulness of clinical examination, FNAC and USG of thyroid in the management of thyroid nodules and compare the efficacy of each of the investigation.

1. Thyroid nodules are common in females of age group 31 to 40 years.
2. Commonest presenting complaint is swelling in the anterior aspect of neck
3. In our study, the sensitivity and specificity of FNAC was 80%and 93.75% respectively. All malignant lesions on FNAC were confirmed by histopathology indicating its excellence. Therefore FNAC helps in planning the correct management and avoids second surgery.
4. In our study, the sensitivity and specificity of USG was 70%and 83.33% respectively. If USG shows cystic lesion, it can be aspirated and used as a therapeutic procedure .USG could diagnose malignancy in two patients, where FNAC failed to achieve the correct diagnosis. Therefore use of ultrasound along with FNAC will improve the diagnostic accuracy to higher level and helps in better management
5. All solitary thyroid nodules needs surgery and minimal surgery is "Hemithyroidectomy". This was undertaken in all cases, which helped in establishing the histopathological diagnosis and in comparing the efficacy of above investigations.
6. The ideal test should have a sensitivity and specificity of 100%. The closest method to ideal test is, thus, FNAC which has high sensitivity and specificity. However, a combination of both FNAC and Ultrasound will give optimal results and avoids mismanagement.

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Annexure – I

Informed Consent

ANNEXURE – I

SAMPLE INFORMED CONSENT FORM

TITLE OF PROJECT: FINE NEEDLE ASPIRATION CYTOLOGY & ULTRASOUND AS DIAGNOSTIC MODALITY IN CLINICOPATHOLOGICAL EVALUATION OF THYROID NODULES.

GUIDE: Dr. M. B. PATIL M.S.
Professor of Surgery
B.L.D.E. University's
Shri B.M. Patil Medical College & Research Centre,
BIJAPUR - 586103

P.G. STUDENT: Dr. DEEPIKA PATIL
Department of General Surgery

PURPOSE OF RESEARCH:

I have been informed that this study will analyze the clinical study and management of Thyroid nodules. This study will thus help the investigator better understand for the management of above condition.

PROCEDURE:

I understand that relevant history will be taken. I will undergo detailed clinical examination after which necessary investigations will be done whenever required, which would help the investigator for appropriate management.

RISKS AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and

the procedures of this study are not expected to exaggerate these feelings, which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation in the study will have no direct benefit to me other than potential benefit of the treatment.

CONFIDENTIALITY:

I understand the medical information produced by this study will become part of my hospital record and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigator's research file. If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers, such as photographs will be used only with my special written permission. I understand that I may see the photographs before giving the permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time, Dr. Deepika Patil at the department of Surgery is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr.Deepika Patil may terminate my participation in this study at any time after she has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly then appropriate treatment would be available to me. But no further compensation would be provided by the hospital.

I understand that by my agreement to participate in this study and not waiving any of my legal rights.

We have explained to _____ the purpose of the research, the procedures required and the possible risks and benefits to the best of our ability.

_____	_____	_____
Dr. Deepika Patil	Dr. M. B. Patil	(Date)
(Investigator)	(Guide)	

I confirm that Dr. Deepika Patil, has explained to me the purpose of the research, the study procedure that I will undergo and the possible risks and discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

_____ _____

(Participant) (Date)

_____ _____

(Witness to signature) (Date)

Annexure – II

Proforma

ANNEXURE – II

SCHEME OF CASE – TAKING

Name:

Age: IP.NO:

Sex: D.O.A:

Occupation: D.O.S:

Address: D.O.D:

Chief complaints:

1. Swelling in the neck:
2. Difficulty in breathing:
3. Difficulty in swallowing:
4. Pain in the swelling:
5. Palpitation:
6. Others:

History of Presenting Illness

1. Site:
2. Duration:
3. Mode of onset: gradual/ sudden
4. Pain& Sudden increase in the size of the swelling:
5. Pressure symptoms: a} Pain and discomfort:

   b} Dyspnoea:

c} Dysphagia:

d}Change of voice:

6. Fever:
7. Others:

Toxic symptoms:

