COMPREHENSIVE

STUDY OF THYROTOXICOSIS

Dissertation submitted to

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the degree of

M.S.degree

Branch- I

M.S. GENERAL SURGERY

March 2007

CERTIFICATE

This is to certify that **Dr.R.SUDHAGAR** postgraduate student (2004-2007) in the department of General Surgery, Kilpauk Medical college, Chennai has done this dissertation titled **"COMPREHENSIVE STUDY OF THYROTOXICOSIS"** under the direct guidance and supervision in partial fulfillment of the regulations laid down by the Tamilnadu Dr.M.G.R. medical university, Chennai, for M.S., Branch – I General Surgery degree examination.

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ACKNOWLEDGEMENT

I wish to thank our Dean **Dr.THIAGAVALLI KIRUBAKARAN, M.D.,** for having permitted me to conduct this study in this hospital.

I am ever grateful to my unit Chief **Prof.Alagappan, M.S,.M.Ch.,** for his generous help , kind guidance , valuable advice & expert supervision & encouragement throughout my carreer & for the preparation for this dissertation.

I am grateful to the Professor and Head of the Department of Surgery **Prof.P.Kulothungan, M.S.,** for his expert advice & help in preparing this dissertation.

I thank all the surgical unit chiefs **Prof.Dr.R.N.M.Francis,**M.S, **Prof.Dr.Gunaselan, M.S., Prof.Dr.M.L.Shyamala, M.S., Prof.Dr.P.Ravi, M.S.,** I thank my assistant professors **Dr.Padmanabhan**, M.S. and **Dr.Madhivadhanan**, M.S., I also thank all the assistant professors of the department of surgery for their guidance.

I also thank my co post graduates & CRRIs for their co operation. Last but not the least I express my gratitude to all the patients for their co operation.

CONTENTS

INTRODUCTION

Thyrotoxicosis is a syndrome which is caused by excessive secretion of thyroid hormone.

Goitre is derived from the *Latin word Guttur* which means throat.

The thyroid gland is first documented by Italians of the renaissance period.

The term Thyroid (*Greek Thyreoeides, Shield Shaped*) is attributed to Thomas Wharton.

Bernard courtois discovered iodine in the ash of burnt seaweed.The first accounts of thyroid surgery dates back to Roger Frugardi in 1170.

The most notable thyroid surgeons were Emil Theodor Kocher (1841 – 1917) & Theodor Billroth (1829 – 1894).

Emil Theodor Kocher of Berne is regarded by many as *Father Of Thyroid Surgery* .

In 1909, *Kocher Received The Nobel Prize* for medicine in recognition "for his works on physiology , pathology , & surgery of thyroid gland "

AIM OF STUDY

1. Review the data regarding the prevalence of Thyrotoxicosis & its association with standard variables.

2. Discuss the various clinical presentations of thyrotoxicosis.

3. Discussion of etiopathogenesis in thyrotoxicosis

4. Discussion of various treatment modalities

5. Evaluate a cost effective treatment for a country like ours

6. Discuss the complications of treatment & follow up

ANATOMY OF THYROID

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 normally weighs about 15 – 20 gm.

The gland consists of two symmetrical lobes , united in front of 2^{nd} , 3^{rd}, 4 th tracheal rings by an isthmus of the gland. The extent of thyroid gland is from thyroid cartilage to the 5^{th} or 6^{th} tracheal ring or from C3 to T1.

The lobes are approximately 4 cm long , 2 cm wide , 20 to 40 mm thick , with the isthmus 2 to 6 mm thick. Each lobe is pear shaped , consisting of a narrow upper pole & a broader lower pole. The thyroid gland is covered by fascia & strap muscles , & more laterally it is tucked under the diverging anterior borders of the sternomastoid muscles & adjacent to the lobes on the medial side , is the carotid sheath.

PYRAMIDAL LOBE

It is present in 80 % of individuals , usually to the left of midline, extending upwards from the isthmus along the anterior surface of the thyroid cartilage. It is a remnant of thyroglossal cyst.

The gland moves upwards on deglutition , because of its facial attachments. The normal gland is impalpable though it can palpated in thin individuals.

FACIAL COVERINGS

The strap muscles are ensheathed by investing layer of deep cervical fascia. These muscles are applied to the anterior surface of the gland & separated by a loose condensation of fascia derived from the pretracheal fascia. This false capsule covers the gland which is enclosed by its true capsule with its rich blood supply.

The pretracheal fascia is attached above to the thyroid cartilage & cricoid cartilage & this suspension of thyroid from the larynx accounts for its movement on deglutition.

During surgery, the investing layer of deep cervical fascia is opened in the midline vertically which is relatively avascular. The space between the gland & strap muscle is entered & the strap muscles are retracted.

The strap muscles are supplied from the cervical roots 1,2,& 3 via the Ansa Cervicalis. These enter the muscle at its lateral border & on the deeper surface & the muscles can be divided transversely to facilitate access to the gland , provided they are resutured , there does not appear to be any functional impairment.

BLOOD SUPPLY:

ARTERIAL SUPPLY:

ARTERY	ORIGIN
➢ Superior thyroid artery	→ External Carotid artery.
➢ Inferior thyroid artery	→ thyrocervical trunk from 1st part of subclavian artery
➢ Thyroidea ima artery	→ arch of aorta or innominate artery

The superior thyroid artery descends down from its origin & runs to the superior pole . And as it reaches the gland it divides into anterior & posterior branches.

The inferior thyroid artery passes behind the carotid sheath & runs transversely across the space between the thyroid & carotid sheath to enter the deeper surface of the gland as separate branches. The recurrent laryngeal nerve usually lies posterior to these branches or sometimes inbetween or anterior to them.

VENOUS DRAINAGE:

A rich venous plexus forms underneath the capsule & drains correspondingly as follows:

VEIN	→	DRAINS
➢ Superior thyroid vein	→	internal jugular vein
➢ Middle thyroid vein	→	internal jugular vein
➢ Inferior thyroid vein	→	brachio cephalic vein

The middle thyroid vein runs a short course, passes from middle lobe directly to internal jugular vein.

From the isthmus & lower pole the inferior thyroid vein forms a plexus that lies in the pre tracheal fascia & drains into the brachio cephalic vein.

LYMPHATIC DRAINAGE:

The lymphatic drainage of the thyroid is principally to the internal jugular nodes. The superior pole & the medial isthmus drain to the superior group, and the inferior drain the lower gland & empty into pretracheal & paratracheal nodes.

NERVE SUPPLY:

- SYMPATHETIC → Superior & middle cervical sympathetic ganglia
- PARASYMPATHETIC→ Laryngeal br. Of Vagus
    - Superior laryngeal nerve (external & internal)
    - Recurrent laryngeal nerve.

The sympathetic nerves travel along the blood vessels to the thyroid & are vasomotor in action.The thyroid gland's relation to the recurrent laryngeal nerve & external laryngeal nerve is of major significance. Identification of these nerves rather than avoiding should be a standard practice for the surgeon.

The recurrent nerve supplies the intrinsic muscles of larynx except the cricothyroid which is supplied by the external laryngeal nerve. Cricothyroid is a tensor of vocal cord & affects the pitch of the voice.

Recurrent laryngeal nerve:

Right: On the right the recurrent nerve originates from the vagus where it crosses the 1st part of the subclavian artery .The nerve then loops the subclavian artery & ascends slightly obliquely to enter the larynx at the level of cricoid cartilage & posterior to the cricothyroid muscle.

Left : The nerve originates from the vagus as it crosses the aortic arch & loops posteriorly around the ligamentum arteriosus before it ascends medially in the tracheo oesophageal groove to enter the larynx opposite the contralateral nerve.

Nerve in tracheo oesophageal groove

right → 64 %

left → 77 %.

Nerve in relation to the inferior thyroid artery

Posterior to artery → right → 53 %

→left → 69 %.

In others the nerve is either anterior or in between the branches. The most meticulous step during thyroid surgery is during the dissection where the recurrent nerve passes through the Berry's ligament. It is here the nerve is in close proximity to the thyroid gland , tethered down by the ligament , & it is here the nerve is most commonly injured.

Non recurrent recurrent laryngeal nerve:

- Exclusively on the right
- 1% of individuals
- associated with anomaly of subclavian artery
- nerve runs directly to larynx after its origin from vagus.

EXTERNAL LARYNGEAL NERVE :

The nerve runs on the lateral surface of the inferior constrictor muscle to innervate the cricothyroid muscle & lies in close proximity to the superior pole vessels.

Nerve supplies the cricothyroid muscle which tensor of vocal cord which affects the pitch of the voice.In 80 % of individuals the nerve can be found over the cricothyroid muscle.

HISTOLOGY OF THE THYROID GLAND:

Microscopically the gland is divided into lobules that contain 20 to 40 follicles.These are roughly 3×10^6 follicles in each gland. Follicles are spherical & averages 30μm in size. Follicle is lined by cuboidal epithelium& contains a central core of colloid secreted from the epithelial cels.

When the gland activity is more as in the case of hyperthyroidism ,the follicular epithelium is high & columnar & the colloid is reduced.

Sparsely intermingled between the follicular cells & also within the interfollicular spaces are the PARAFOLLICULAR or C CELLS which secrete calcitonin.

The C cells are mostly concentrated in the superior pole , reflecting their origin as neuroectodermal cells derived from the Ultimobranchial bodies , & are a part of APUD series described by Pearse.

EMBRYOLOGY OF THYROID:

The thyroid develops as an endodermal tubular structure from the posterior aspect of fetal tongue , and grows downwards in front of the developing hyoid & larynx , bifurcating & fusing with growth elements from the 4^{th} branchial pouch . The stem of the down growth forms the thyroglossal duct whose upper end remains as foramen caecum of the tongue , the lower end forms the pyramidal lobe . Thyroglossal duct usually atrophies but may remain in whole or in part & produce abnormalities.

It is joined laterally by a pair of components originating from the Ultimobranchial bodies of the 4^{th} & 5^{th} pharyngeal pouches. These lateral components supply the C cells of the thyroid which secrete calcitonin.

The superior parathyroids develop from the 4^{th} pharyngeal pouch & it is in close relationship to the superior aspect of thyroid.

The inferior parathyroids develop from the 3^{rd} pharyngeal pouch & is developmentally related to thymus.

PHYSIOLOGY

IODINE METABOLISM:

The average daily requirement of iodine is 0.1 mg. Iodine in the stomach & duodenum is converted to iodide & is absorbed . It is actively transported to thyroid by an ATP dependent process. The normal serum to thyroid Iodine ratio is about 1:5 . But can be as high as 1: 500. Thyroid hormones T 4 & T 3 are bound to thyroglobulin within the colloid.

Synthesis is as follows :

- Trapping of organic iodide
- Oxidation of iodide to iodine
- Binding of iodine with tyrosine to form iodotyronine
- Coupling of monoiodotyrosine (MIT) and diiodotyrosine (DIT) to form T3 , T4 ,Rt3.

All the above steps in thyroid synthesis is accelerated by TSH acting through a specific membrane receptor via the Cyclic amp second messenger system.

The coupling & oxidation of iodide are catalysed by peroxidase enzyme which is inhibited by propylthiouracil & carbimazole.

The hormones so synthesized are stored in colloid within the thyroglobulin. When the hormones are required the complex is reabsorbed into the epithelium by endocytosis & broken down by the lysosomes. This results in the formation of T4,T3,Rt3, MIT,DIT.

The MIT & DIT are deiodinated & Iodine is reused. The T3 & T4 enter the circulation & transported bound to Thyroxine binding globulin (TBG), Thyroxine Binding Pre Albumin (TBPA) & albumin .

99.98 % of thyroid hormones are bound to protein & only 0.02 % is free & active physiological form . r T3 is biologically inert. The circulating level of T4 to T3 is 10: 1 to 20: 1. T3 is more potent , less lightly bound to protein , 3 – 4 times more active than T4. About 75 % of T3 is produced from peripheral conversion of T4 to T3 which is inhibited by β blockers.

HYPOTHALAMO PITUITARY THYROID AXIS:

Synthesis & liberation of thyroid hormones is controlled by Thyroid stimulating hormone (thyrotropin) TSH secreted by basophil cells of anterior pituitary. The TSH is in turn controlled by thyrotropin releasing hormone (TRH) secreted by the hypothalamus.

MOLECULAR BASIS OF THYROID HORMONE ACTION:

The thyroid hormones are transported across the plasma membrane of the tissues by ATP dependent transport system .

Uptake by the tissue is rate limited by the amount of free hormone avilableat the tissur level .

At the cellular level T3 is the active hormone , & its activity is mediated through T3 receptors located in the cell nucleus .

OUTLINE OF THYROTOXICOSIS

Syndrome that results when excessive levels of thyroid hormones are secreted into circulation. The term thyrotoxicosis is retained because symptoms due to raised level of hormone is not responsible for all the manifestations of the disease.

CLASSIFICATION

I) BASED ON ETIOLOGY:

A)Primary Alteration Within The Thyroid:

Graves' disease

Toxic MNG

Toxic adenoma

B)CNS Disorders – Increased Tsh Secretion

II)BASED ON HORMONE SECRETION

With Increased Thyroid Hormone

Secretion

Graves' Disease - Primary Thyrotoxicosis

Toxic Nodular Goitre

Toxic Thyroid Adenoma

Jod – Basedow Hyperthyroidism

Without Increased Thyroid

Hormone Secretion

Subacute Thyroiditis

Factitious Hyperthyroidism

Functioning Metastatic Ca Thyroid

Struma Ovarii (ovarian teratoma containing thyroid)

Molar Pregnancy – increased beta HCG

ETIOPATHOGENESIS GRAVES' DISEASE

(DIFFUSE TOXIC GOITRE)

Originally described by Caleb Pary – Welsch Physician – 1825. Named after Robert Graves - Ireland – 1835.

It is the most common form of thyrotoxicosis.

Affects young adults (20 – 40 yrs) .

6 times more common in females.

EXTRA THYROIDAL MANIFESTATIONS :

Ophthalmopathy, Pretibial Myxedema,Vitiligo, Thyroid Acropathy is common.

AETIOLOGY :

It is an autoimmune disorder. The disease was originally thought to be due to *LATS (LONG ACTING THYROID STIMULATING ANTIBODY*) described by Adams & Parves in 1956.

It is recently demonstrated that the disease is due to wide range of antibodies termed as TRAb (THYROID RECEPTOR ANTIBODIES).Thyroid stimulating antibodies or Ig are directed at TSH receptor on follicular cells.

