Hyperthyroidism and Thyrotoxicosis

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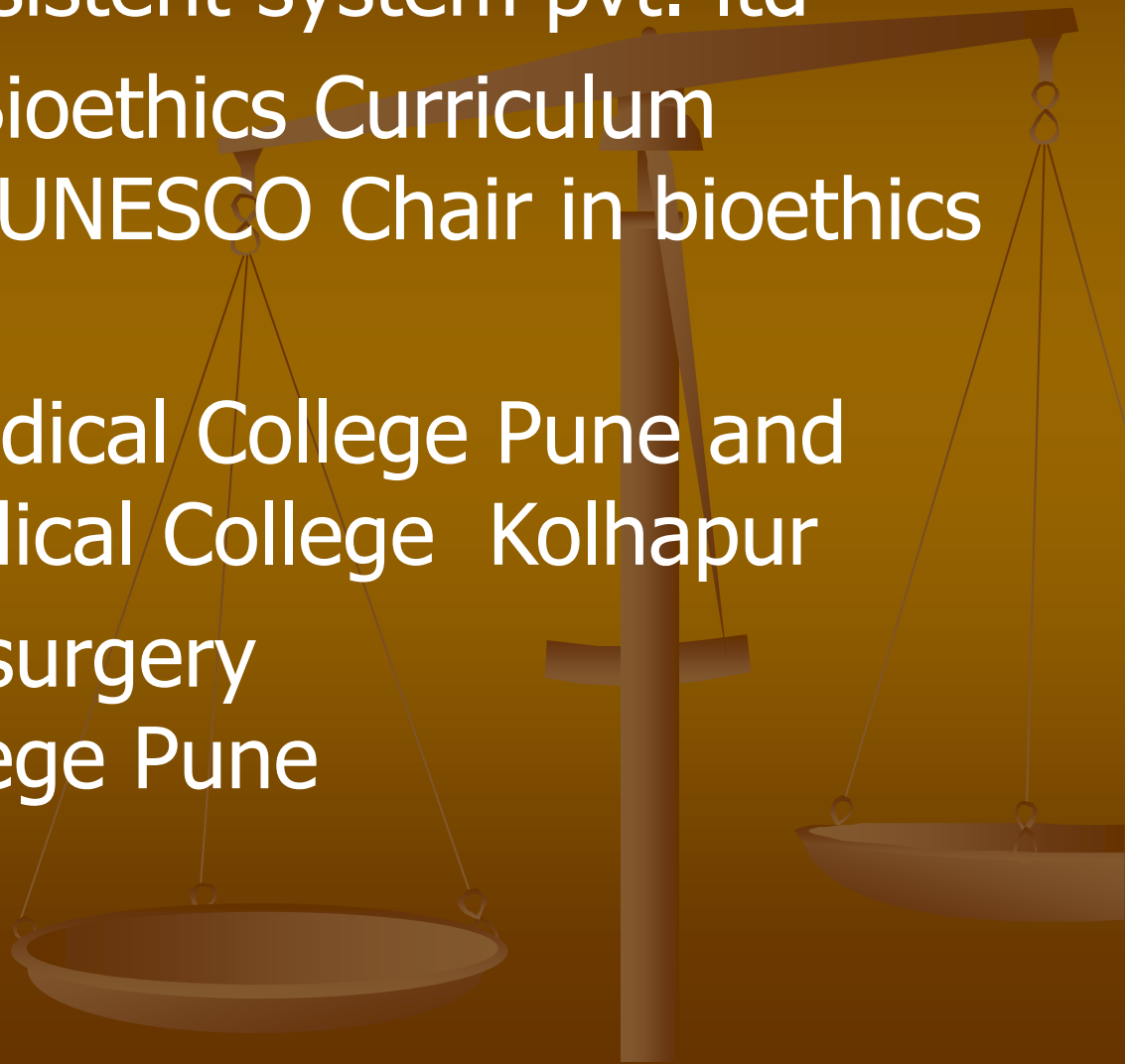
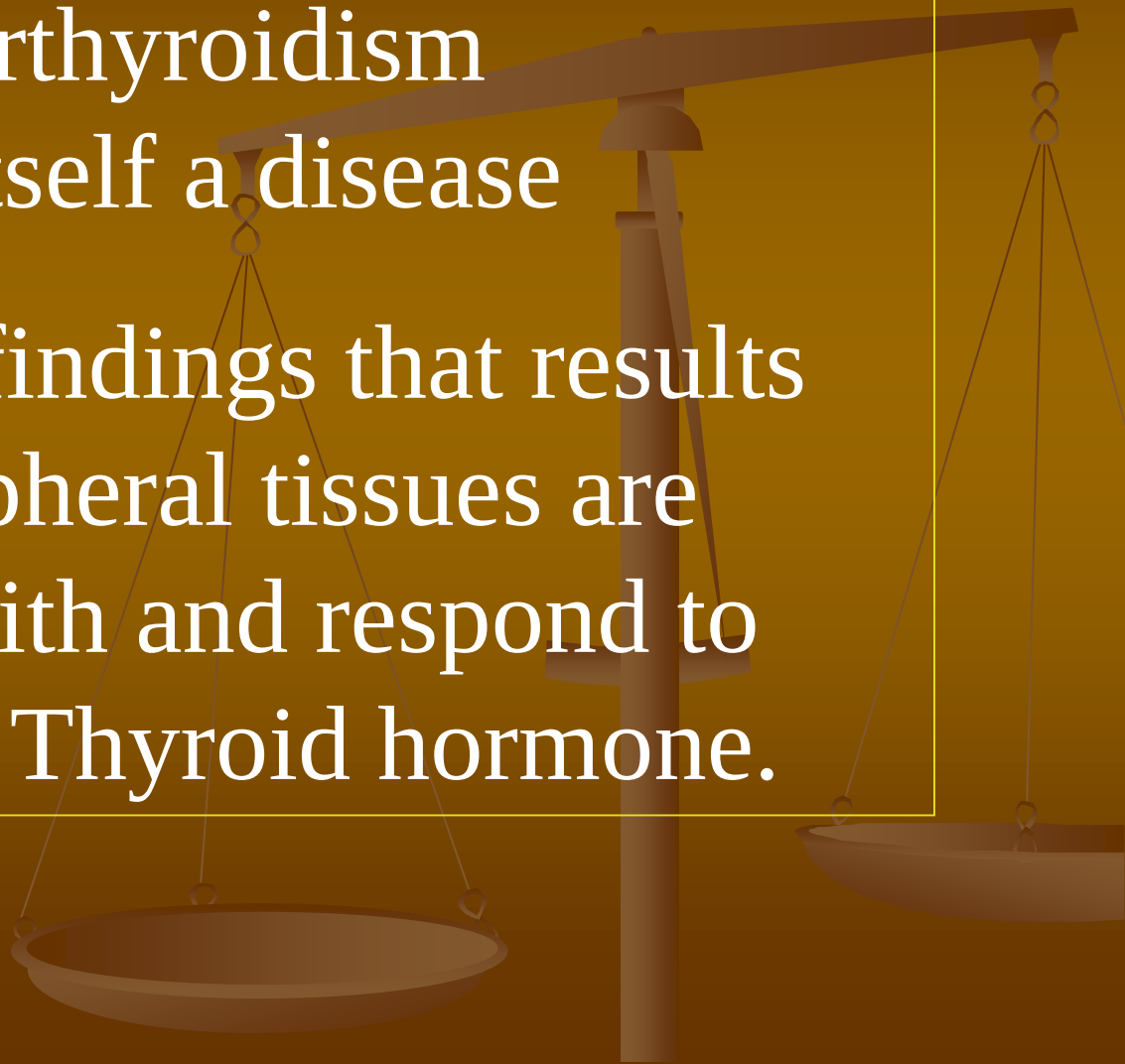
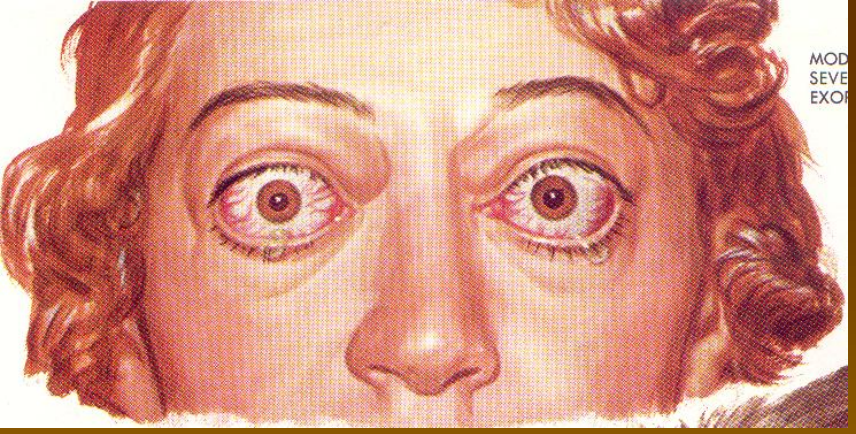