1. Appetite: Increase/decrease
2. Weight: increase/decrease
3. Intolerance: Heat/Cold
4. Sweating:
5. Anxiety:
6. Fear:
7. Behaviour changes:
8. Tremors:
9. Lethargy:
10. Palpitation:
11. Precordial pain:
12. Loss of hair:
13. Diplopia:

Past history:

1. Previous drug intake:
2. Radiotherapy or surgery:
3. Others:

Personal history:

a. Diet[brassica family, sea fish]

b. Appetite:

c. Bowel:

d. Micturition:

e. Menstrual history(in female patients):

f. Habbits:

Family history:

GENERAL PHYSICAL EXAMINATION:

1. Built:Well/moderate/poor
2. Nourishment:Well/moderate/poor
3. Facies: normal/anxious/dull
4. Hands:normal/warm and moist/cold and dry.
5. Pulse:Rate /min, Rhythm ,Volume,sleeping pulse rate
6. B.P: mmHg.
7. Pallor:
8. Icterus:
9. Clubbing:
10. Pedal edema:
11. Pretibial edema:
12. Lymphadenopathy:Regional/generalised.

Local examination:

A. Inspection

1. Site
2. Number:
3. Size:

4. Shape:
5. Extent:
6. Borders:
7. Lower border:Seen/not seen.
8. Surface:
9. Skin over the swelling:
10. Visible veins: Over the swelling/Over the chest.
11. Movement with deglutition:
12. Movement with protrusion of tongue:
13. Pulsation:
14. Surrounding area:
15. Congestion of face on lifting handsup{Pembertson's sign):
16. Horner's syndrome:

B. Palpation

1. Local rise of temperature:
2. Tenderness:
3. Size:
4. Shape:
5. Extent:
6. Borders:
7. Lower border:Made out/Not made out
8. Surface:Smooth/nodular.
9. Consistency:Soft/firm/cystic/hard,Uniform/Variable
10. Skin pinchable:yes/no.
11. Rest of gland:

12. Mobility:

13. Pulsation and thrill

14. Carotid pulsation: Present/Absent{Berry's sign)

15. Position of trachea:

16. Kocher's test:Present/Absent.

17. Regional lymphnodes:

C. Percussion over manubrium sternii:

D. Auscultation:

E. Eye Signs:

Lid retraction:

Exophthalmos:

Vongraefe's sign:+/ -

Joffroy's sign:+/ -

Stellwag's sign:+ / -

Moebius sign:+/ -

Dalrympte's sign:+ / -

Ophthalmoplegia:

Chemosis:

Systemic examination:

a. Cardiovascular system:

b. Central nervous system:

c. Respiratory system:

d. Abdomen:

e. Bones(skeletal system):

Clinical diagnosis:

Investigations:

1. Blood: Hb %:

Total count:

Differential count:

ESR:

Random Blood Sugar:

Blood urea:

Serum Creatinine:

Blood grouping and Rhesus typing:

Bleeding time: Clotting time:

2.Urine: Albumin:

Sugar:

Microscopy:

3.Thyroid function test: T3

T4

Thyroid Stimulating Hormone

4. Fine-Needle Aspiration Cytology of Thyroid nodule:

5. Ultrasound of thyroid: Right lobe Left lobe

Measurement:

Focal lesions:

Margin:

Capsule:

Halo sign:

Cystic areas:

Isthmus:

Lymph nodes:

Arteries:

Veins:

6. X-Ray neck: If needed

7. Indirect laryngoscopy:

8. Electro-cardio-gram

9. Chest X-ray

IMPRESSION:

TREATMENT:

SURGERY: Type

Operative findings:

Histopathological diagnosis:

Gross:

Microscopy:

IMPRESSION:

POSTOPERATIVE PERIOD: Eventful/Uneventful

Recurrent Laryngeal nerve injury:

Hypoparathyroidism:

Any others:

RESULT:

FNAC	USG	Histopathology

Annexure – III

Colour Plates

CLINICAL PHOTOGRAPHS

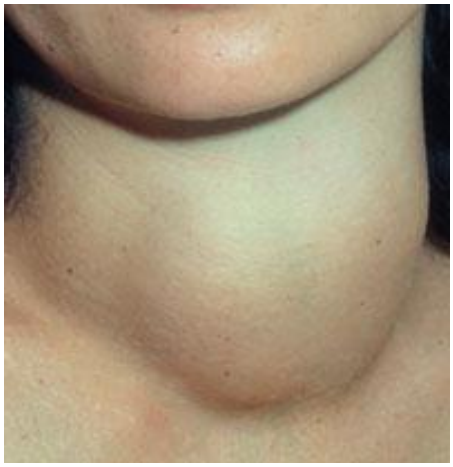


Photo 1: Solitary thyroid nodule

Photo 2: Multinodular goiter

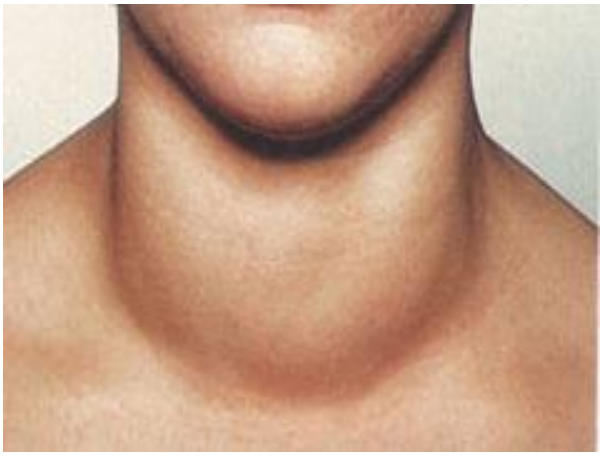


Photo 3: Solitary Thyroid Nodule

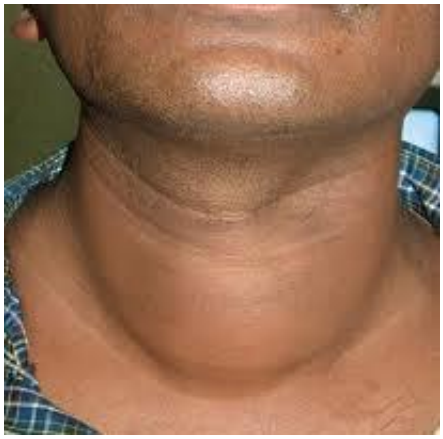
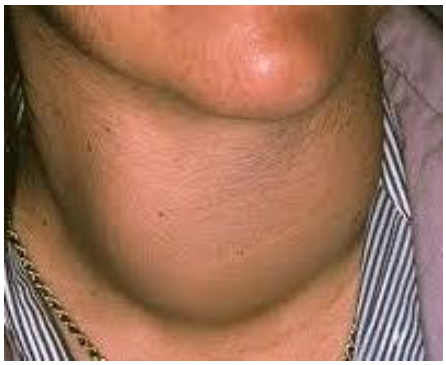