TSI or TSAb -thyroid stimulating Ab or Ig stimulate TSH receptors on follicular cells.

TSII or TBIA- TSH binding inhibiting Ig or Ab . All these Ab are grouped as TRAb.

What iniates the Graves' & Ab production is unclear. Various theories:

1) Defect in the T suppressor cell .

2) Immune response is launched to altered antigens on the follicular cell surface.

3) Genetic factors- Twins have increased chance. Probably due to increased frequency of association with HLA b8 & DR3 in Caucasians : HLA – Bw35 in Japanese.

Family history of autoimmune disease, graves' disease, hashimoto's disease may be associated .

PATHOLOGY

MACROSCOPIC APPEARANCE

Gland is diffuse, symmetrical, smoothly enlarged with increased vascularity.

MICROSCOPIC APPEARANCE

Cells are hyperplastic with columnar epithelium , papillary projections & mitosis & with aggregates of lymphoid tissue. Colloid is reduced .

Many follicles are empty. Some contain vacuolated colloid with the characteristic scalloped pattern adjacent to thyrocytes.

TOXIC MULTINODULAR GOITRE

(SECONDARY THYROTOXICIOSIS)

Toxic Nodular Goitre – Plummer's Disease.

Long standing MNG becomes hyper active over long period.

Middle or elderly aged females.

Hyperthyroidism is relatively mild .

Not associated with extra thyroidal manifestations .

Gland is nodular & eye signs are less common.

In many cases it is the internodular tissue that is active & nodules are inactive. In some cases the nodules are active & here the toxicosis is due to autonomous nodules as in toxic adenoma.

SOLITARY TOXIC NODULE

TOXIC ADENOMA

One or more nodules trapping & organifying more iodine & secreting more hormone thereby producing hyperthyroidism independently of TSH control.

It is autonomous -- not due to TRAb. TSH secretion is suppressed by high levels of circulating hormones. Normal thyroid tissue surrounding the nodule is suppressed & inactive.

Adenoma is usually >3 cm in dia.

Pathogenesis Of Dermopathy & Ophthamopathy Is Immune Mediated But Not Due To TRAb & Less Well Understood

PATHOGENESIS OF GRAVES' OPHTHALMOPATHY

It is an Autoimmune disorder—immunologically mediated, but not due to TRAb. Cross reaction between the thyroid antigens & ocular muscle antibodies.

Fibroblasts proliferation in orbit leading to accumulation of hydrophilic glycosaminoglycans in the retro orbital tissues which leads to increased interstitial fluid content . And there is also chronic inflammatory cell infiltration in the retro orbital tissue. All these lead to swelling of extra ocular muscle & increased retro orbital pressure leading Exophthalmos & optic nerve compression.

CLINICAL MANIFESTATION

AGE : Graves' disease 20 – 40 yrs

Toxic MNG middle or elderly

Toxic Adenoma >40 yrs

SEX : All thyroid diseases are common in females.

Clinical features are the same in graves' or toxic MNG except that Graves' disease is associated with more severe toxicity & with extra thyroidal manifestation. There may be Family history of other autoimmune diseases.

In Graves' – the onset is sudden, associated with remissions & exacerbation & more of neurological symptoms. In toxic MNG - the onset is insidious & may be associated with cardiac failure or atrial fibrillation & more of cardiovascular manifestations.

There is an increased caloric turnover & hyper metabolic state. The most significant symptoms are loss of weight despite increased appetite, preference to cold & palpitation, heat intolerance & excessive sweating.

GASTRO INTESTINAL SYMPTOMS:

Increased bowel motility, increased transit time

Diarrhoea/hyperdefecation & weight loss despite good appetite. Anorexia & vomitting

CARDIOVASCULAR SYSTEM:

Increased heart rate , B.P ,cardiac output & blood volume. Widened pulse pressure (corrigan's pulse).

Chest pain, dyspnea, palpitation, pedal edema, cardiomyopathy , CCF.

Cardiac rhythm abnormalities –

Sinus tachycardia

Multiple extrasystole

Paroxysmal atrial tachycardia & atrial fibrillation

Persistent atrial fibrillation not responding to digoxin.

NEUROLOGICAL

Nervousness,irritability,restlessness,excitability,

Emotional liability,psychosis

Tremor,hyper reflexia,illsustained clonus.

MUSCULAR SYSTEM:

Muscle weakness,proximal myopathy

Periodic paralysis (only noted in chinese)

HAIR: Brittle & fine leading to hair loss

NAIL: Onycholysis;clubbing.

REPRODUCTIVE SYSTEM:

Amenorrhea, oligomenorrhea Infertility, spontaneous abortion, Loss of libido & impotence.

DERMATOLOGICAL:

Pretibial myxedema, increased sweating, pigmentation vitiligo, thyroid acropathy, spider naevi, palmar erythema.

OTHER FEATURES:

Fatigue, apathy, gynaecomastia, osteoporosis(elderly).

NECK SWELLING:

Graves' – diffuse symmetrically enlarged goiter

Toxic mng – multi nodularity, firm nodules

Toxic adenoma- single nodule palpable

PRETIBIAL MYXEDEMA:

Incidence 3-5 %. Nearly always associated with true exophthalmos & high levels of TRAb. Infiltrative dermopathy- mucin like deposit in the skin causing skin thickening.

Symmetrical in the early stage ; characterized by shiny red plaque of thickened skin with coarse hair which may be cyanotic when cold. In Severe cases the skin of whole leg , foot & ankle are involved. Associated with clubbing of fingers & toes (thyroid acropathy).

Treatment: rarely requires treatment. Local injection of Triamcinolone or betamethasone ointment under occlusive dressing may be effective.

OCULAR MANIFESTATION

Some degree of exophthalmos is common in all the cases. True exophthalmos is proptosis of eyes caused by infiltration of retrobulbar tissues with fluid ,round cells & spasm of upper eyelid. Levator palpebra superioris is partly innervated by sympathetic & its over activity causes lid retraction & lid lag.

AMERICAN THYROID ASSOCIATION CLASSIFICATION OF EYE SIGNS IN GRAVES' DISEASE

N	0	No Signs Or Symptoms
O	1	Only Signs
S	2	Signs & Symptoms
P	3	Proptosis
E	4	Extra Ocular Muscle Involvement
C	5	Corneal Involment
S	6	Sight Loss(Optic Nerve Damage)

EYE SIGNS :

I) Lid lag & lid retraction

II)Signs of Exophthalmos:

Von Graefe's sign : lid lag .

Dalrymple's sign : lid retraction –upper sclera is visible

Joffroy's sign: Absence of forehead wrinkling when pt looks up

Stellwag's sign: staring look & infrequent blinking ,widened palpebra.

Moebius' sign: absence of eyeball convergence due to muscle weakness.

III)Ophthalmoplegia*:*

Most commonly involved muscle is elevators of eye –inferior oblique & superior rectus. Diplopia commonly occurs at upward & outward gaze.

IV) Chemosis:

Conjuctiva is edematous , congested. Edema of eyelids, conjuctival injection & chemosis are aggravated by compression of ophthalmic veins causing increased lacrimation & photophobia.

MALIGNANT EXOPHTHALMOS:

The above mentioned features are severe & progressive it is termed malignant exophthalmos. Papilledema, corneal ulceration & optic nerve damage & vision loss occurs.

Examination of exophthalmos:

1)Look from above for eyeball protrusion - Naffzieger's method.

2)From front – look for scleral rim around cornea.

EXOPHTHALMOMETER (HERTEL):

Measures the distance between lateral bony orbital margin to anterior surface of cornea.

COMPARISION BETWEEN PRIMARY & SECONDARY THYROTOXICOSIS

Features	Primary Thyrotoxicosis	Secondary Thyrotoxicosis
Age	20 – 40 years	Middle or elderly
Pre existing goiter	Not prominent	Long standing goiter
Goiter	Diffuse , smooth	nodular
Exophthalmos	More common	Less common
Extra thyroidal manifestations	Yes	No
Neurological symptoms	More pronounced	Less
Cardiovascular symptoms	less	More pronounced

UNUSUAL CAUSES OF HYPERTHYROIDISM

THYROTOXICOSIS FACTITIA*:*

Hyperthyroidism induced due to excess intake of thyroxine. It occurs only if the dose exceeds the daily requirement. Doses below the daily requirement only suppress the normal thyroid function. RAIU Radio iodine uptake is low.

Treatment : To stop the drug & treat with carbimazole or propranolol.

JOD BASEDOWS THYROTOXICOSIS;(JOD German word for Iodine)

Diffuse toxic goiter is also called Basedows disease. Large doses of iodine given to hyperplastic endemic goiter which is iodine avid causes temporary hyperthyroidism.

DEQUIRVAINS' THYROIDITIS AND AUTOIMMUNE THYROIDITIS (HASHITOXICOSIS)

During the early stage there is hyperthyroidism due to leakage of hormone from the gland.

FUNCTIONING METASTATIC THYROID Ca:

Rarely causes hyperthyroidism.

NEONATAL THYROTOXICOSIS:

Babies born to hyperthyroid mother have high titres of TSH & TRAb. Since both TSH & TRAb will cross the placenta.

It gradually subsides in about 3 weeks time & Ab titre gradually comes down.

POST PARTUM THYROIDITIS

Causes hyperthyroidism in the early stage.

TT3 THYROTOXICOSIS:

The TT4 is normal & T3 alone is ↑.

RAIU is normal.

Commonly occurs in endemic goitre with solitary nodule.

INVESTIGATIONS

ASSESMENT OF THYROID FUNCTION:

TSH:

Normal level is 0.15 – 4.2 μU /ml.

Done previously by Radioimmuno assay. Nowadays it is done by Immunochemiluminometric Assay using monoclonal antibodies.

TSH ↓ - hyperthyroidism

TSH ↑ - hypothyroidism.

If TSH is alterd , T3 & T4 has to be measured.

Many consider that TSH is the most sensitive assay of thyroid function.

TOTAL THYROXINE (TT4) & FREE THYROXINE (FT4)

TT4 : Normal level 55 – 150 nmol/L

FT4 : Normal level 12 – 28 pmol/L

FT4 is ↑ in early hyperthyroidism in which the TT4 is normal.

TOTAL T3 (TT3) & FREE T3 (FT3*)* :

TT3 ; Normal level 1.5 – 3.5 nmol/L

FT3 : Normal level 3 – 9 pmol/L

FT3 is ↑ in early hyperthyroidism where the TT3 is normal. T4 is bound to globulin, albumin & other carrier proteins. Pregnancy, oestrogen intake & ocp intake all increase the carrier protein level.Increase in TBG level → ↑ TT4 & TT3 level leading to false positive results but FT4 & FT3 remains the same. So in those persons it is ideal to measure the free hormone level.

In some centres total hormonal assay has been obsolete & only free hormone assay is done. But in some places it is still in place. Low T3 syndrome occurs in starvation & propranolol intake.

ANTIBODY ASSAY:

Antimicrosomal Ab & antithyroglobulin Ab are raised in 70% of hyperthyroid patients. TRAb is detected in 90% of graves' disease.

THYROID SCAN: ISOTOPE SCAN

(RADIO IODINE UPTAKE STUDY)

Thyroid scanning is carried with either radio active I^{123} or Tc^{99m}. I^{131} is used for radio ablation of thyroid.

Usually after 24 hours the gland takes up 16 – 48 % of isotope and is detected.

But when the uptake is >48 % $\rightarrow$ hyperthyroidism.

USG or isotope study is not useful in graves' disease except in the case of post partum thyroiditis. Routine Isotope scan is inappropriate to differentiate between benign & malignancy.

Its principal value is in Toxicity with nodule or nodularity. Localization of overactivity of the gland will differentiate between the Toxic Adenoma & Toxic MNG.

GRAVES DISEASE	Diffuse ↑ in uptake
TOXIC MNG	Internodular tissue is overactive. Remaining gland in suppressed
TOXIC ADENOMA	Nodule is over active. Remaining gland is suppressed

According to uptake it is divided into as follows:

WARM	Uptake similar to adjacent thyroid tissue
HOT	Overactive nodule than surrounding thyroid
COLD	Nonfunctional / hypofunctional

RAIU ↑ UPTAKE :

- Graves' disease
- Toxic MNG
- Toxic Adenoma

RAIU ↓ UPTAKE

- Thyroiditis – early phase
- Iodine induced - Jod Basedows
- Hashimoto' s disease

ULTRASONOGRAM OF THYROID

High frequency USG delineates the cysts & nodules. And detects unpalpable nodules.

Any thyroid nodule has to subjected to FNAC & Cysts can be diagnosed when aspiration is attempted as part of investigating a nodule on FNAC & so ultrasound is not absolutely necessary to diagnose cysts of thyroid. The value of USG of thyroid is decreasing nowadays.

FINE NEEDLE ASPIRATION CYTOLOGY:

It is not usually required for toxic thyroid unless there is palpable nodule & in which carcinoma cannot be ruled.

Done with 23 or 24 g needle & 10 or 20 cc syringe. In a single prick , multiple passes are made inside the thyroid tissue.

Some slides are alchohol (70%) dried & some are air dried & papanicolou stained. FNAC is Highly sensitive to rule out malignancy.

X – RAY NECK AP & LATERAL VIEWS:

Will show anteroposterior compression of trachea, lateral deviation of trachea, calcification of thyroid, shadow of thyroid gland & retro sternal goiter.

C.T. SCAN & M.R.I. SCAN:

Shows Retro sternal extension

X RAY CHEST:

Asses cardio pulmonary status , retro sternal extension, lung metastasis in malignancy.

ELECTRO CARDIOGRAM & ECHO CARDIOGRAM

To assses the cardiac status & find out any arrythmias.

IDL SCOPY (INDIRECT LARYNGOSCOPY*):*

Assess the vocal cord status pre operatively for clinical & medico legal purposes.

SERUM PROTEIN BOUND IODINE:

It is cheap & can be easily assessed but lacks specificity as it measures the non hormonal forms of iodine in the blood. In euthyroid state , the range is 3.5 – 8 μg per 100 ml.

False positive results → pregnancy, person taking various forms particularly contrast media, expectorants containing iodides & oral contraceptive pills.

False negative results → salicylates , androgens , hydantoin like drugs & in nephritic syndrome.

FREE THYROXINE INDEX (FTI *)*

This is calculated from the formula

FTI = Serum T4 (or PBI) × T3 uptake percent.

The normal range is from 3.5 to 8.

This correlates closely with the level of free T4 in serum & thus accurately reflects the thyroid status of the person.