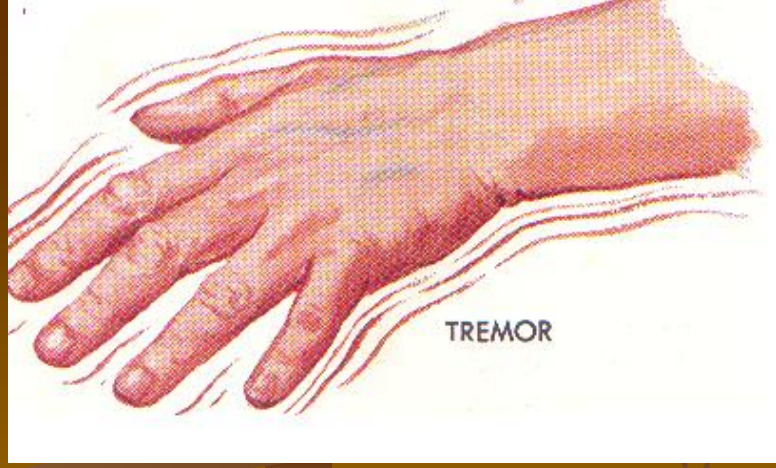
Hyperthyroidism

Hyperthyroidism
is not itself a disease

Complex of findings that results when peripheral tissues are presented with and respond to an excess of Thyroid hormone.





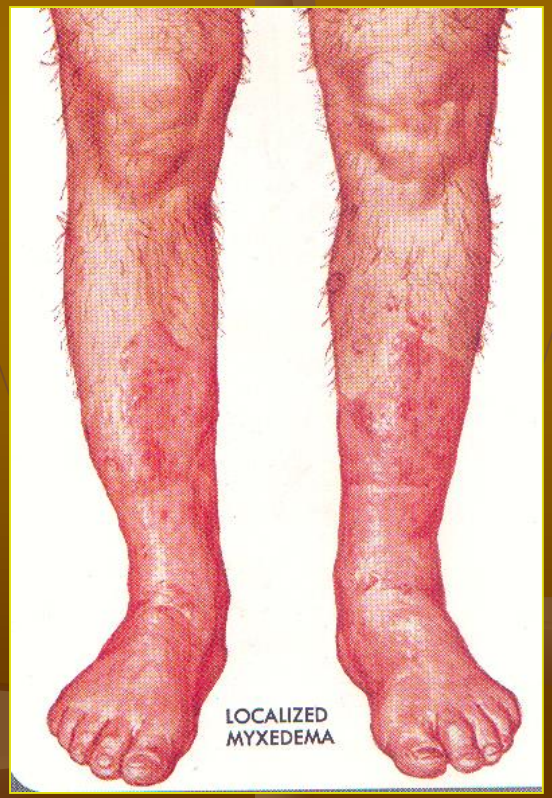


THYROTOXICOSIS

Exopthalamos

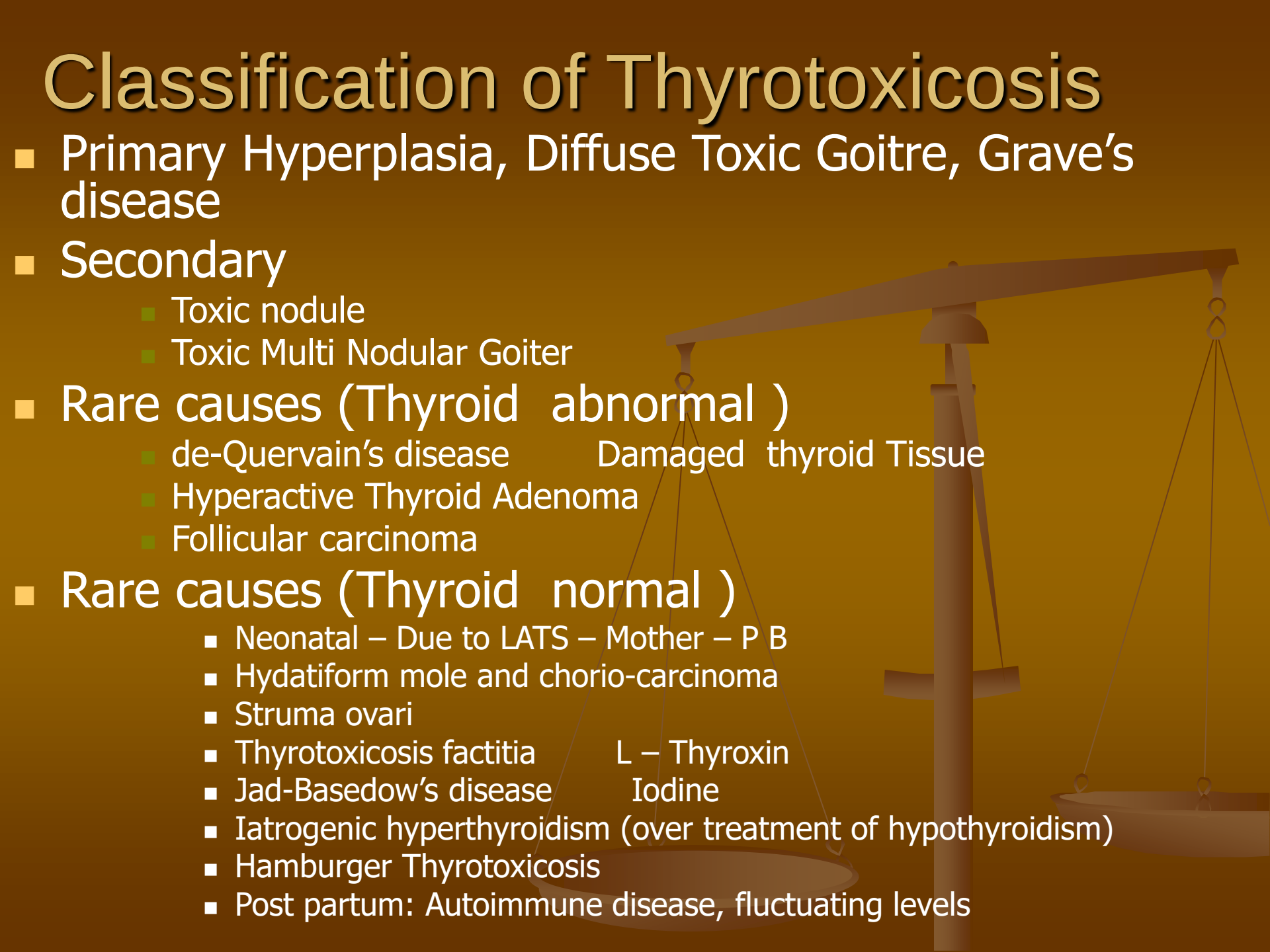
Tremors

Pre-Tibial Myxoedema



Classification of Thyrotoxicosis

- Primary Hyperplasia, Diffuse Toxic Goitre, Grave's disease
- Secondary
  - Toxic nodule
  - Toxic Multi Nodular Goiter
- Rare causes (Thyroid abnormal)
  - de-Quervain's disease Damaged thyroid Tissue
  - Hyperactive Thyroid Adenoma
  - Follicular carcinoma
- Rare causes (Thyroid normal)
  - Neonatal – Due to LATS – Mother – P B
  - Hydatiform mole and chorio-carcinoma
  - Struma ovari
  - Thyrotoxicosis factitia L – Thyroxin
  - Jad-Basedow's disease Iodine
  - Iatrogenic hyperthyroidism (over treatment of hypothyroidism)
  - Hamburger Thyrotoxicosis
  - Post partum: Autoimmune disease, fluctuating levels