Photo 4: Multinodular goiter

Photo 5: Solitary Thyroid Nodule



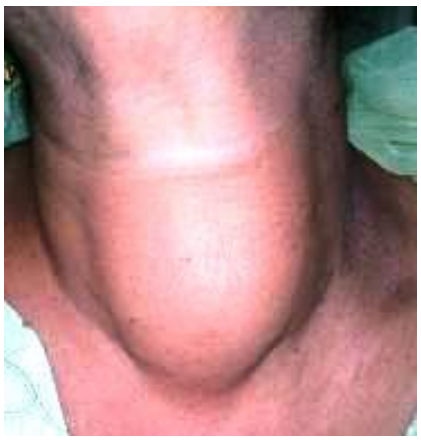


Photo 6: Solitary Thyroid Nodule

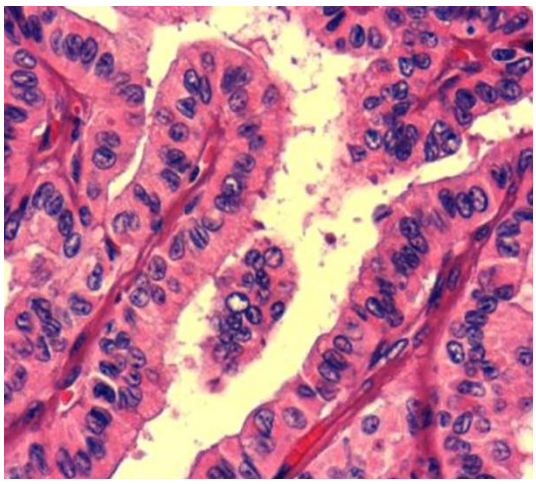


Photo 7: Histopathology

Papillary Carcinoma

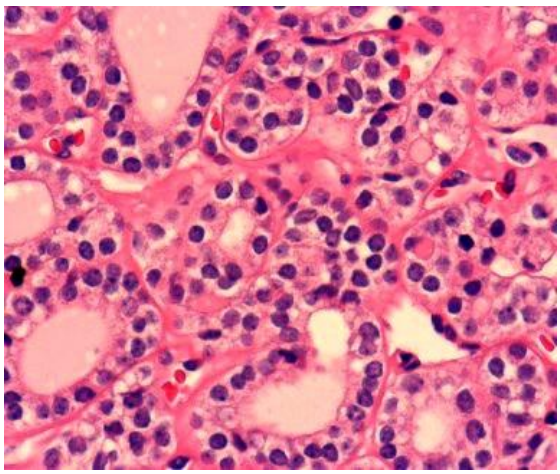


Photo 8: Histopathology

Follicular Carcinoma