T3 RESIN UPTAKE

The patient serum is incubated with radio active T3 so that the latter becomes fixed to any thyroid binding protein not carrying the hormone. The amount fixed can be measured & thus the number of binding sites in the serum that are unoccupied can be measured.

Naturally in hyperthyroidism the number of free binding sites is low & in hypothyroidism this number is high. The secondary binder , where the unutilized radio active T3 become fixed can be resin ,or thyopac.

The fraction of labeled T3 taken up by the resin can be compared with that of a standard serum & this test is called as RESIN UPTAKE RATIO.

The normal range is 0.91 – 1.21 µg. While using thyopac method one may 100 percent as the mean normal value for free binding sites. In this case ≤ 85 % will suggest hyperthyroidism as in this case the number of free sites will be less. And a figure of ≥ 120 % suggests hypothyroidism as the number of free sites is high.

TSH STIMULATION TEST:

Measures the response of pituitary to I.V administered TRH, the hypothalamic stimulator of TSH. TRH dose given is 400 µgm or 1.73µgm / sq m. In euthyroid persons who normal pituitary function , a prompt ↑ in TSH which peaks at 20 – 30 minutes. In hypothyroidism , basal TSH is elevated . Following TRH administration , the reaction is more & TSH often reaches 100 – 200µU/L at 30 minutes. In thyrotoxicosis, TSH response is absent when TRH is administerd.

TEST FOR HYPOTHALAMO PITUITARY THYROID AXIS:

When TRH is given I.V in a dose of 200 µg to a normal individual , the level of TSH rises from basal level to 1µU/ml to a mean peak of 10 µU/ml at 20 min & return to normal in 120 min.

In hypothyroidism there is an exaggerated rise of an already elevated TSH , but hyperthyroidism there is no response of a depressed level.

T3 SUPPRESSION TEST (Werner):

This test differentiates thyrotoxicosis from other causes of raised uptake e.g . iodine deficiency & autonomous nodules.

BASAL METABOLIC RATE (BMR): BMR is ↑ in thyrotoxicosis.

S.CHOLESTEROL & CREATININE : cholesterol is ↓ in hypothyroidism & creatinine is ↑ in hypothyroidism.

MANAGEMENT

THREE MODALITIES:

Antithyroid Drugs

Surgery

Radio Iodine Ablation

ANTITHYROID DRUGS:

Drugs that inhibit hormone synthesis : Propylthiouracil, Carbimazole, Methimazole.

Drugs that inhibit iodine trapping : Thiocyanate, perchlorate, nitrates

Drugs that inhibit hormone release : Iodides of sodium & potassium, iodine

β Blockers propranolol,nadolol

PROPYLTHIOURACIL & CARBIMAZOLE:

Inhibit peroxidase → inhibit iodination & coupling.

Hormone synthesis is affected. Propylthiouracil also inhibits the peripheral conversion of T4 → T3. Carbimazole is converted to its active metabolite Methimazole. In U.S.A Propylthiouracil & Methimazole are commonly used ; in U.K carbimazole is used.

All these drugs have no effect on the underlying disease process.

DRUG	*DOSE/DAY*
Propylthiouracil	*100 – 300 mg tds*
Methimazole	*10 – 30 mg tds*
Carbimazole	*40 - 60 mg*
Propranolol	*40 - 60 mg tds*

Initial Response is attained in 2 weeks. After attaining response the dose is reduced to maintenance dose.

BLOCKING REPLACEMENT REGIMEN

Usually after giving the initial high dose, the drug dose is reduced to maintenance dose. But in this regimen the initial high dose is continued & Thyroxine is supplemented is Blocking – replacement regimen.

SIDE EFFECTS:

a)Skin rashes, pyrexia, peripheral neuritis, vasculitis, arthritis, hepatitis

b)sore throat , fever

c)Granulocytopenia – reversible if drug is discontinued

d)Agranulocytosis – incidence is 1 in 250

e)Aplastic anaemia rarely.

When agranulocytosis occurs , it can treated with rh G-CSF. If side effects occurs for one drug, the therapy can be switched on to another drug as there is no cross reaction between the drugs.

ADVANTAGES:

a)No surgery

b)No radiation

DISADVANTAGES:

- 50 % relapse rate
- toxicity & drug side effects
- teratogenecity : all the drugs cross the placenta & secreted in milk
- Long term follow up is necessary
- Poor patient compliance – unsuitable for illiterate people.

β BLOCKER:

PROPRANOLOL:

No action on the gland. Inhibits peripheral conversion of T4 → T3. Inhibits sympathetic activity & results in alleviation of sympathetically mediated symptoms like tremor, excitability, nervousness. There is rapid improvement of toxicity & rapid symptomatic improval. Can be used for rapid correction to euthyroid state before surgery. Dose is 40 mg 8^{th} hourly.

NADOLOL :

Is a long acting β blocker single daily dose of 160mg/day

IODIDES:

Inhibits hormone release

Lugols Iodine → 5% Iodine in 10% Potassium Iodide solution. Reduces vascularity . Makes the gland firmer & easier to handle & less

bleeding during surgery. Usually given 10 days before surgery in a dose of 5 drops 8^{th} hourly mixed with milk or water. Alternatively potassium iodide tablets can be given at 60 mg tds /day.

ANTITHYROID DRUGS USED IN 3 MAIN WAYS:

a) As a definitive form of treatment

b) In pre op preparation for thyroidectomy

c) In association with Radio iodine ablation

DRUG THERAPY IS UNSUITABLE FOR THE FOLLOWING:

Large diffuse glands

Toxic MNG

On discontinuing the drug after attaining response it results in high rate of recurrence & definitive treatment in the form of Surgery or Radio iodine ablation is indicated in the above mentioned conditions.

RADIOIODINE ABLATION THERAPY

I^{131} is the most commonly used drug. Therapeutic dose is higher than the tracer dose. First used by Hertz & Roberts.

Affinity of the hyper plastic thyroid gland to Iodine forms the basis for treatment. The Radio iodine I^{131} is given as oral drink, which disintegrates within the gland & emits β particles which destroys the acinar cells. These β particles penetrate the other tissue for few mm only & so the recurrent laryngeal nerve , Parathyroid & cartilages are not affected. The gamma radiation is too small to cause to any damage.

PROCEDURE:

USUAL DOSE OF RADIOIODINE I^{131}

500 – 750 mBq or 10 mCi or 8500 cGy

All patients should be made euthyroid before therapy with antithyroid drugs. Stop the antithyroid drug about 2 – 3 weeks before therapy to allow Iodine uptake of thyroid . Radioiodine is given in the form of oral drink of $I^{131.}$ After single dose of therapy the response rate is 75%. Response is slower usually occurs in 8 – 12 weeks time If necessary & if the response does'nt occur in 12 weeks, the therapy can be repeated. Higher the initial dose given , higher is the hypothyroidism incidence & earlier is the onset of recurrence .

Response occurs after a period of 4 – 12 weeks & during this lag period antithyroid drug is given. Before ablation a isotope scan is done is done to assess the size of the gland.

SUITABLE FOR :

- small or moderate sized goiter
- relapse after drug or surgery
- in whom surgery or drugs are contra indicated
- older patients treated with radio iodine ablation .

CONTRAINDICATIONS :

- ABSOLUTE : Pregnancy & lactation
- RELATIVE : Ophthalmopathy Isolated thyroid nodules or toxic nodular goiter
- Young age – children & adolescent

DISADVANTAGES:

Increased incidence of leukemia, thyroid malignancy & other malignancy.

Long term follow up is essential

Repeated doses may be required.

COMPLICATIONS:

- exacerbation of thyrotoxicosis, arrythmias & precipitation of CCF
- Thyroid storm, Hypothyroidism, hyperparathyroidism
- Worsening of eye signs : incidence is greater than after surgery
- Fetal damage in pregnancy

SURGERY

Surgical Procedures For Thyroid Disorders [8]

- Total Lobectomy
- Subtotal Lobectomy
- Isthmusectomy

Total Thyroidectomy	2× total lobectomy + isthmusectomy
Subtotal Thyroidectomy	2× subtotal lobectomy + isthmusectomy
Near Total Thyroidectomy	Total lobectomy + isthmusectomy + subtotal lobectomy
Lobectomy	Total lobectomy + isthmusectomy

SUBTOTAL THYROIDECTOMY

Leaving behind ⅛ th of the gland.

5 cubic cm of gland is left or 4 – 5 gm of tissue is left.

Small remnant of gland if left on either side of the Trachea.

NEAR TOTAL THYROIDECTOMY

Leave <2 gm of thyroid .Remove one lobe completely & leave <2 gm on the other side(Dunhill Procedure) , so that the chance of damage to Recurrent laryngeal nerve is reduced in subsequent surgery if there is any recurrence.

PRE OPERATIVE PREPARATION TO EUTHYROID STATE:

Carbimazole:

Usually carbimazole is given in a dose of 10 mg 8^{th} hourly .And response starts usually at about 2 weeks. Euthyroid state attained in about 6 – 8 weeks. The drug is given till the last evening before surgery.

Propranolol:

It is given in a dose of 40 mg 8^{th} hourly for rapid control of symptoms. Response is faster & patients become euthyroid earlier. Used when surgery is planned earlier.

LUGOLS IODINE

Given in dose of 5 – 10 drops 8^{th} hourly in milk. Usually given in the Last 10 – 14 days before surgery is planned.

RECOMMENDED TREATMENT:

GRAVES DISEASE:

Large diffuse glands & young patients $\rightarrow$ *Surgery*

Small, moderate sized glands $\rightarrow$ *Radioiodine Ablation*

The standard treatment is subtotal thyroidectomy after adequate control of toxicity. But following subtotal thyroidectomy it was studied that there was 10 % recurrence rate & 70 % of patients developed hypothyroidism on 10 years follow up. So current consensus is to do Total Or Near Total Thyroidectomy & put them on thyroxine[9]

TOXIC MNG:

Antithyroid drug or Radio iodine therapy is less effective. *Surgery Is The Treatment Of Choice.* And in this too the original standard treatment is subtotal thyroidectomy. But now the current trend is total thyroidectomy & thyroxine replacement.[9]

TOXIC ADENOMA:

Total lobectomy of the affected side is the treatment of choice. Radio iodine ablation can be given in elderly & unfit patients.

RECURRENT THYROTOXICOSIS:

Radio Iodine Ablation Therapy Is The Treatment Of Choice

Further surgery has little place [10]

THYROTOXICOSIS IN CHILDREN

Radio iodine therapy is contra indicated . Following Surgery - there is ↑ recurrence as the follicular cells are active. So treat them with drugs until late teens & failing which surgery can be done.

THYROTOXICOSIS IN PREGNANCY:

It is difficult to diagnose & also to treat. Radio iodine ablation is absolutely contraindicated because of fetal damage. So the therapeutic option is between Surgery & drugs. Surgery has high rate of miscarriages. If it is planned it can be carried out in 2nd trimester. So the mode of treatment is with antithyroid drugs until the 2nd trimester & do surgery. Following surgery the patient should be replaced with thyroxine as required to avoid hypothyroidism as it is also equally hazardous. Both TSH & drugs cross the placental barrier& the baby born will be goitrous.

Both carbimazole & propylthiouracil can used , but many favour propylthiouracil. Propylthiouracil crosses the placenta less than carbimazole. And T3 to be given to the mother along with propylthiouracil to avoid goiter in neonate. Propranolol given causes sustained contraction of the uterus muscle tone & might result in small placenta & IUGR. And also causes Depression after birth, post natal bradycardia & hypoglycaemia in mother.

TREATMENT OF EXOPHTHALMOS:

Spasm & retraction usually disappear when hyperthyroidism is controlled. Recurrent hyperthyroidism & hypothyroidism will increase exophthalmos. Treatment is as follows:

- Sleeping propped up
- Wearing glasses during day
- Tape the eyes during the night

- Artificial tears to the protect against drying
- Guanethedine eye drops & steroid eye drops
- Massive doses of steroid (Prednisolone 60 mg/day) reduces the Chemosis
- Orbital decompression or retro orbital radiation – may be required to save the eye when it is in danger.
- Orbital decompression can be done by temporal approach (Rowbotham's) or frontal approach (Naffzieger's).
- Retro orbital Radiation by Supervoltage X rays
- Lateral tarsorraphy to oppose the eyelids & prevent further ulceration & keratitis.
- Some reports say Total thyroidectomy alleviates the eye disease. It is unproved whether Total thyroidectomy is preferable to Near total or subtotal thyroidectomy. Total thyroidectomy should be undertaken only in patients with severe exophthalmos when well prepared.

SUBTOTAL THYROIDECTOMY

ANAESTHESIA : General Anaesthesia & Controlled Ventilation

POSITION : Neck Extended Position (Rose Position)

INCISION : Low Collar Transverse Skin (or) Crease Incision (Kocher)

SUBPLATYSMAL FLAPS :

UPPER FLAP $\rightarrow$ upto thyroid cartilage

LOWER FLAP $\rightarrow$ Upto suprasternal notch

Investing layer of deep cervical fascia is incised vertically in midline. Strap muscles are retracted or cut if gland is large & as required. Thyroid gland is dissected bluntly from the adjacent sternothyroid muscle.

- Middle thyroid vein : isolated , ligated & divided in between the ligatures.
- Superior thyroid pedicle*:* is skeletonized , doubly ligated on patient side, close to the capsule with vicryl or silk. Care is taken not include or injure the *superior laryngeal nerve. Superior laryngeal nerve is seen on the cricothyroid muscle in 80 % of persons.* Then the gland is mobilized.
- Inferior thyroid artery*:* is skeletonized & branches to parathyroid is preserved. Main artery is not ligated to avoid the parathyroid branches. Individual branches are then ligated with vicryl or silk close to the capsule. Care is taken not to include or injure the Recurrent laryngeal nerve.
- Recurrent laryngeal nerve should be identified rather than avoiding *:* enters the larnx at the level of cricothyroid , passing under & through the berry's ligament deep to the cricothyroid muscle.
- Parathyroids should be preserved: upper : at the level of cricothyroid . lower : found where the recurrent laryngeal nerve crosses the inferior thyroid artery. In 80 % the lower gland is located within 1 cm of the artery .
- If parathyroid or blood supply is damaged , the gland is minced & reimplanted into sternohyoid .
- Gland is removed & cut ends of the gland sutured with the capsule with vicryl
- Wound is closed with or without drain.