Classification of Thyrotoxicosis

- Thyrotoxicosis associated with state of hyperthyroidism
- Thyrotoxicosis not associated with state of hyperthyroidism

Thyrotoxicosis associated with state of hyperthyroidism

- State of TSH excess :
  - Tumourous : TSH secreting tumours.
  - Non-Tumourous : Thyrotroph resistance to thyroid hormone
- Abnormal thyroid stimulator :
  - Graves Disease : TSH receptor antibody
  - Trophoblastic Tumour : HCG like thyroid stimulator
- Intrinsic Thyroid Autonomy :
  - Toxic adenoma : Benign tumor
  - Toxic Multinodular Goiter : Foci of functional autonomy

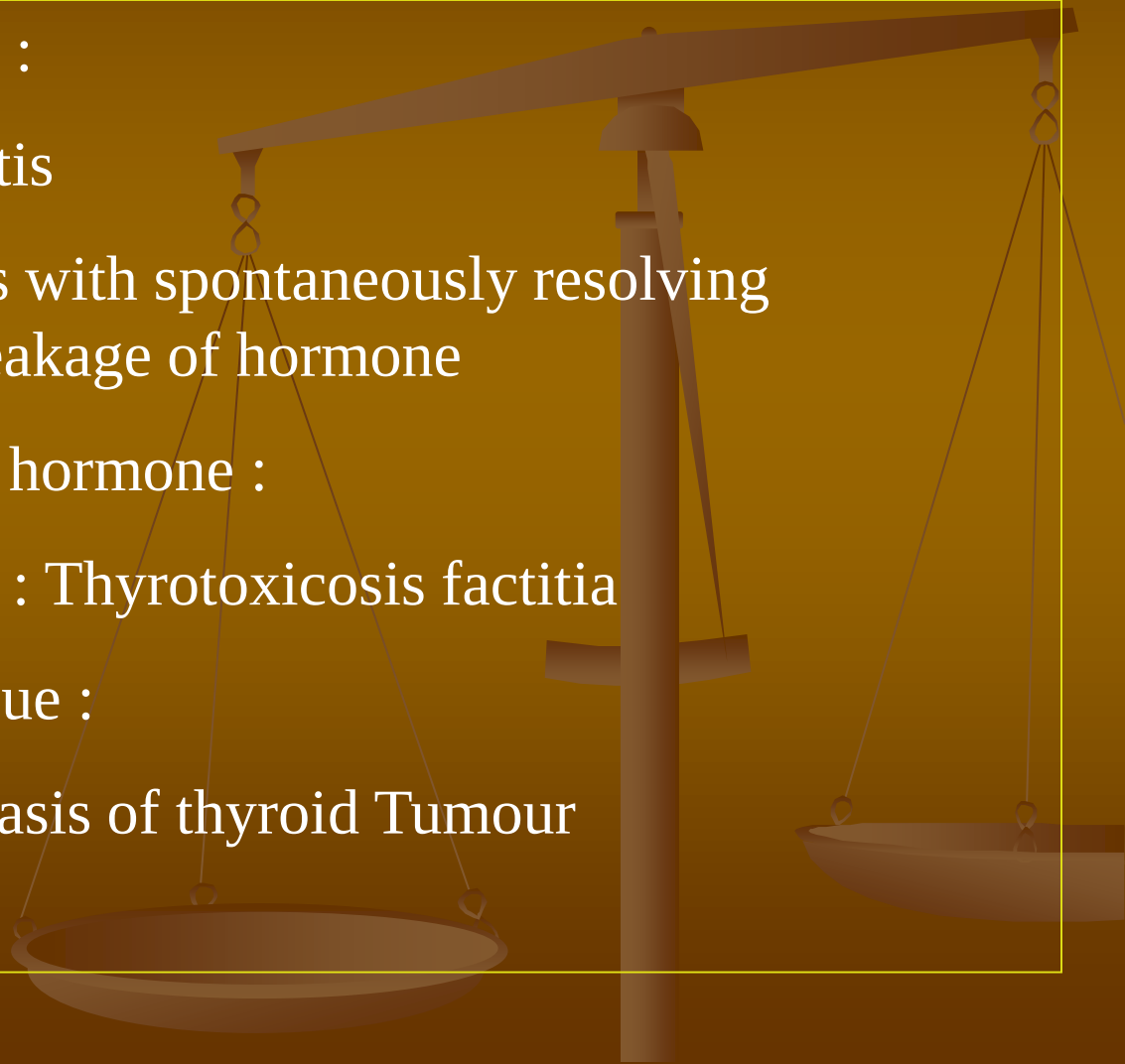
Thyrotoxicosis not associated with state of hyperthyroidism.

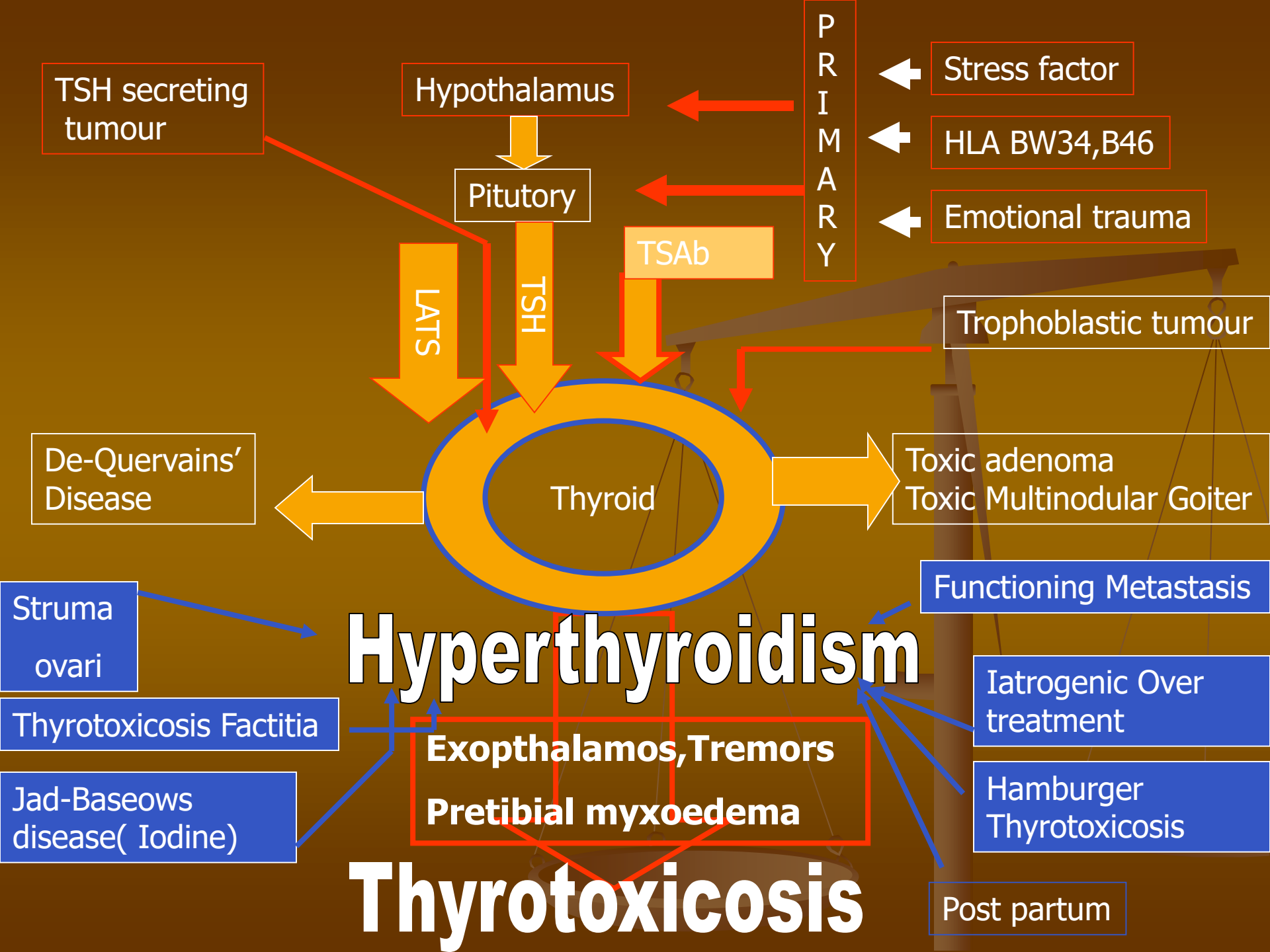
a) Inflammatory Diseases :