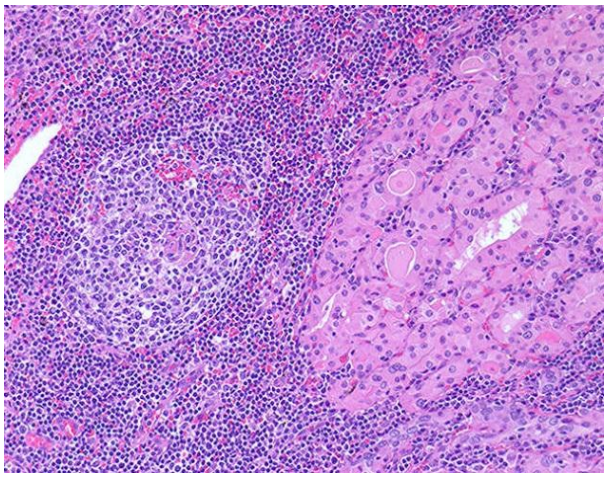


Photo 9: Histopathology

Hashimoto’s thyroiditis

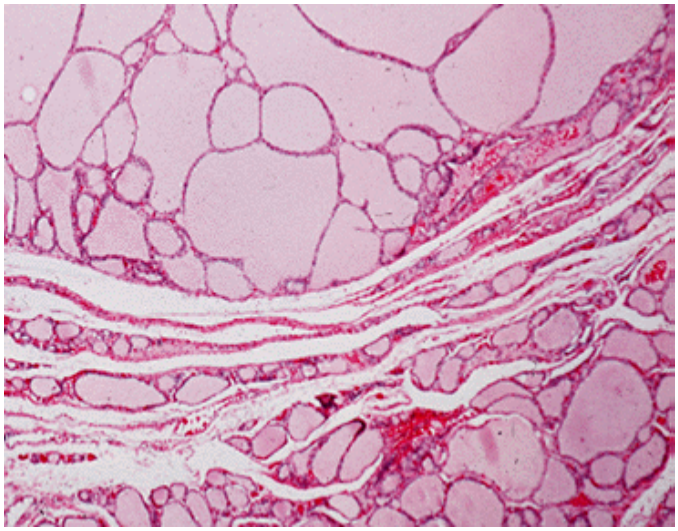


Photo 10: Histopathology

Colloid nodule

Photo 11: Histopathology

Follicular Adenoma

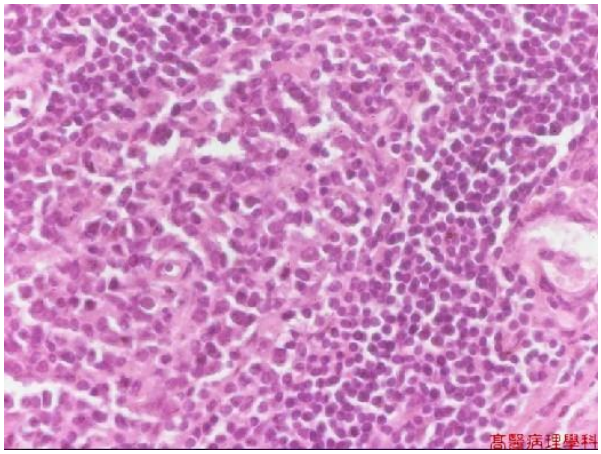
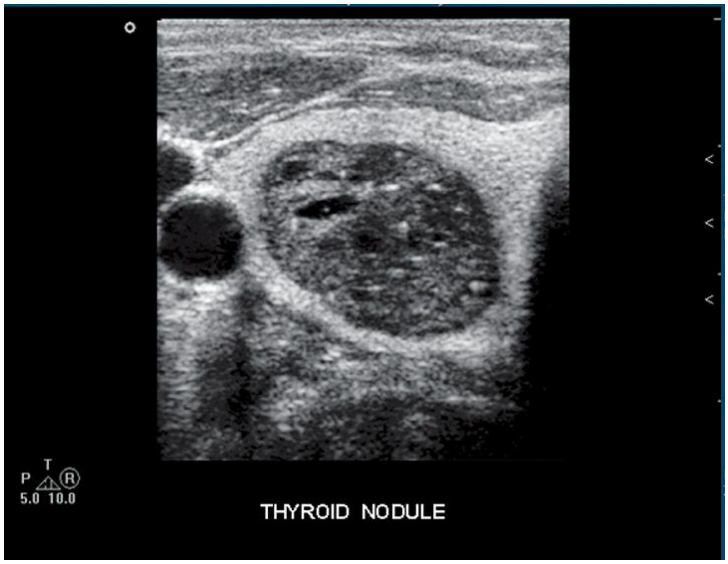
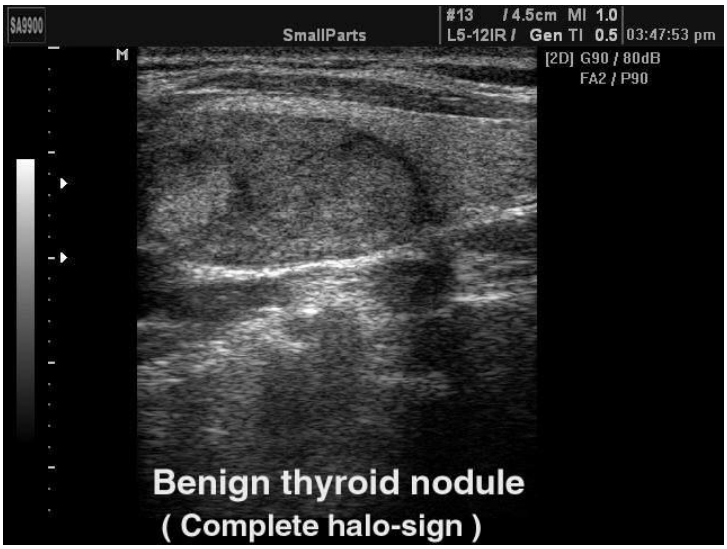