COMPARITIVE STUDY OF THREE TREATMENT MODALITIES

CRITERIA	ANTITHYROID DRUGS	SURGERY	RADIO IODINE ABLATION
Mortality	Nil	Less than 1 %	Nil
Speed of control	8 – 12 weeks	Immediate	
Response rate	50 %	85 – 95 %	75 %
Goiter	Remains the same or regress	Removed	Destroyed
Hypothyroidism	Occasional but temporary	10 % after 1 year , may reach 30 % later.70 % after 10 years	50 % after 10 years
Ocular changes	Improved	Improvement after total thyroidectomy (not proved).May be worsened.	If severe exohphthalmos → excacerbation rate more than surgery
In Patient (I.P) treatment	Not usually necessary unless severe	Essential before surgery	Essential
Discomfort	nil	Yes	Yes
Tetany	Nil	Transient 3 % Permanent 1 -2 %	Less
Cord palsy	Nil	Present	Nil
Drug reactions	Yes	Less as the drugs are discontinued before surgery	Less as the drugs are discontinued

POST OPERATIVE COMPLICATIONS

TENSION HEMATOMA

Hematoma is deep to the deep cervical fascia.

Usually due to slippage of ligature of superior pedicle. Causes respiratory difficulty & the wound is opened to let the hematoma out even before shifting the pt to theatre. And the hematoma is evacuated & bleeding point ligated.

RESPIRATORY OBSTRUCTION

Commonly due to laryngeal edema .The most important cause of laryngeal edema is tension hematoma. Trauma to larynx due to intubation & surgery are contributory. Recurrent laryngeal nerve palsy causes stridor if bilateral .If the respiratory difficulty is not relieved → re intubate the patient immediately .

If intubation is not possible → emergency needle tracheostomy

Tracheostomy is rarely needed.

RECURRENT LARYNGEAL NERVE INJURY

Temporary injury → is due to traction or stretching

Permanent injury → is due to dividing or ligating the nerve

Permanent injury → incidence 1 %

Nerve runs more obliquely on the right side than the left where it lies close on the tracheo oesophageal groove. *Nerve is most commonly injured at the berry's ligament. Where it is tethered down by the ligament* Use of electrocautery in this area should be avoided.

When nerve is not identified during surgery :

Transient paralysis is less common *Permenant damage is 3 – 4 times higher*.

When nerve is identified during surgery :

Transient paralysis is more common *Permenant paralysis is less*

RLN Injury → Vocal Cord Damage →and Cord is in Paramedian Position

BILATERAL NERVE DAMAGE

→ acute respiratory distress /stridor immediately after extubation

→ re intubate immediately

→Tracheostomy (if intubation is not possible)

UNILATERAL NERVE DAMAGE

→ Hoarseness of voice or husky voice

→ Choking & coughing when drinking fluids (as nerve is also sensory to trachea).

If nerve damage is temporary → recovery of cord function occurs in 6 months to 1 year.

If recovery does not occur in 12 months opt for

→ Speech therapy

→Teflon injection

Teflon injection is done lateral to the cord & it mobilizes the cord to midline & voice improves.

Disease specific risk factors for RLN injury (in the order of frequency):

- ❖ Recurrent thyroid Ca
- ❖ Recurrent goiter
- ❖ Large retro sternal goiter
- ❖ Chronic lymphocytic thyroiditis
- ❖ Graves' disease
- ❖ Non toxic goiter

EXTERNAL LARYNGEAL NERVE INJURY

Results in difficulty in shouting or singing high note (High note nerve).

To avoid injury Superior thyroid pedicle is ligated close to the capsule. Ext laryngeal nerve lies on the cricothyroid in 80 %.

THYROID INSUFFICIENCY:

Usually occurs within 2 years after surgery. Do hormonal assay & put the pt on thyroxine replacement dose.

PARATHYROID INSUFFICIENCY

Usually transient. Mostly due to ischemia to parathyroid because of bruising or partial interruption of blood supply.

Manifestations

- Tingling & numbness periorally & then in fingers
- CHVOSTEK'S SIGN → twitching of lips when facial nerve is tapped infront of tragus.
- Carpopedal spasm & tetany : occurs when S.Ca <8 mg/dl
- TROSSEAU'S SIGN → inflate the sphygmomanometer above systolic B.P (>200 mm Hg) carpopedal spasm
- Respiratory alkalosis

- Treatment : I.V Calcium gluconate as required Or 1g of Calcium every 4 hour Usually recovers in due course.

STITCH GRANULOMA

Due to use of non absorbable suture material like silk. Incidence is less when absorbable material like vicryl is used.

WOUND INFECTION

HYPERTROPHIC SCAR & KELOID SCAR

THYROID STORM (THYROTOXIC STORM)

Acute exacerbation of thyrotoxicosis. Occurs in thyrotoxic patient in whom preparation is inadequate or following some unrelated surgery.

MANIFESTATIONS:

Features Of Profound Thyrotoxicosis

- Tachycardia Hyperpyrexia, vomiting, diarrhea, dehydration
- Disorientation, mania, coma, death

MANAGEMENT :

- I.V fluids as required, Cool the pt with ice packs, O2
- Diuretics for cardiac failure & digoxin for AF, I.V. hydrocortisone
- I.V. propranolol 2 mg slowly. Or 40 mg orally 6^{th} hourly, Carbimazole 10 -20 mg 6^{th} hourly, Lugols iodine 10 drops 8^{th} hourly
- Avoid aspirin

POST OP FOLLOW UP

Vocal cord examination

If the voice is good & cough is unequivocally occlusive ,it is not mandatory to do IDL scopy & vocal cord examination on discharging the patient.

Screen for parathyroid insufficiency:

S.Ca assay is to be done after 4 – 6 weeks & treat if necessary.

Thyroid hormone assay:

After surgery, Stability of thyroid function takes some time. Biochemical (subclinical failure) is not an indication for thyroxine replacement therapy during 1st year since majority of patients with subclincal failure will ultimately regain normality. Most of the patients will develop hypothyroidism by 2 years.

Recurrent thyrotoxicosis can occur at any time during life & so life long follow is essential.

MATERIALS AND METHODS

This is a prospective study of randomly selected patients who presented with hyperthyroid symptoms , toxic goiter who were diagnosed & treated at KILPAUK MEDICAL COLLEGE HOSPITAL, Chennai during the period of September 2004 – September 2006.

Each patient's symptoms & signs were entered in proforma with detailed clinical examination in relation to thyroid. All the patients were subjected to basic investigations like complete hemogram, blood sugar, urea, urine analysis, chest X-ray.

Thyroid profile TotalT4,TotalT3,TSH done for all the patients. X – ray neck, E.C.G. were taken for the cases. Ultrasonogram of thyroid & Radio Isotope study was not done since the facility is not available in our hospital.

Since Radio Iodine ablation therapy is not available in our hospital , our patients were treated with either antithyroid drugs or surgery.

Surgery was the mode of treatment offered to all the patients. But out of 50 cases , surgery was done for only 45 cases & for rest of the 5 patient surgery was deferred due to various reasons & those five patients were treated with antithyroid drugs only.

The 45 patients who were planned for surgery were put on anti thyoird drugs as part of pre operative preparation to euthyroid status & to prevent thyrotoxic crisis. They were monitored by daily sleeping pulse chart, periodic

weight monitoring, & by symptomatic improval. Surgery was done after pre operative preparation to euthyroid state with anti thyroid drugs.

Pre Op Preparation : Most of our patients required an average dose of Carbimazole 10 mg 8^{th} hourly . And propranolol was also given in a dose of 40 mg 12 th hourly for patients with severe toxic symptoms. And 10 days prior to surgery, Lugol's iodine 5 – 10 drops 8^{th} hourly was given to patients. Few patients were given Colloidal iodine instead of Lugol's iodine. Night sedation was given with Dizepam or Alprazolam.

SURGERY in the form of → SUBTOTAL or NEAR TOTAL or TOTAL THYROIDECTOMY was done.

Post operative complications were analysed & the patients regularly followed up.

The patients in whom surgery was deferred were treated with antithyroid drugs.

Total T4 level 3 months after surgery (for 45 patients)& Total T4 level 3 months after medical therapy (for 5 patients) were measured & analysed.

All the observations were analysed & compared with standard results.

CASE ANALYSIS

AGE INCIDENCE:

Youngest age encountered was 23 years and the oldest age is 46 years. The case frequency according to age group.

AGE IN RANGE (years)	No. of CASES (total 50)	PERCENTAGE
20 - 30	14	28%
31 - 40	28	56%
41 – 50	8	16%

Average Age - 33 years

SEX INCIDENCE:

Thyrotoxicosis is common in females. In our series females predominate. The overall male : female ratio is 1: 9

The sex incidence in our study is as follows:

CASES	Total cases (50)	Percentage
Male	5	10
Female	45	90

FAMILIAL INCIDENCE:

In this study no family or hereditary incidence was noted.

CLIMATIC VARIATIONS:

A seasonal variation in the intensity of toxicity was suggested in studies. But in our study, no such climatic variation is noted.

CLINICAL PRESENTATION

Goitre was present in all the cases . And the frequency of each type in our study is :

TYPE OF GOITRE	No. of Cases (50)	PERCENTAGE
Diffuse Toxic goiter (D)	15	30%
Toxic MNG (M)	35	70%

Out of 50 cases, 35 patients presented with toxic MNG , 15 patients had Diffuse Toxic goiter & no patient had Solitary toxic nodule.

CLINICAL FEATURES:

All the cases studied had goiter. The incidence of various thyrotoxic symptoms in our study is tabulated below :

S.No	PRESENTING SYMPTOMS	No. OF CASES (total – 50)	PERCENTAGE
1	Goitre	all	100 %
2	Tremor	19	38%
3	Palpitation	35	70%
4	Heat intolerance	21	42%
5	Excitability	20	40%
6	Sleep disturbances	30	60%
7	Weight loss	32	64%
8	Diarrhea	32	64%
9	Muscle weakness	19	38%
10	Ophthalmopathy	11	22%
11	Bruit	5	10%
12	Menstrual abnormalities	3	6%

Few patients had menstrual abnormalities like oligomenorrhea which got corrected once the patients were brought to euthyroid state. None of the patients included in the study had chest pain , dyspnea or any other cardiac symptoms or pressure symptoms like dysphagia , hoarseness of voice.

GRADE OF TOXICITY

The toxicity has been graded according to pulse rate as 1st degree , 2nd degree & 3rd degree. And the incidence in our study is as follows :

SEVERITY OF TOXICITY	PULSE RATE (per min)	No. OF CASES (total 50)
1st DEGREE	< 90	4
2nd DEGREE	90 - 110	16
3rd DEGREE	> 110	30

TREATMENT AND FOLLOW UP

In our series surgery was done for 45 patients. In the rest of 5 patients surgery was deferred for the following reasons : 3 were not willing for surgery , 2 were anaesthetically unfit for surgery . Those 5 patients were treated with antithyroid drugs.

All the patients who were planned for surgery were put on anti thyroid drugs as previously stated to attain euthyroid status before surgery.

Control Of Toxicity After Pre-Op Preparation

Duration for control of toxicity is analysed. Some patients with mild toxicity & early cases became euthyroid in 2 weeks. And in others it ranged from 3 to 6 weeks to control the toxicity. For few patients it took around 8 weeks for controlling toxicity.

SURGICAL TREATMENT :

Surgery done was Subtotal Thyroidectomy , Near Total Thyroidectomy, Total Thyroidectomy. For most of the patients Subtotal thyroidectomy was done. TT4 level measured in all the cases 3 months after surgery.

SURGERY DONE	No. of CASES (45)
Subtotal Thyroidectomy	33
Near Total Thyroidectomy	8
Total Thyroidectomy	4

MEDICAL TREATMENT WITH ANTITHYROID DRUGS:

In the 5 patient in whom surgery was deferred , antithyroid drug therapy was started. They were given Tab.Carbimazole 10 – 20 mg 8^{th} hourly & Tab. propranolol 40 mg 12^{th} hourly & night sedation with diazepam . TT4 level measured in all the cases 3 months after therapy.

COMPLICATIONS :

During surgery & in the post operative period the complications that were encountered are summarized:

Two Patients Developed Hypoparathyroidism: It manifested as :

- Tetany
- Carpo pedal spasm
- Chvostek's sign positive
- Trousseau's sign positive
- One patient developed symptoms on the 2^{nd} day , other on the 3rd day.

They were managed as follows:

- Serum Calcium estimation
- Serum phosphorus
- Oral Calcium
- I.V. Calcium gluconate as required.

Two Patients Had Unilateral Recurrent Laryngeal Nerve Palsy :

It manifested as :

- Hoarseness of voice
- Coughing on taking liquid drinks
- Subsequent IDL scopy showed the paralysed vocal cord in para median position
- They did not develop aspiration.
- They were treated with I.V. steroids (dexamethasone & hydrocortisone
- They improved symptomatically subsequently.
- They were advised reassurance & did not develop any further complication

One Patient Developed Stitch Granuloma;

It presented as;

- Continuous serous discharge from a sinus in the scar for about 3 months in the post operative period.
- Wound was explored under Local Anesthesia & there was found to be silk suture protruding in the sinus.

- The silk was cut as low as possible & the scar excised & wound resutured.

- Inference: Use of non absorbable suture material causes stitch granuloma & sinus.

- Two patients developed wound gaping & were treated with dressing, resuturing etc…

- Two patients developed subcutaneous serous collection / haematoma, they were treated by aspiration.

There was no incidence of Thyroid Storm or Respiratory Distress or Tension Hematoma or Recurrent Thyrotoxicosis. All the patients are living peacefully.

COMPLICATION RATE

Ranges of results of surgery	**From Hershman ranges of percentage**	**In our series percentage**
Mortality	< 3.1 %	Nil
Vocal Cord Palsy	0.0 – 4.4 %	4 %
Hypoparathyroidism	0.0 – 3.6 %	4 %
Recurrent thyrotoxicosis	0.6 – 17.9 %	Nil
Hypothyroidism	4 – 29.7 %	20 %

DISCUSSION

Most of the patients who were diagnosed to have thyrotoxicosis were in the age group of 31 – 40 years. Most of the patients who presented with graves' disease were in the age group 20 – 30 years. Most of the cases with toxic MNG were in the age group of 30 – 45 years .

In our study, incidence of thyrotoxicosis in females was high & the male to female ratio in our study was 1: 9.There was no familial incidence in our study.

Of the types , most of the patients had Toxic MNG (35 patients) & none of our cases included in the study had Solitary toxic nodule.

All the patients had goiter. The most significant clinical features were palpitation, weight loss , hyperdefecation, sleep disturbances, excitability & heat intolerance in the order of frequency. With regard to pulse rate , most of the cases had severe toxicity 3rd degree with pulse rate >110 / min .