- Sub acute Thyroiditis
- Chronic Thyroiditis with spontaneously resolving Thyrotoxicosis –Leakage of hormone

b) Extra Thyroid source of hormone :

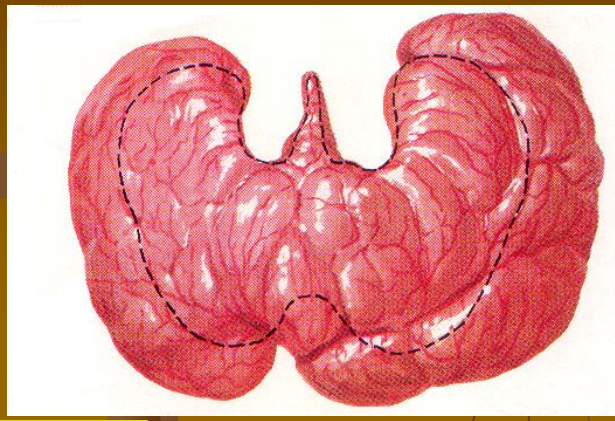
- Hormone ingestion : Thyrotoxicosis factitia
- Ectopic thyroid tissue :
- Functioning metastasis of thyroid Tumour
- Struma ovarii

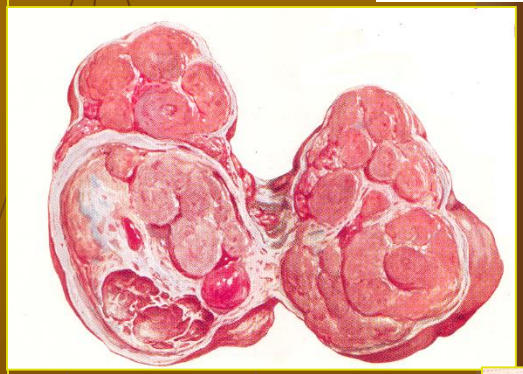


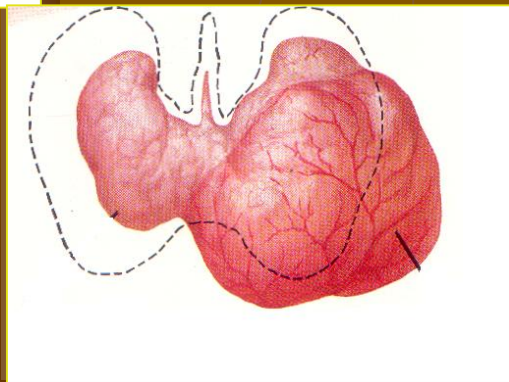

TSH secreting tumour
Hypothalamus
Pitutory
PRIMARY
Stress factor
HLA BW34,B46
Emotional trauma
TSAb
LATS
TSH
Trophoblastic tumour
De-Quervains' Disease
Thyroid
Toxic adenoma
Toxic Multinodular Goiter
Struma ovari
Functioning Metastasis
Hyperthyroidism
Thyrotoxicosis Factitia
Iatrogenic Over treatment
Exopthalamos,Tremors
Pretibial myxoedema
Jad-Baseows disease(Iodine)
Hamburger Thyrotoxicosis
Thyrotoxicosis
Post partum

Clinical types

- Diffuse toxic goiter
- Toxic Multinodular Goiter
- Toxic nodule







PATHOGENESIS OF THYROTOXICOSIS

- Thyroxin :

All s/o Thyrotoxicosis except ocular, skin, pretibial Myxoedema

- T S H :

Depressed , Grave's disease persists in hypophysectomised patient. Unlikely to be due to Hypothalamo – pituitary axis
Two chains alpha and beta common for TSH,HCG,LH,FSH

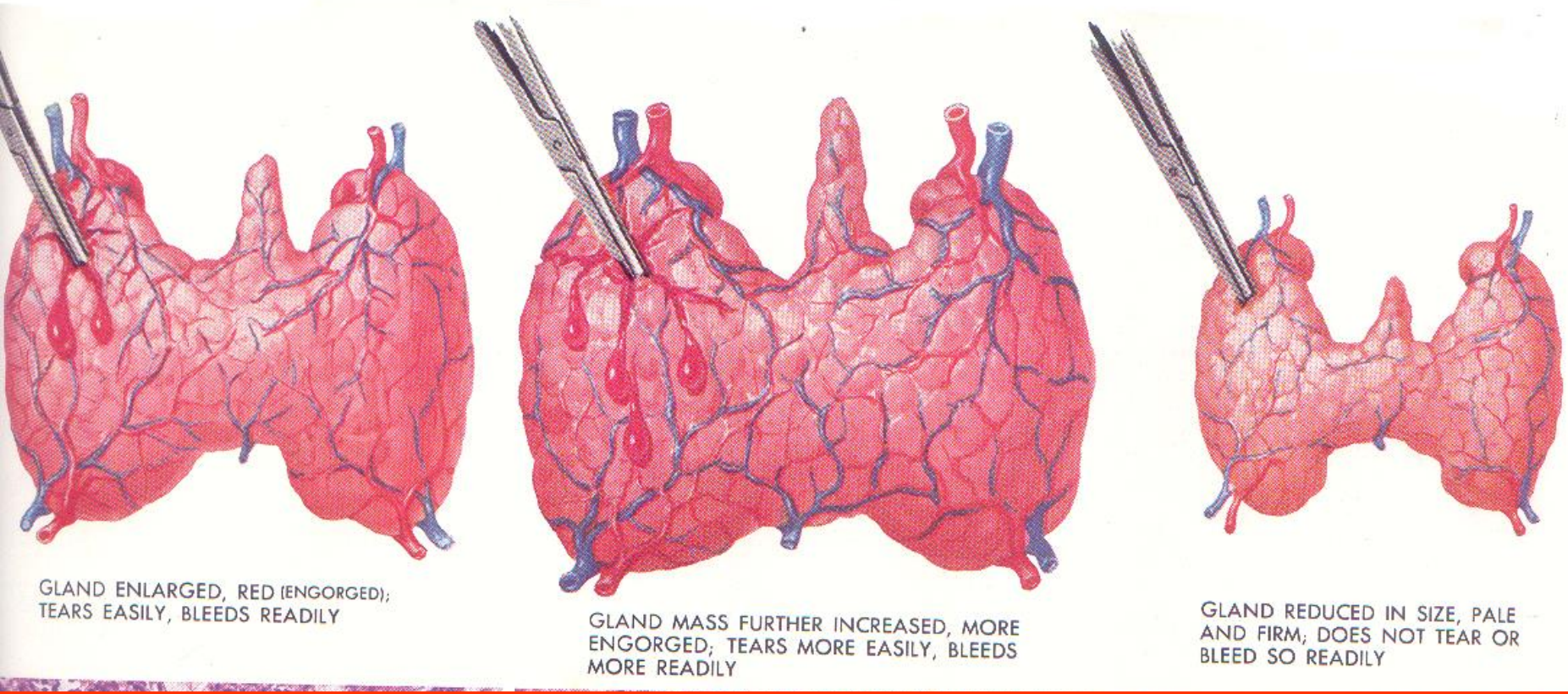
- L A T S : LONG ACTING THYROID STIMULATOR

  75 Ig G
  Persistent action : 16 Hrs.
  80% Toxic patient
  Crosses placental barrier.

PATHOGENESIS OF THYROTOXICOSIS II
Thyroid Stimulating Antibody; T.S.I.