Photo 12: Ultrasound of Thyroid





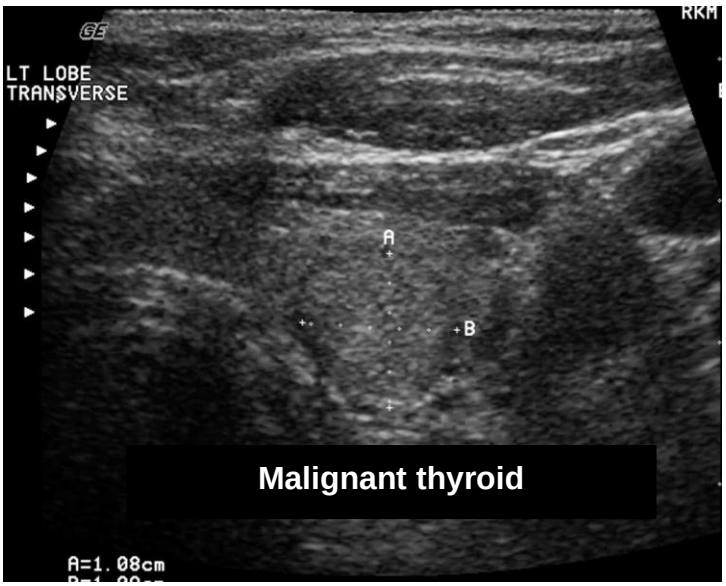
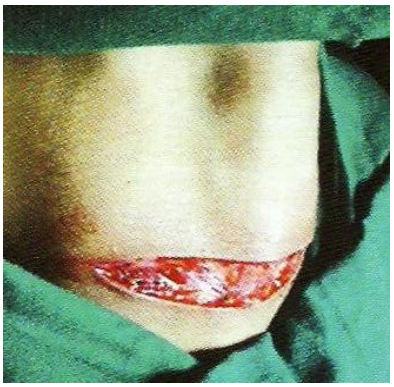
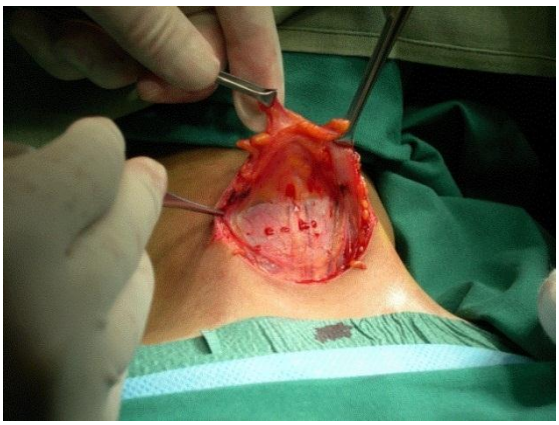


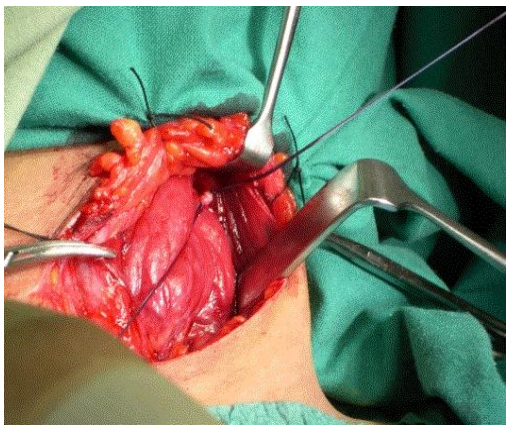
Photo 13: Operative photographs



A. Incision taken

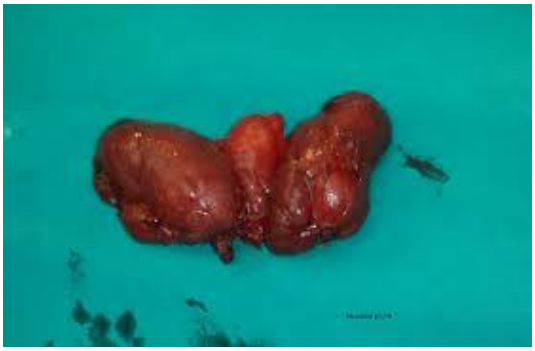
B. Upper flap raised





C. Dissection of thyroid gland

D. Specimen of total thyroidectomy



Annexure – IV

Key To Master Chart

& Master chart

ANNEXURE – IV

KEY TO THE MASTER CHART

DOA	Date of Admission
DOS	Date of Surgery
FNAC	Fine Needle Aspiration Cytology of the thyroid nodule.
USG	Ultrasonography of Neck
HPR	Histopathological Report of the resected specimen.