TSH, Total T4 ,Total T3 was done for all the cases . In all the cases the TSH was reduced & T4 & T3 was raised confirming the hyperthyroid state & indicating the severity of the disease. TT4 repeated for all cases 3 months after therapy (both surgery & drug).

All the patients in whom surgery was planned , were given antithyroid drugs & taken up for surgery after adequate control of toxicity . This prevented the complication of thyroid storm in the per operative & in the post operative period. After giving antithyroid medications , euthyroid state was attained on an average of 3- 4 weeks with a minimum of 2 weeks & maximum of 8 weeks

Most of cases underwent Subtotal thyroidectomy. All the cases were followed up in the post operative period until the study period . It was noted that none of our patients had recurrent thyrotoxicosis & there was no mortality with a little morbidity . The patients who underwent total thyroidectomy were given thyroxine replacement in the form of Eltroxin tablets in a dose of 0.1mg/day. The histopathology of operated specimen was studied . And there was no evidence of malignancy in the Histo Pathology of the operated specimen .

The mean T4 level for patients treated with surgery & for patients treated with antithyroid drugs was analysed 3 months after therapy. The T4 level in the patients treated with surgery was reduced significantly to normal level or to just below normal level in the range of 2-4 µU /ml (Nl level 4.5 – 12µU/ml). But in cases treated with antithyroid drugs the T4 level was reduced to an average level of 12 - 14µU/ml which is just above the normal level stated above.

Out of the 5 patients treated with anti thyroid drugs only 1 came for routine follow up & other 4 patients did not turn up after 3 months. And the significance of drug therapy in them could not be assessed properly.

From the available data , in general it can be stated that surgery is the appropriate form of treatment that can be safely offered to patients with thyrotoxicosis in our set up since most of the patients do not come for routine & regular follow up .

CONCLUSION

In this study a comprehensive account of history , anatomy, physiology with a detailed account of the clinicopathological aspects, presentations & various modalities of treatment of thyrotoxicosis have been dealt with. 50 cases of thyrotoxicosis have been dealt with.

From the evidence, it is clear that after adequate control of toxicity with anti thyroid drugs, surgery is the modality of treatment that can be safely offered to patients with thyrotoxicosis in our set up.

This present study confirms the observation made by the reputed authors & emphasizes the importance of perfect & sufficient pre operative preparation, meticulous surgical technique, detailed knowledge about anatomy of thyroid , parathyroid & associated nerves assures complete remission with negligible morbidity & nil mortality.

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THYROTOXICOSIS CASE PROFORMA

Name : Age : Sex

Address: Occupation

I.P no. :

D.O.A : D.O.S : D.O.D :

COMPLAINTS

H/O PRESENT ILLNESS

SYMPTOMS

Swelling

Mode of onset

rate of growth

pain

Increased appetite & weight loss heat intolerance & preference to cold, excessive sweating, excitablity, irritablity, restlessness, Insomnia, tremor of hands, palpitation, muscle weakness, visual disturbance,diplopia, protrusion of eyes, Chest pain, dyspnea, dysphagia,hoarseness of voice

H/O PAST ILLNESS

HT, TB, DM

PERSONAL HISTORY

Smoking ,Alchohol

Intake of brassica vegetables

Family history:

Menstrual history:

Obstetric history:

Treatment history;*drug intake

*irradiation

*surgery

GENERAL EXAMINATION:

Built Nutrition anaemia dyspnea jaundice cyanosis

Generalized lymphadenopathy

Tremor of hands & tongue

Leg edema(pretibial myxedema)

Eye signs: Lid retraction & Lid lag

Exopthalmos – Von graefe's sign, Joffroy's sign, Stellwag's sign, Moebius sign, Dalrympte's sign, Ophthalmoplegia, Chemosis

PR; Sleeping PR RR B.P Temp CVS RS ABD CNS

LOCAL EXAMINATION OF NECK

INSPECTION

Swelling

Site

Size

Shape

Extent

Borders

Movement with deglutition

Movement with protrusion of tongue

Skin over the swelling

Surface

On sternomastoid contraction -

Trachea position

PALPATION

Warmth

Tenderness

Site ,size ,shape,extent

Borders

Skin over the swelling

Surface

Consistency

Mobility

Trachea position

Carotid pulsation

Kocher's test

Pemberton's sign

PERCUSSION Over manubrium

AUSCULTATION: Bruit

LYMPH NODES

SKELETAL SYSTEM & SPINE

DIAGNOSIS

INVESTIGATIONS

Hb Tc Dc

ESR

Bl. Sugar Urine R/E

E.C.G ECHOCARDIOGRAM

X – RAY CHEST X– RAY NECK

THYROID FUNCTION TEST

Nl value

TSH, TT4, TT3, FT4, FT3

ANTIBODY, USG THYROID, THYROID SCAN, IDL, FNAC

TREATMENT

MEDICAL

Drug	Dose	Duration	Toxicity
1)			
2)			
3)			

Treatment for drug toxicity

Control of toxicity attained after ……weeks

SURGERY: ……

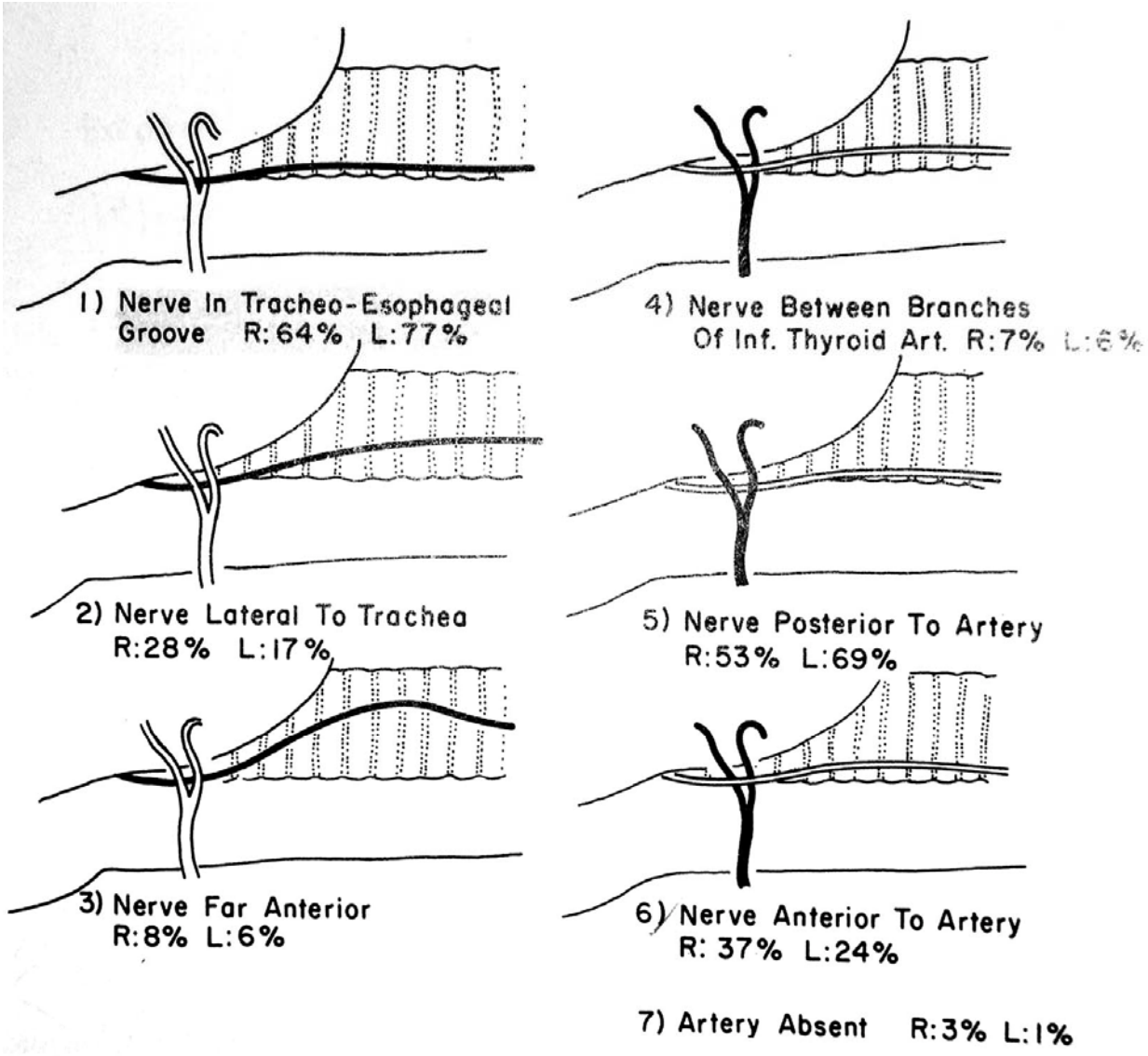
Post op complications:

Type	Treatment
1)……	
2)…….	
3)…….	

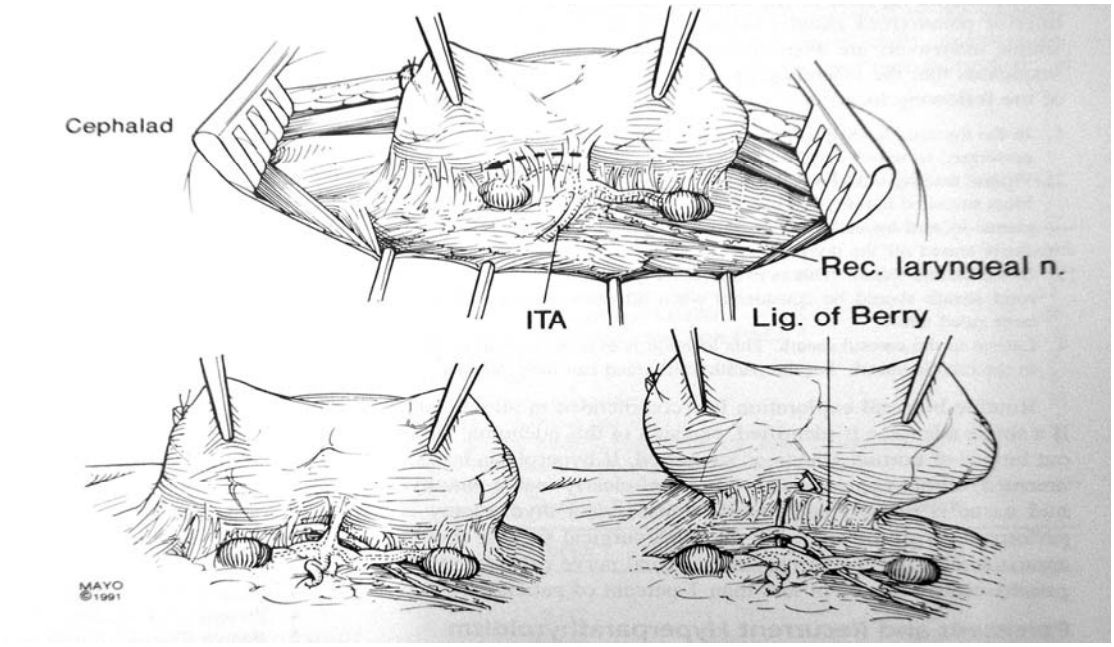
PROPRANALOL continued in the post operative period for 7 days

H.P.E

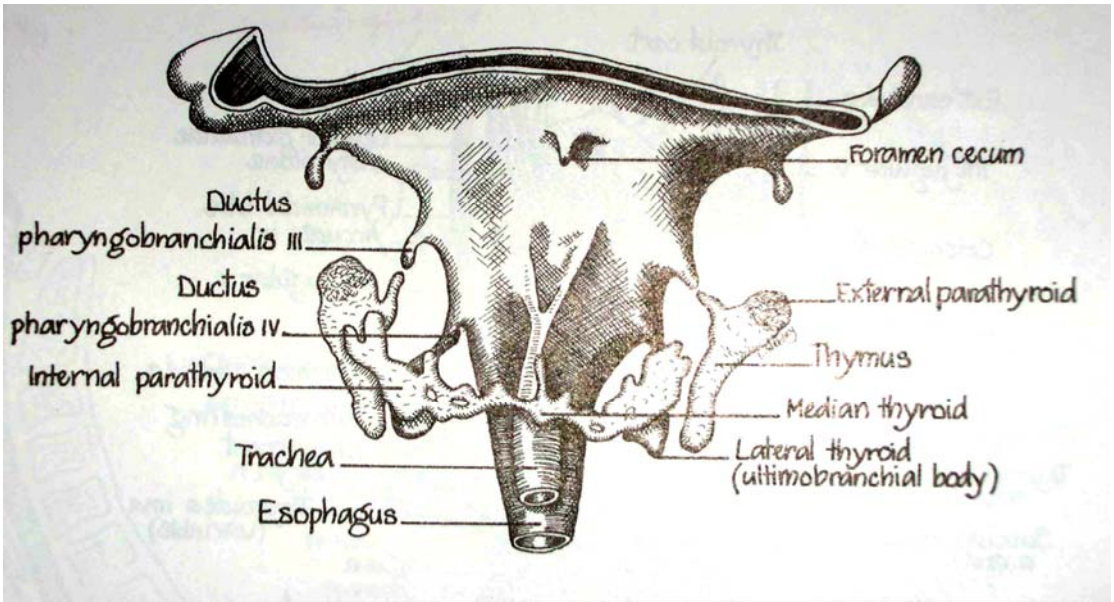
FOLLOW UP



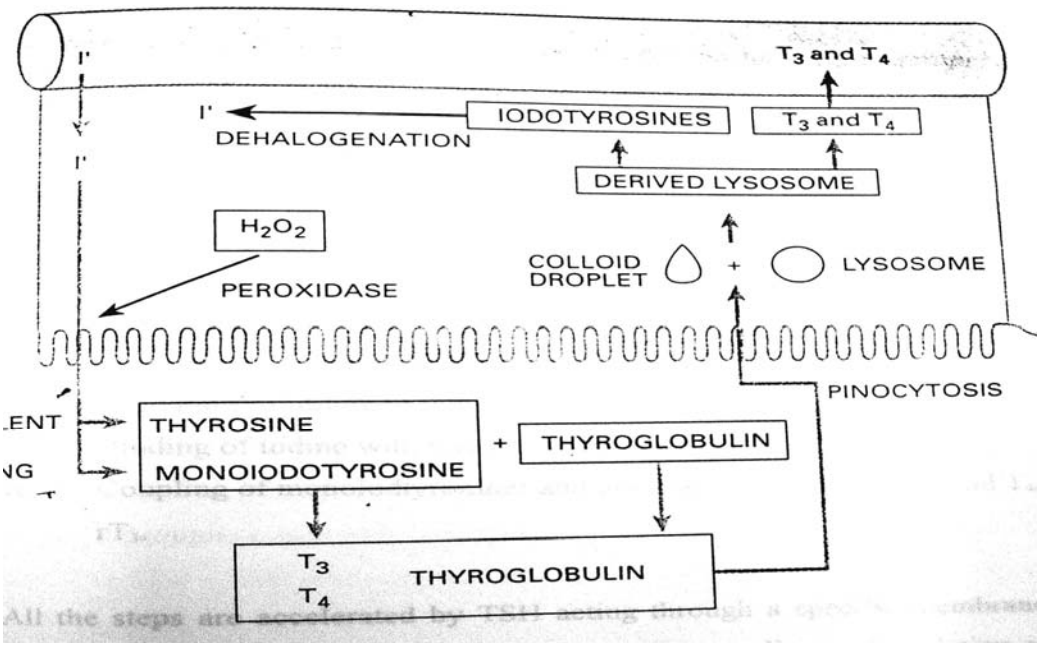
RECURRENT LARYNGEAL NERVE – RELATION WITH TRACHEO ESOPHAGEAL GROOVE & INFERIOR THYROID ARTERY