Antibody against T S H Receptor on Thyroid membrane

- Some are inhibitory others mimic T S H
- Anti-Idiotype Antibody
- Glycoprotein component –
- Ganglioside component – ab 1
- Stimulating Antibody (Type VI) Reaction
- JERNE'S NETWORK HYPOTHESIS
- 70 TO 80% Grave's disease
- If Tsab levels not reduced after surgery or Anti-Thyroid drugs ; Relapse.



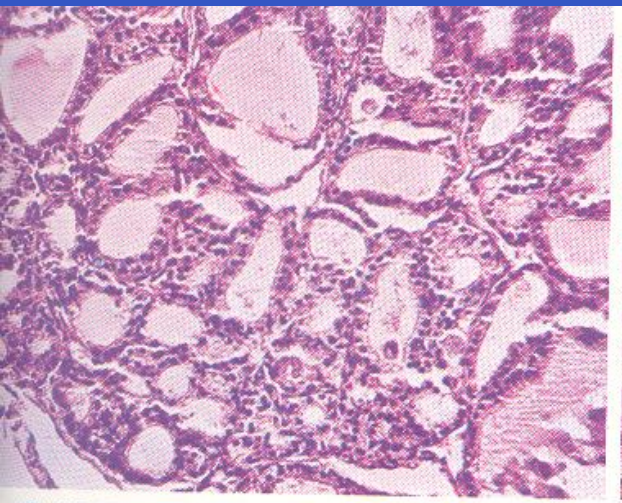
- Thyroid diffusely enlarge, small increase in size
- Untreated firm , dense, opaque, diffuse
- Treated : more translucent, like colloid goiter Intermitant opaque areas

PRIMARY THYROTOXICOSIS : Macrpscopic PATHOLOGY

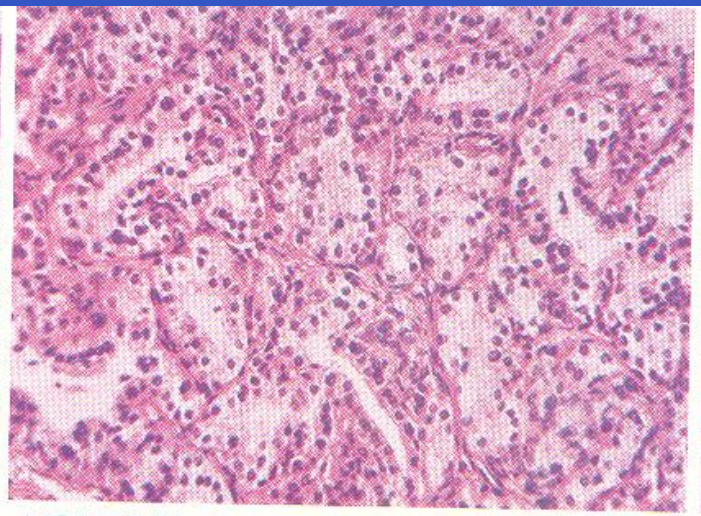
PRIMARY THYROTOXICOSIS : PATHOLOGY

- MICROSCOPY :
  - Diffuse hyperplasia glandular activity increased.
  - EPITHELIUM : Tall columnar, More mitosis, Increased dimensions of ACINAR SPACE
  - PAPILLARY EPITHELIAL PROLIFERATION
  - INFILTRATION OF LYMPHOCYTES ; MILD
  - SECONDARY GERMINAL CENTER ; TSAB

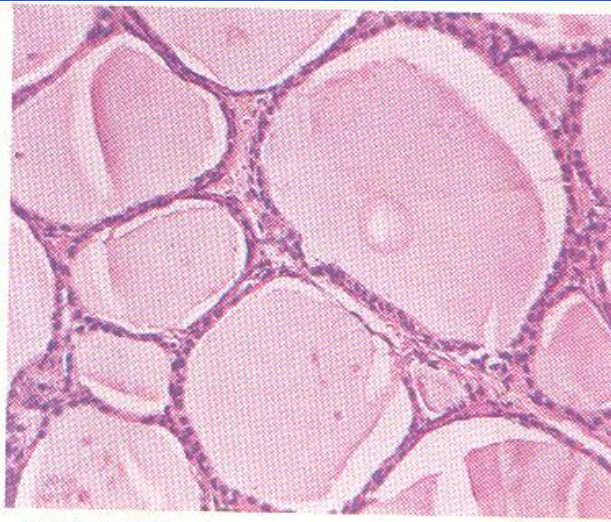
- THIO-URACIL EFFECT – CONGESTED COLLOID DECREASED
  LYMPHOCYTE INCREASED
- LUGOL'S IODINE -VASCULARITY Decreased
  COLLOID GOITRE LIKE INVOLUTION.



ACINAR HYPERPLASIA AND LOSS OF COLLOID (MEAN ACINAR CELL HEIGHT 12 MICRA)



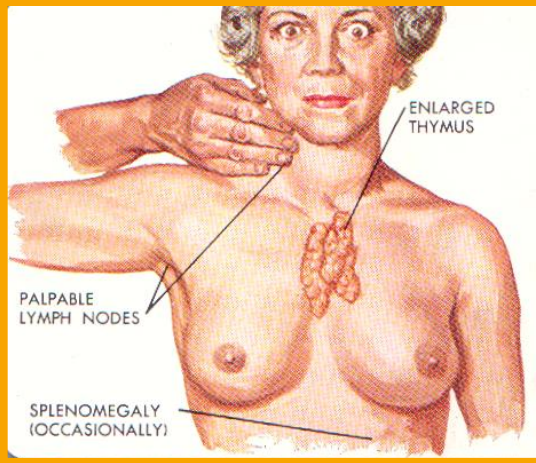
INCREASE IN ACINAR CELL HYPERPLASIA; COMPLETE LOSS OF COLLOID (MEAN CELL HEIGHT 17 MICRA)

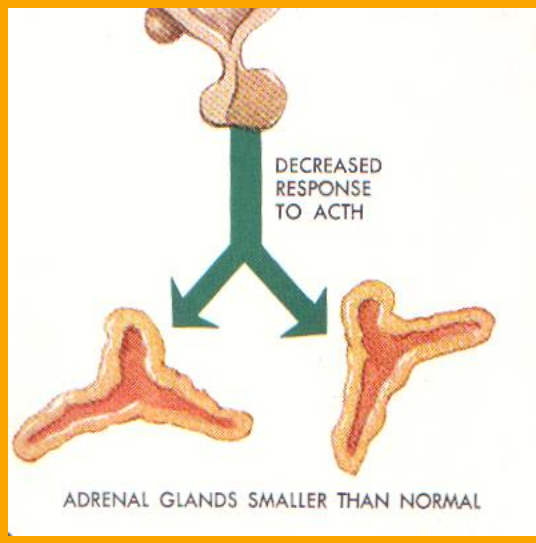


INVOLUTION OF ACINAR EPITHELIUM; STORAGE IODINE–POOR COLLOID (MEAN CELL HEIGHT 9 MICR

PRIMARY THYROTOXICOSIS : PATHOLOGY

- THYMUS : ENLARGED
- HEART : Cardiomegaly
  Myocardial degeneration
- ADRENAL ; Atrophic
- LIVER : Congested, Degeneration
  - Acute Necrosis – Focal, Local
  - Sub acute toxic atrophy
  - Cirrhosis, nodule formation
- BONES : atrophy, Rarefaction
- Fatty degeneration :
  Quadricep's sign



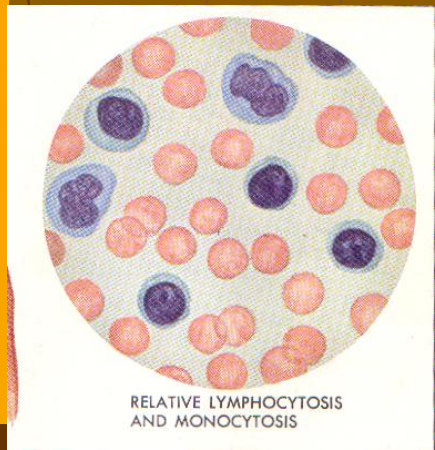


PRIMARY THYROTOXICOSIS : PATHOLOGY

- Subcutaneous Tissue : Mucopolysachride deposition

  Common : lower leg, feet may involve Hand Forearm, cheek, Orbit
- EYE :

  Oedema, Hypertrophy, cellular infiltration fibrosis of Retro orbital muscle.
- Lymphoid Tissue : Hyperplasia of Tonsils, Peyer's patches , Spleenomegaly
- PBS : Relative Lymphocytes.