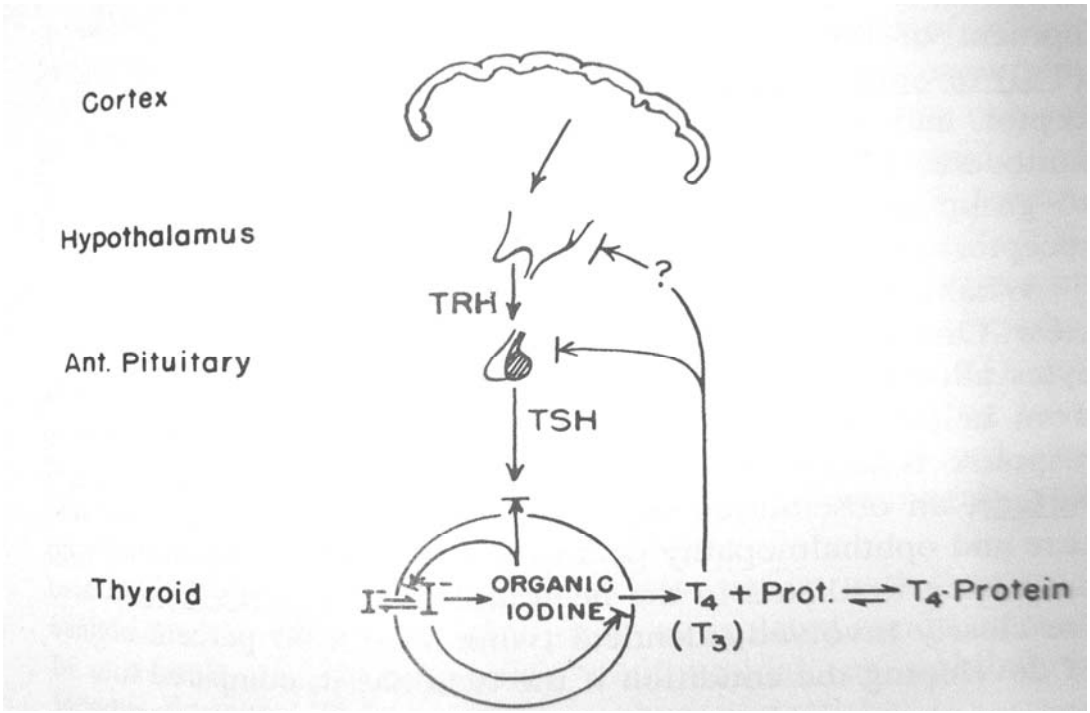
RLN IN RELATION TO INFERIOR THYROID ARTERY & PARATHYROIDS



DEVELOPMENT OF THYROID

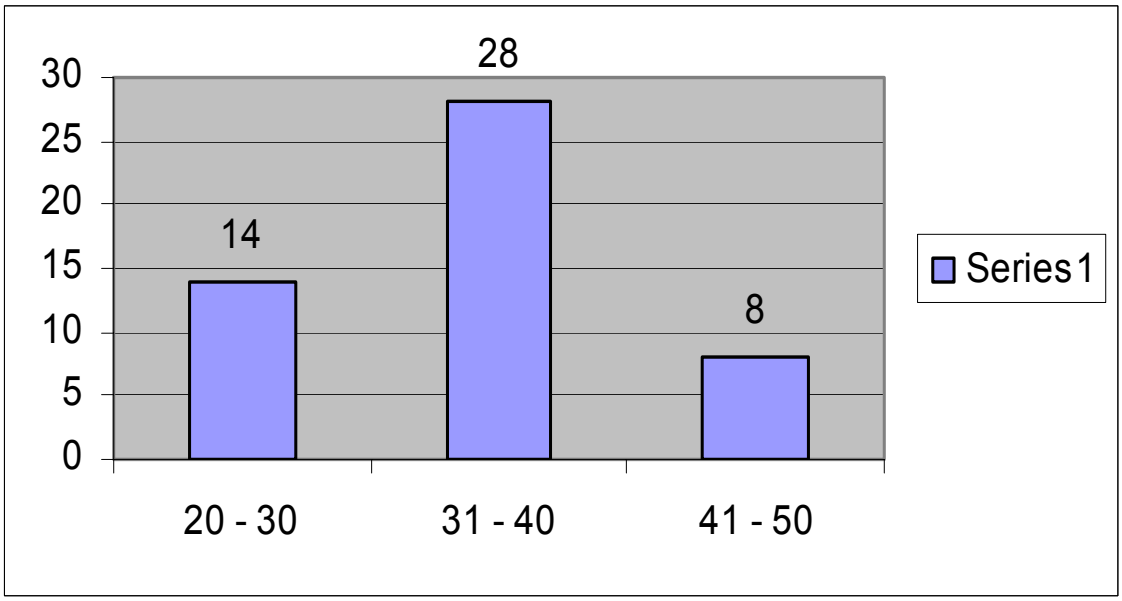


THYROID HORMONE SYNTHESIS

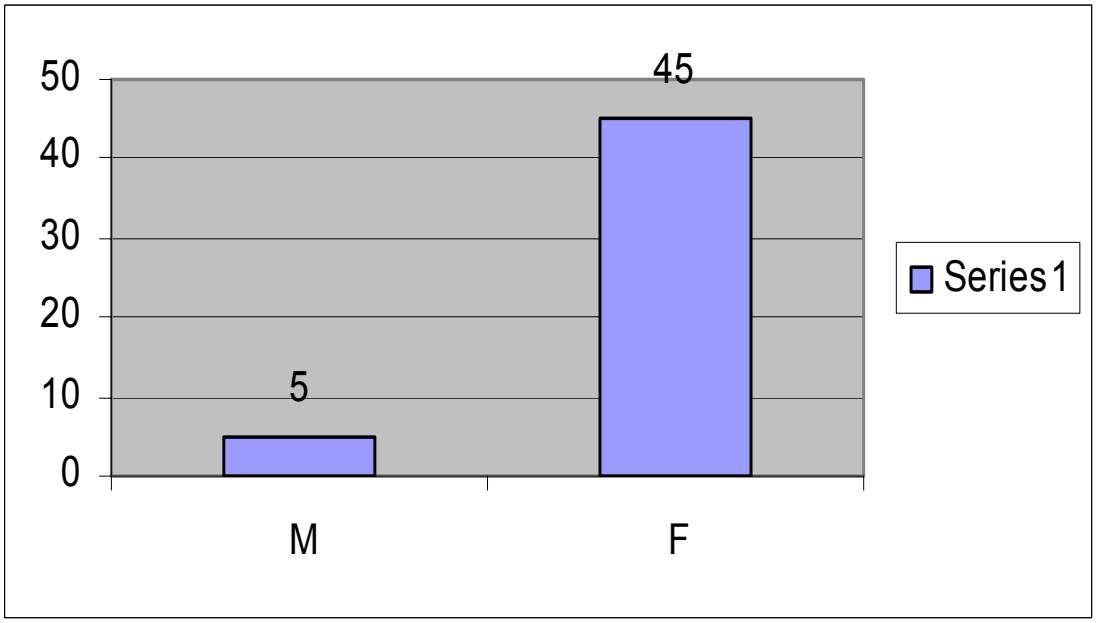


HYPOTHALAMO PITUITARY THYROID AXISp

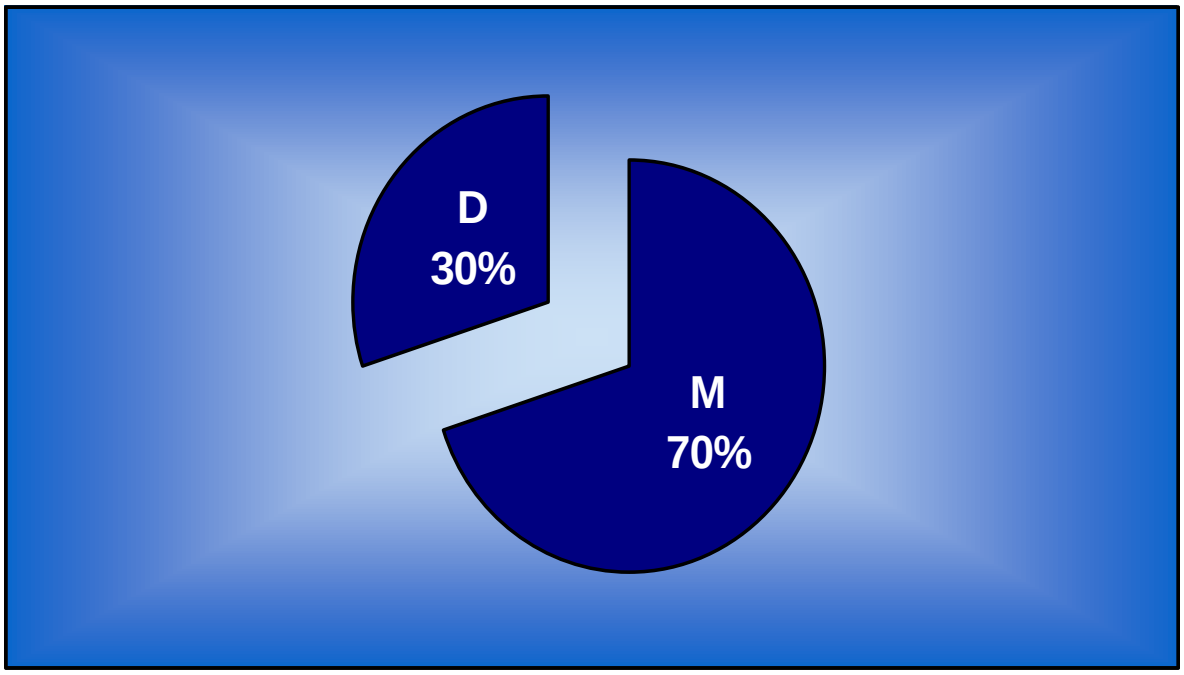
AGE INCIDENCE



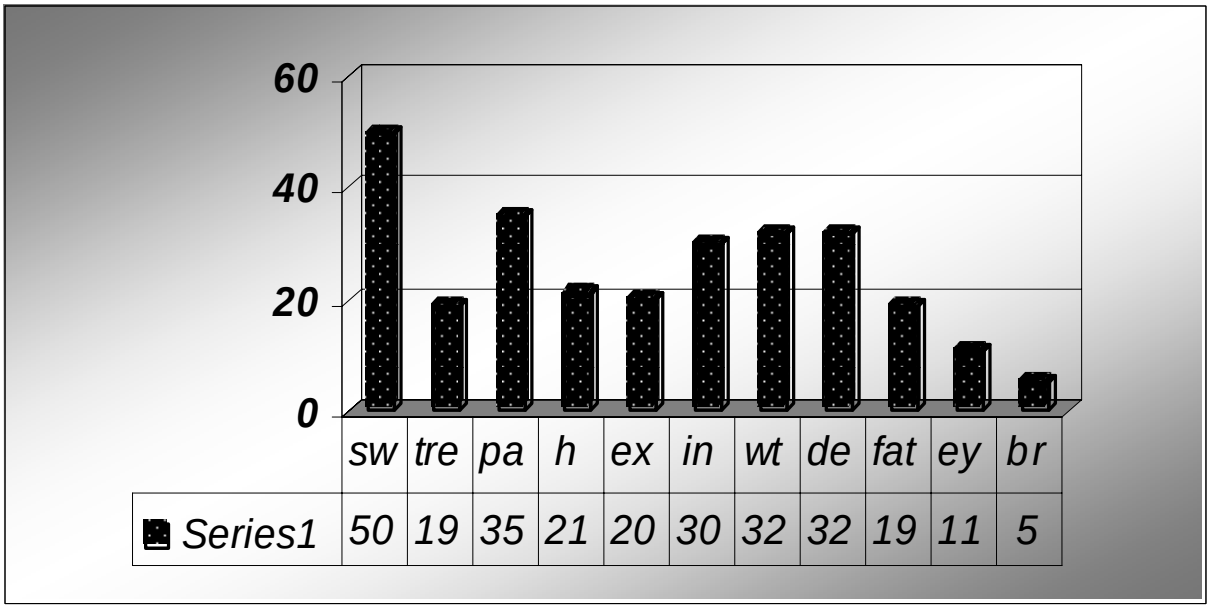
SEX INCIDENCE

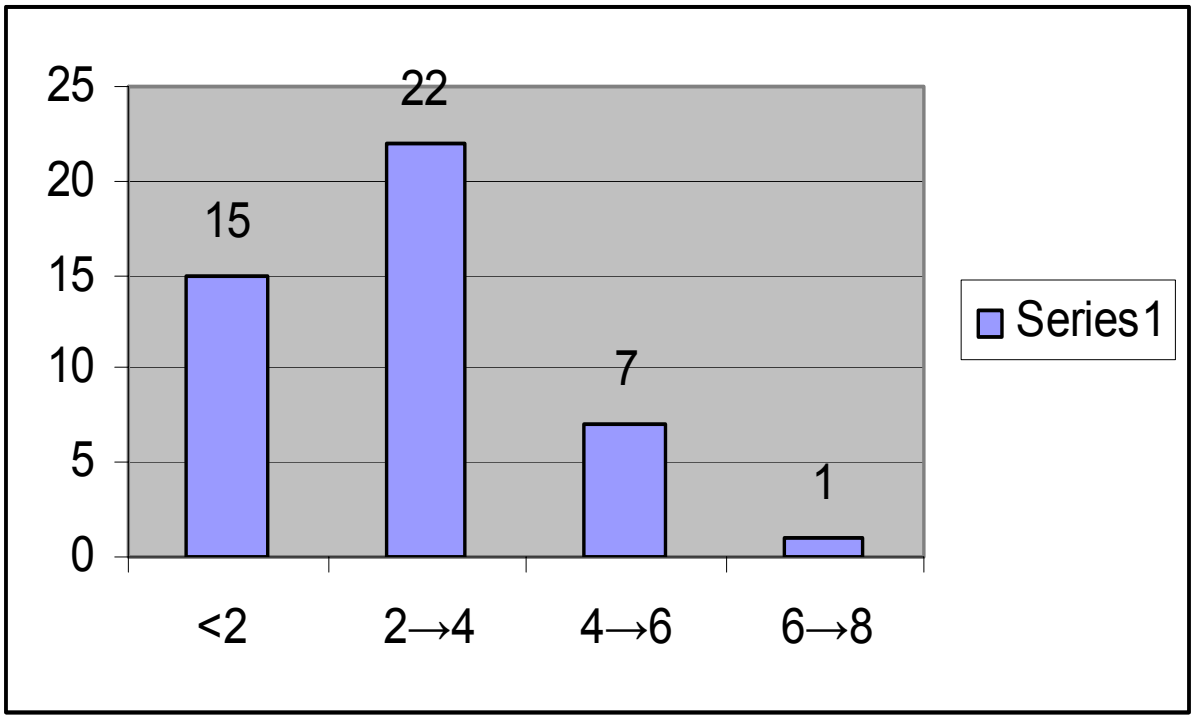


INCIDENCE OF GOITRE



INCIDENCE OF CLINICAL FEATURES

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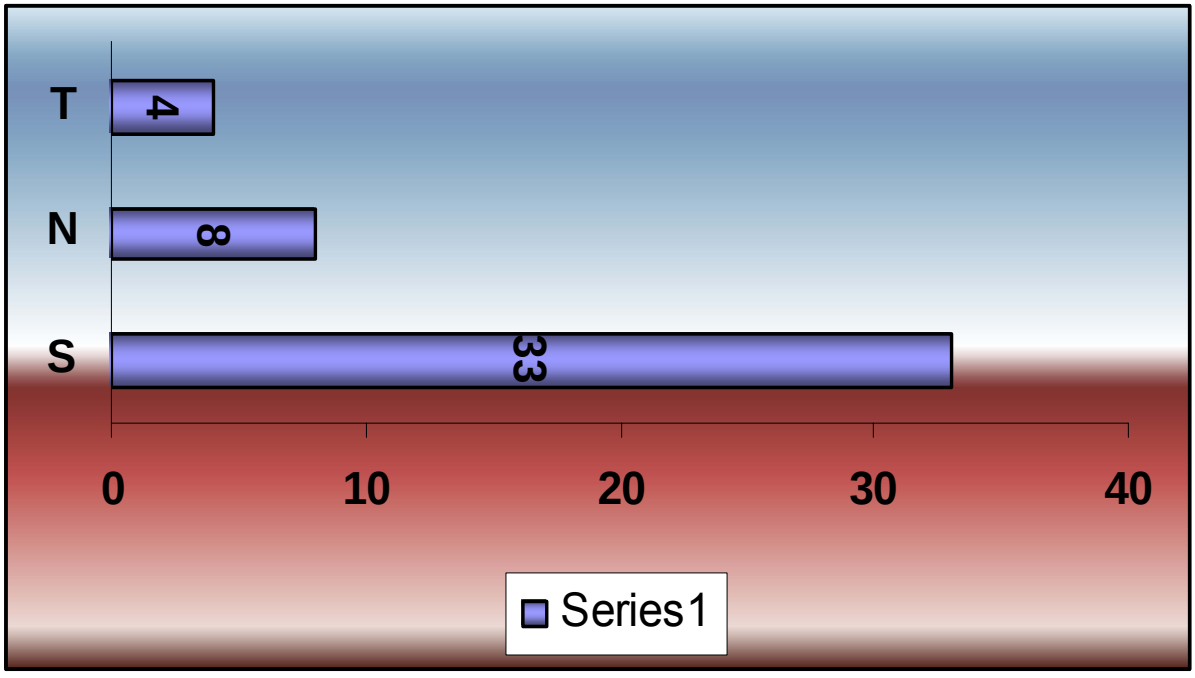
<2
2→4
4→6
6→8
Series1

SURGERY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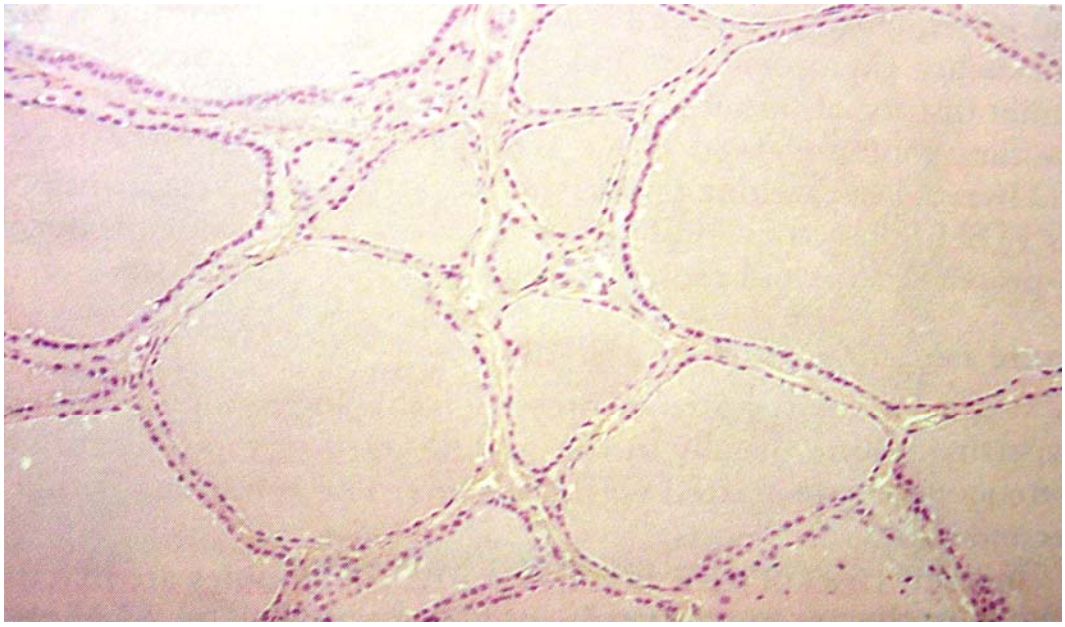
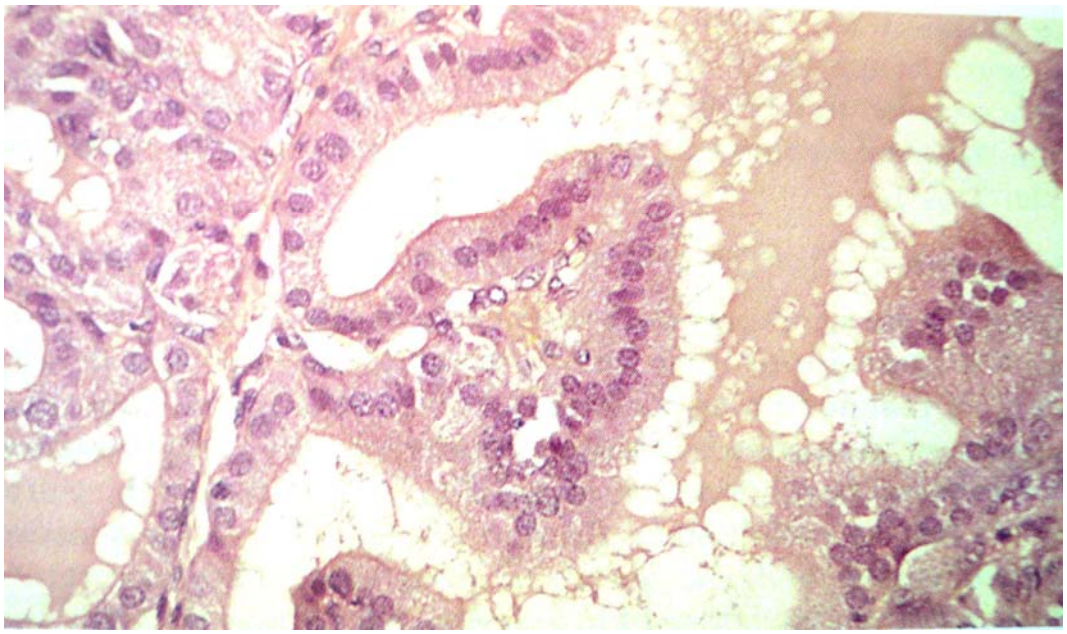
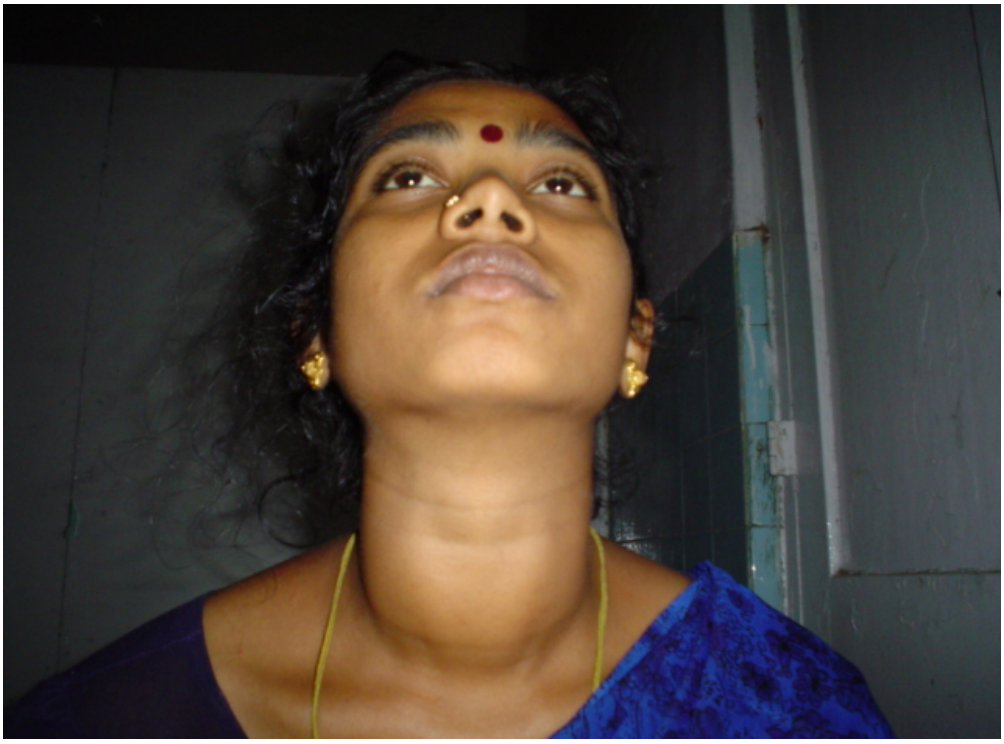