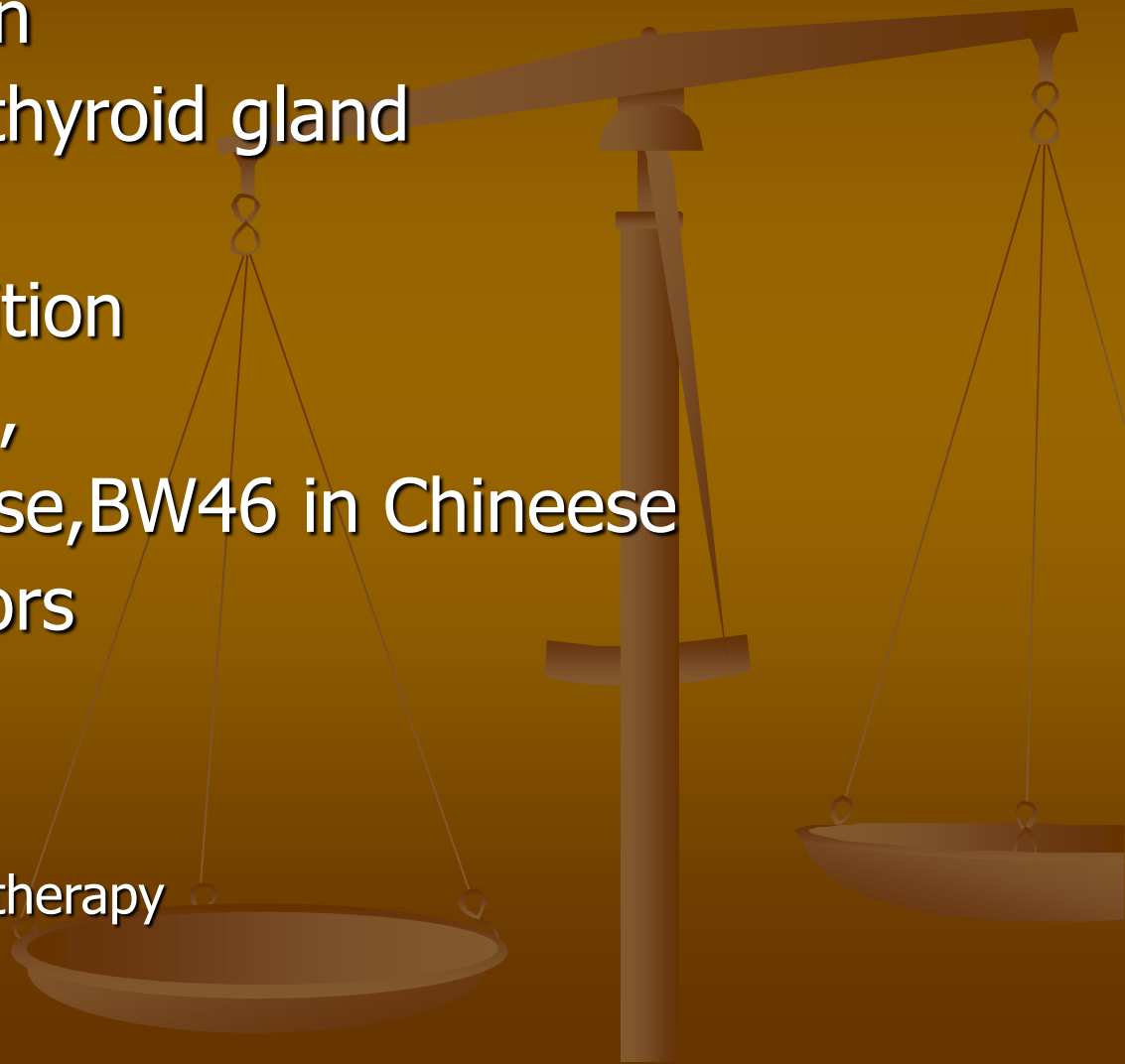


Primary Thyrotoxicosis

- A systemic auto immune disorder
- Constitutional disease
- Psychosomatic disease
- Goitre, Hyperthyroidism, Exopthalamos and Infiltrative pachydermopathy (pretibial lymphoedema)
- One or more features may be absent

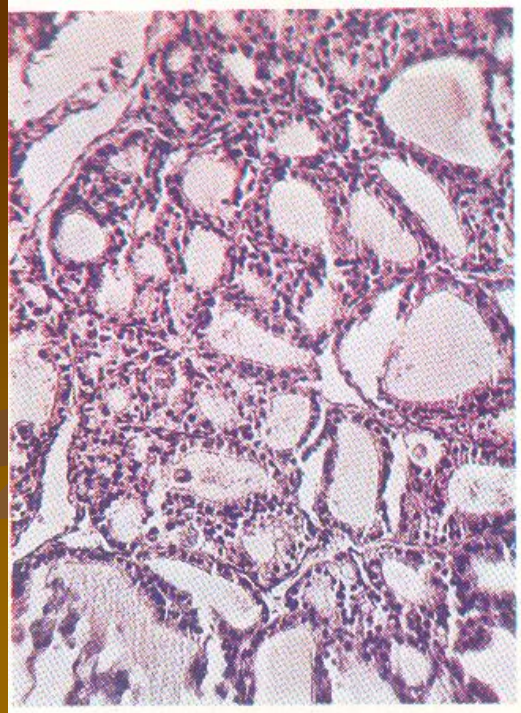
Primary Thyrotoxicosis :Aetiology

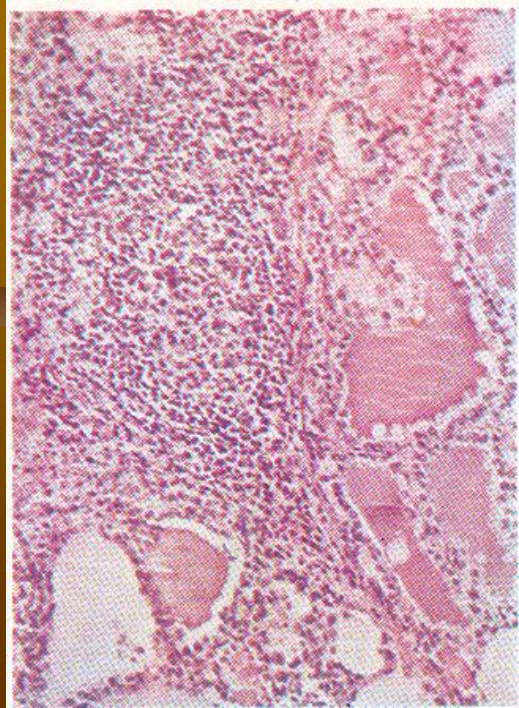
- Not exactly known
- Occurs in normal thyroid gland
- Highly familial
- Genetic predisposition
- HLA A1,B8,DRW3,
- BW35 in Japaneese,BW46 in Chineese
- Precipitating factors
  - Various stress,
  - Emotional trauma
  - Weight reduction
  - Thyroid hormone therapy



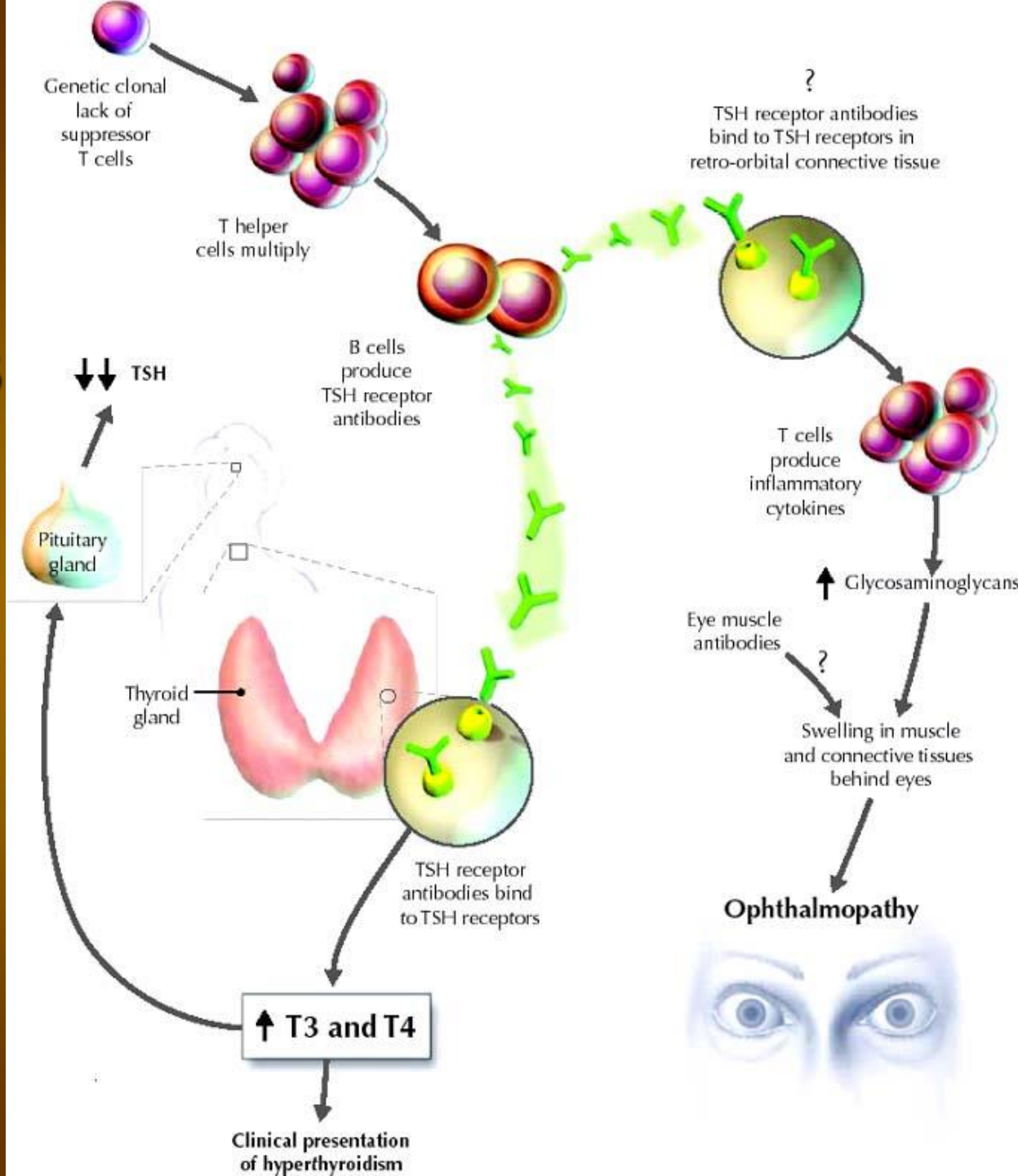
Primary Thyrotoxicosis Aetiology in view of T S Ab

- Thyroid stimulating antibody is produced by Lymphocytes infiltrating in Thyroid in secondary germinal center
- Depression in Suppressor 'T' cell activity which allows escape of forbidden clones capable of Uncontrolled auto antibody formation
- Break down of recognition of self antigen





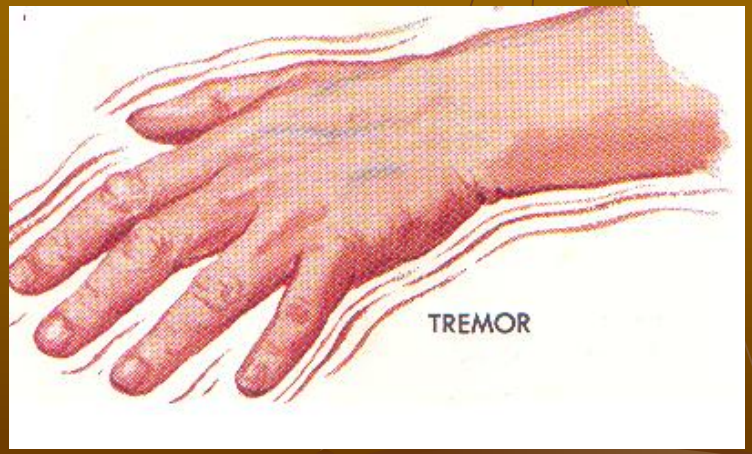
Pathogenesis of Graves Disease



- Hyper metabolic state
- Decreased weight inspite of voracious appetite

C.N.S. :

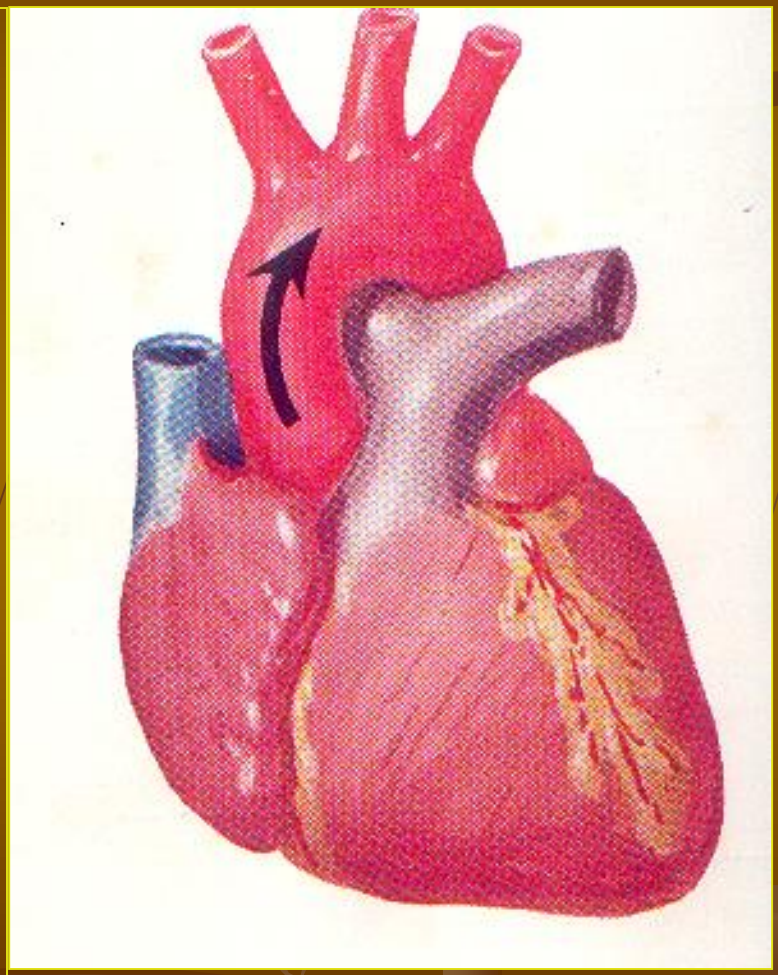
- Irritable, Restless, Excited
- Fine Tremors : Hand , Tongue
- Severe degree : Entire body shake
- Speech : Rapid, Psychosis Reflex : Hyperactive
- **INCREASED NEUROEXCITIBILITY**



Clinical Picture

Cardio Vascular System :