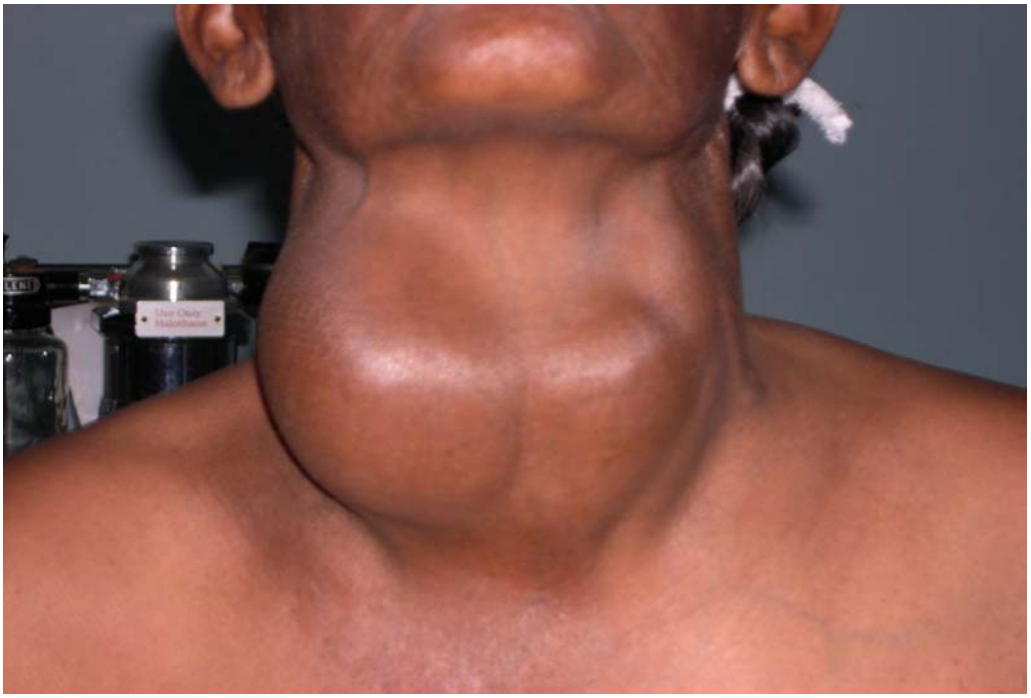
NORMAL THYROID HISTOLOGY



MICROSCOPIC PICTURE IN HYPERTHYROIDISM

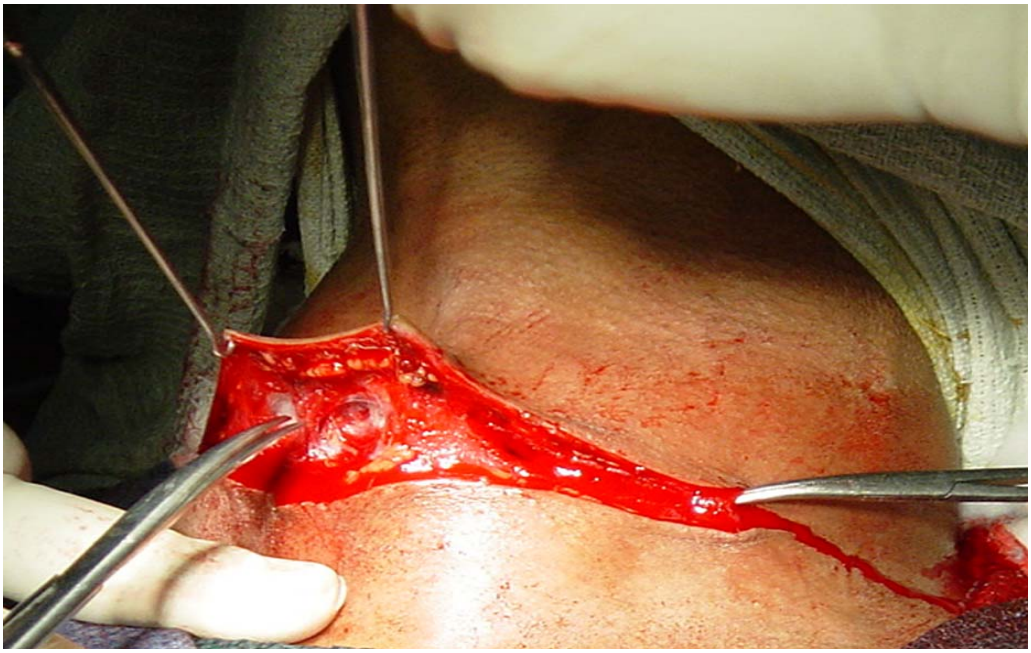


A CASE OF TOXIC MNG

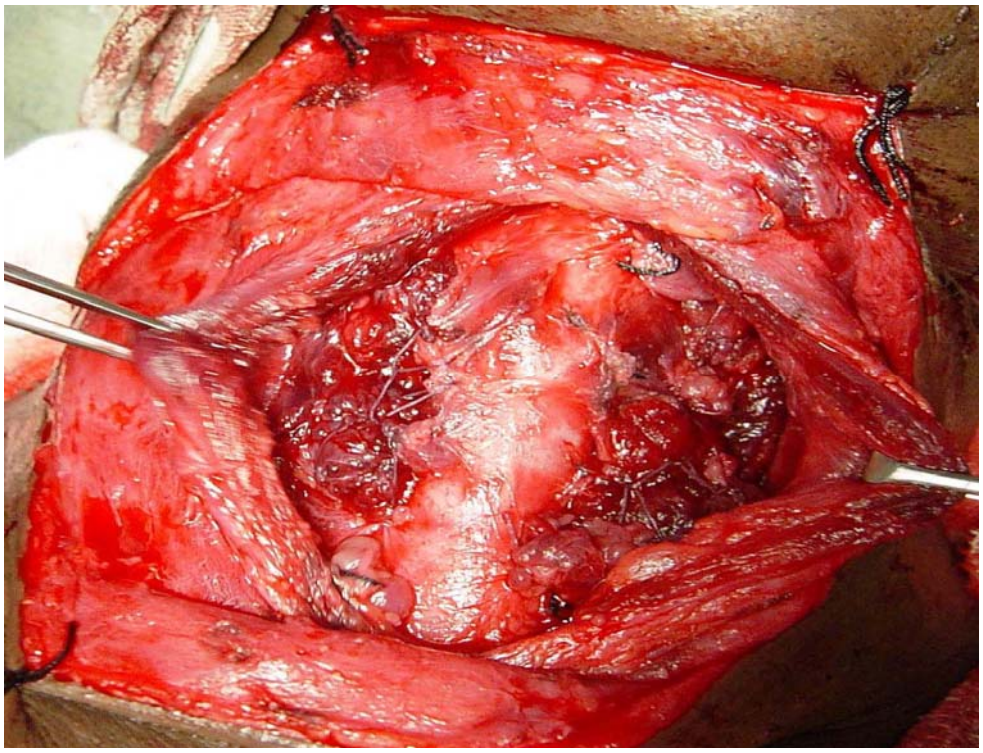


A CASE OF MNG

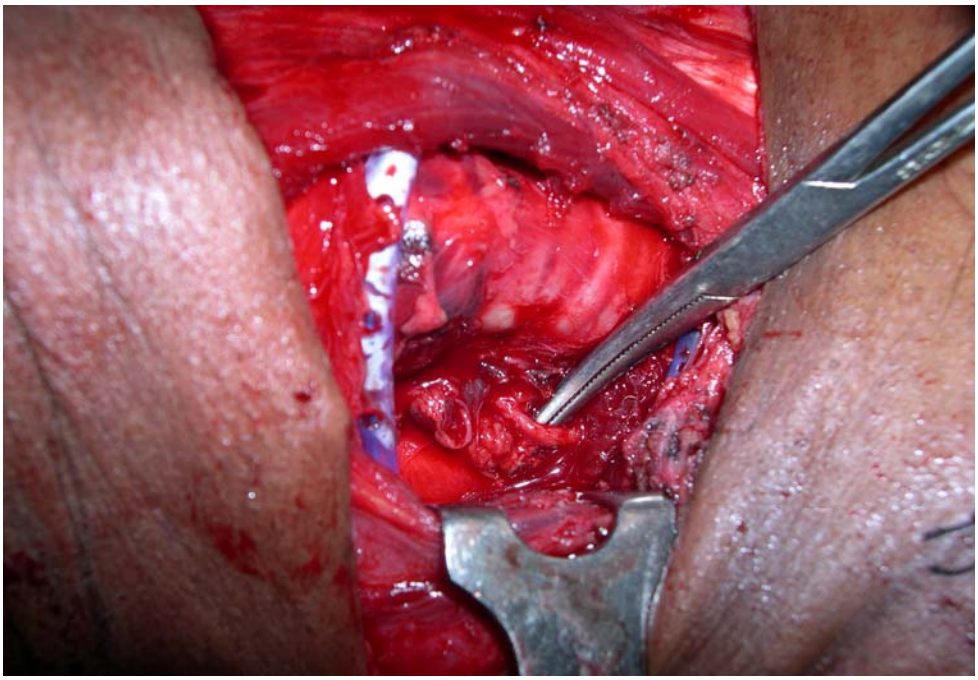
POSITION DURING SURGERY



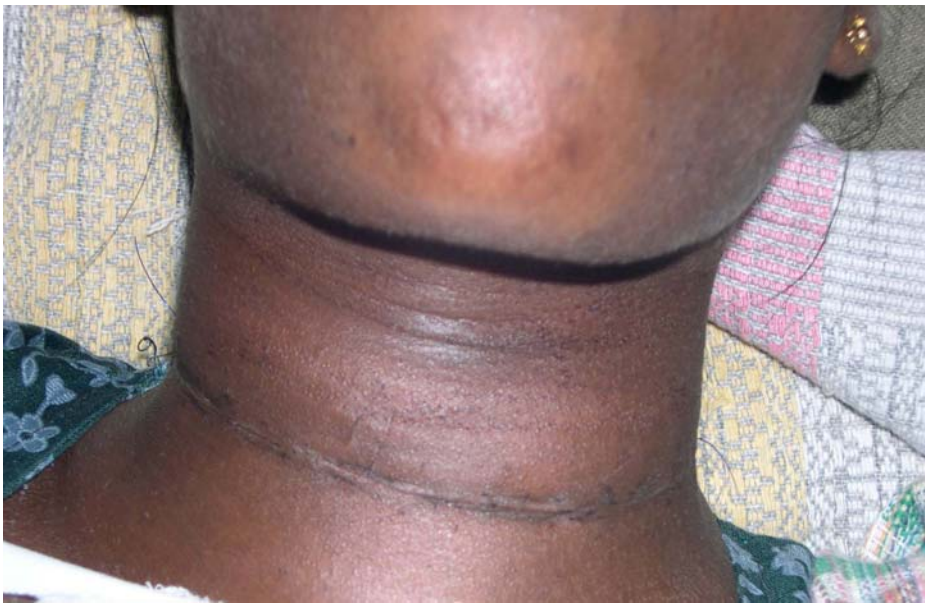
INCISION AND RAISING THE FLAPS



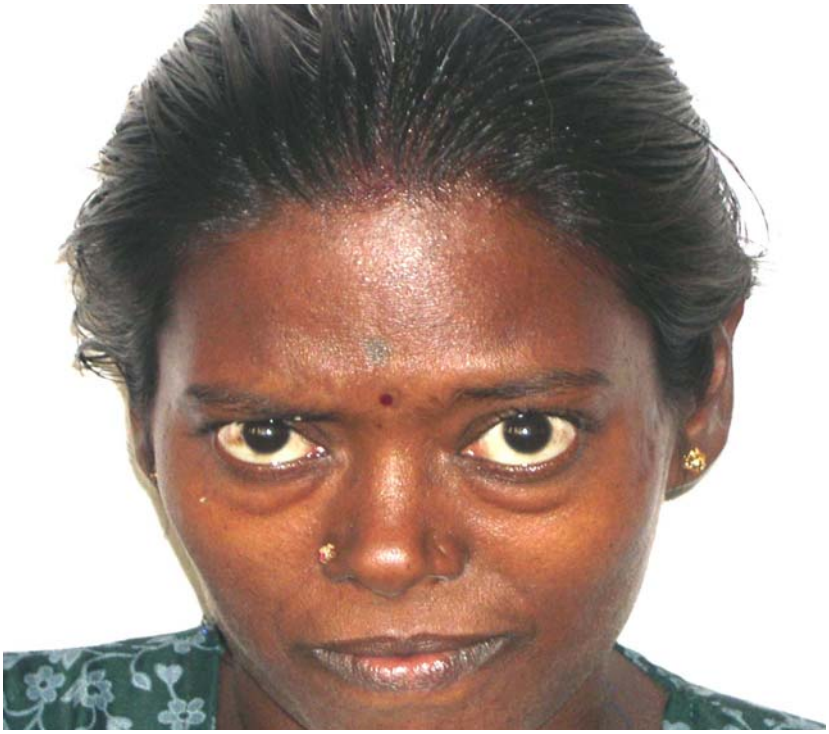
AFTER SUBTOTAL THYROIDECTOMY



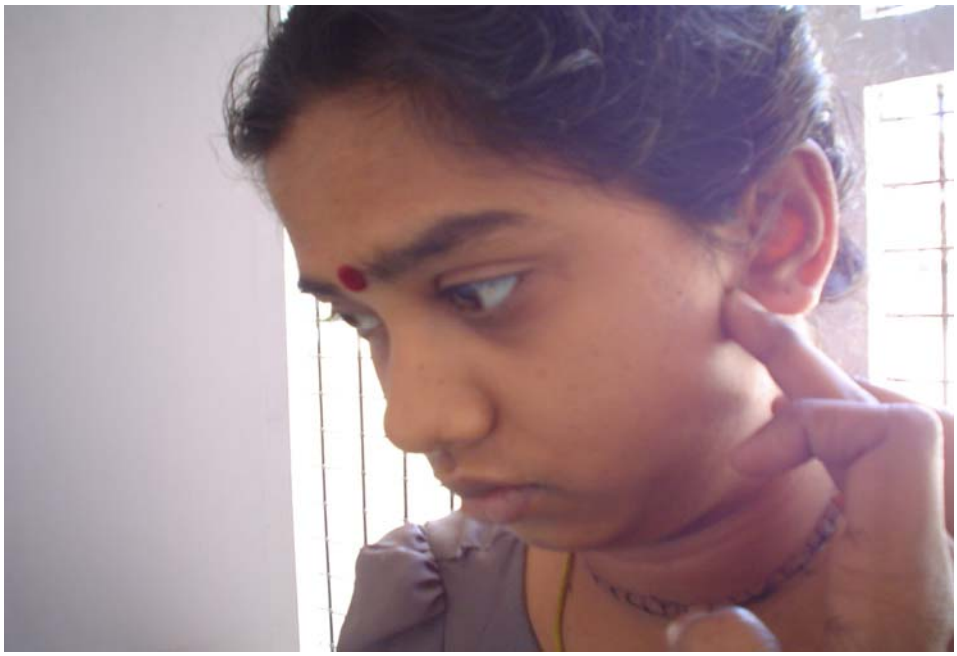
RECURRENT LARYNGEAL NERVE



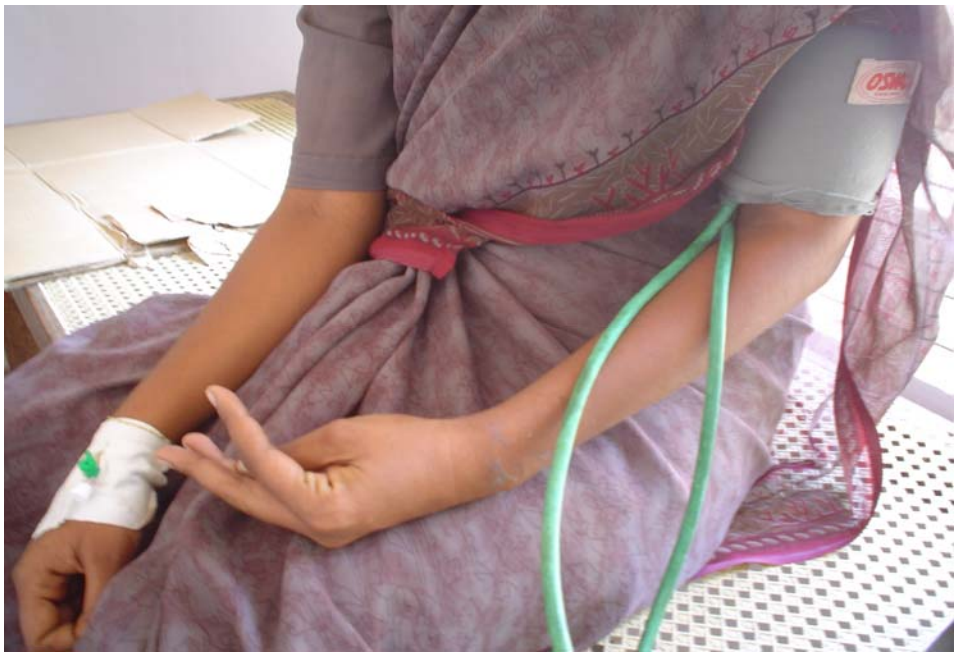
WOUND IN THE POST OP PERIOD



CASE OF TOXIC GOITRE WITH EXOPHTHALMOS



DEMONSTRATION OF CHVOSTEK'S SIGN



DEMONSTRATION OF TROUSSEAU'S SIGN