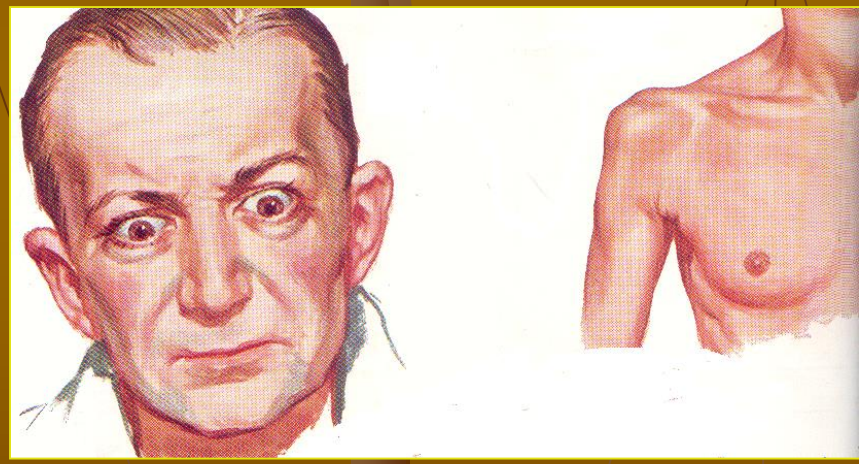
- Pulse pressure increased Tachycardia
- Paroxysmal atrial Tachycardia,
- Paroxysmal atrial fibrillation
- High cardiac output failure
- Digoxin resistant as beyond maximum positive inotropic action



Clinical Picture

Muscle weakness in Thyrotoxicosis

- Fatigue common
- Quadriceps weakness,
- Small muscle atrophy
- Generalized muscle wasting
- Atrophy of should girdle muscle, Temporal muscle
- Sphincter weakness : Rectal prolapse
- Occasionally Myasthenia gravies like picture

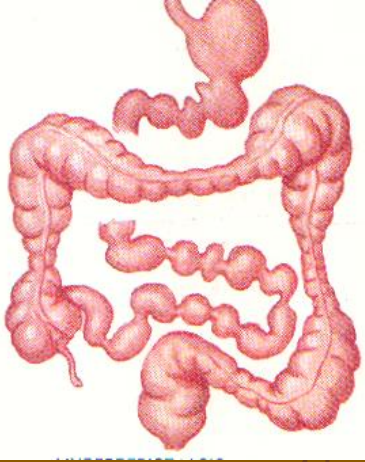


G I T

Intestinal motility Increased.

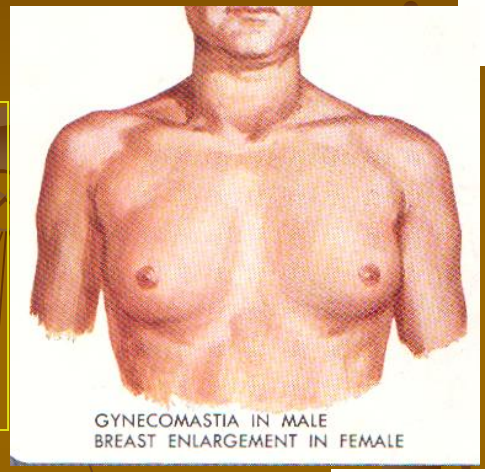
Diarrhea

Late : Toxic Hepatic failure

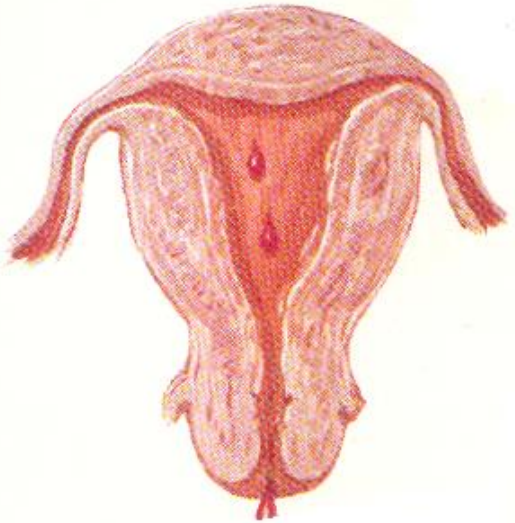


REPRODUCTIVE :

- Gynaecomastia 3 to 5 %
- Breast enlargement
- Libido : decreased

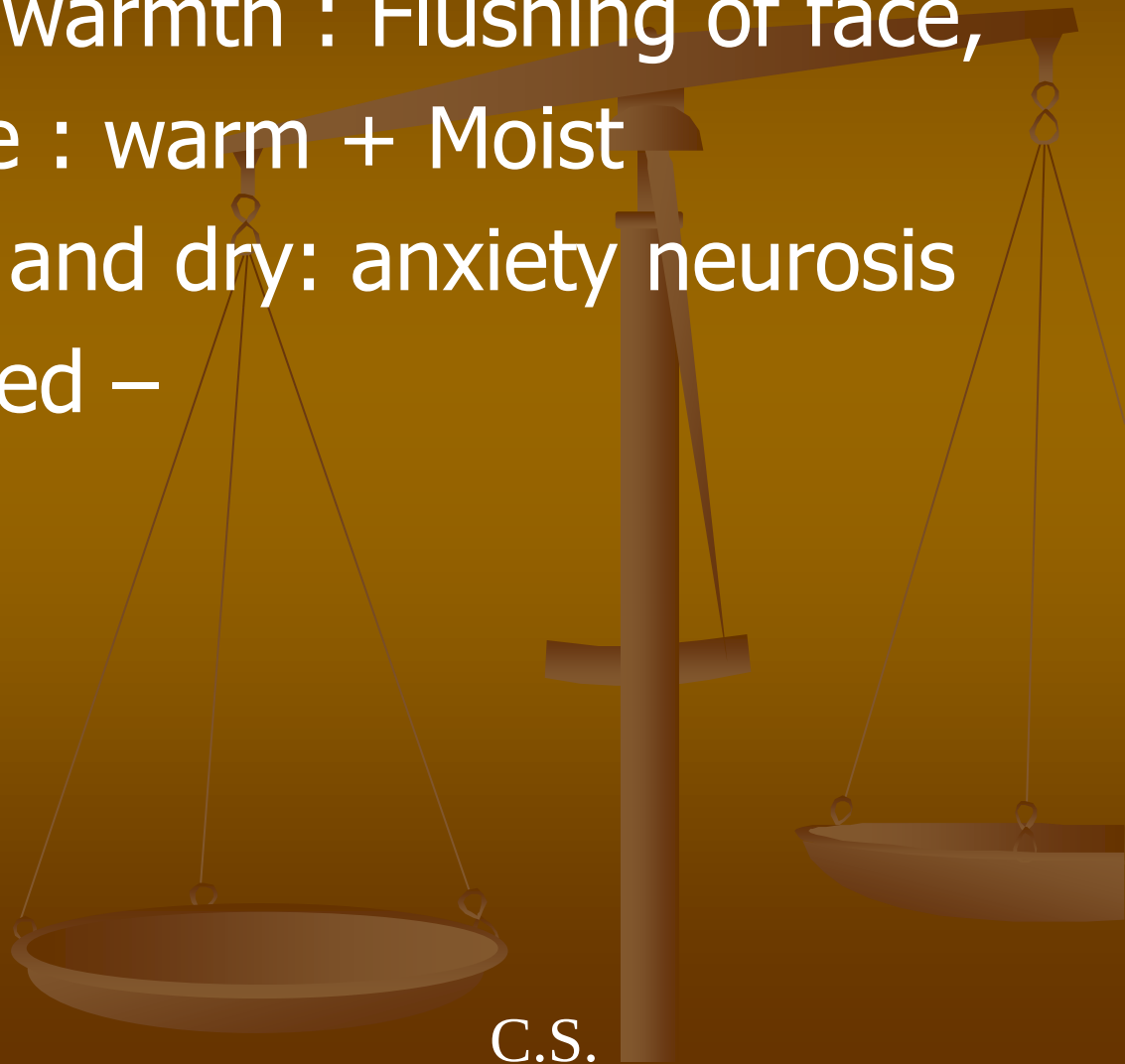


- Fertility decreased
- Menstrual Irregularity
- Flow decreased.



Clinical Manifestation

- Increased body warmth : Flushing of face,
- Warm handshake : warm + Moist
  cold and dry: anxiety neurosis
- sweating increased –
- Thirst increased
- Polyurea



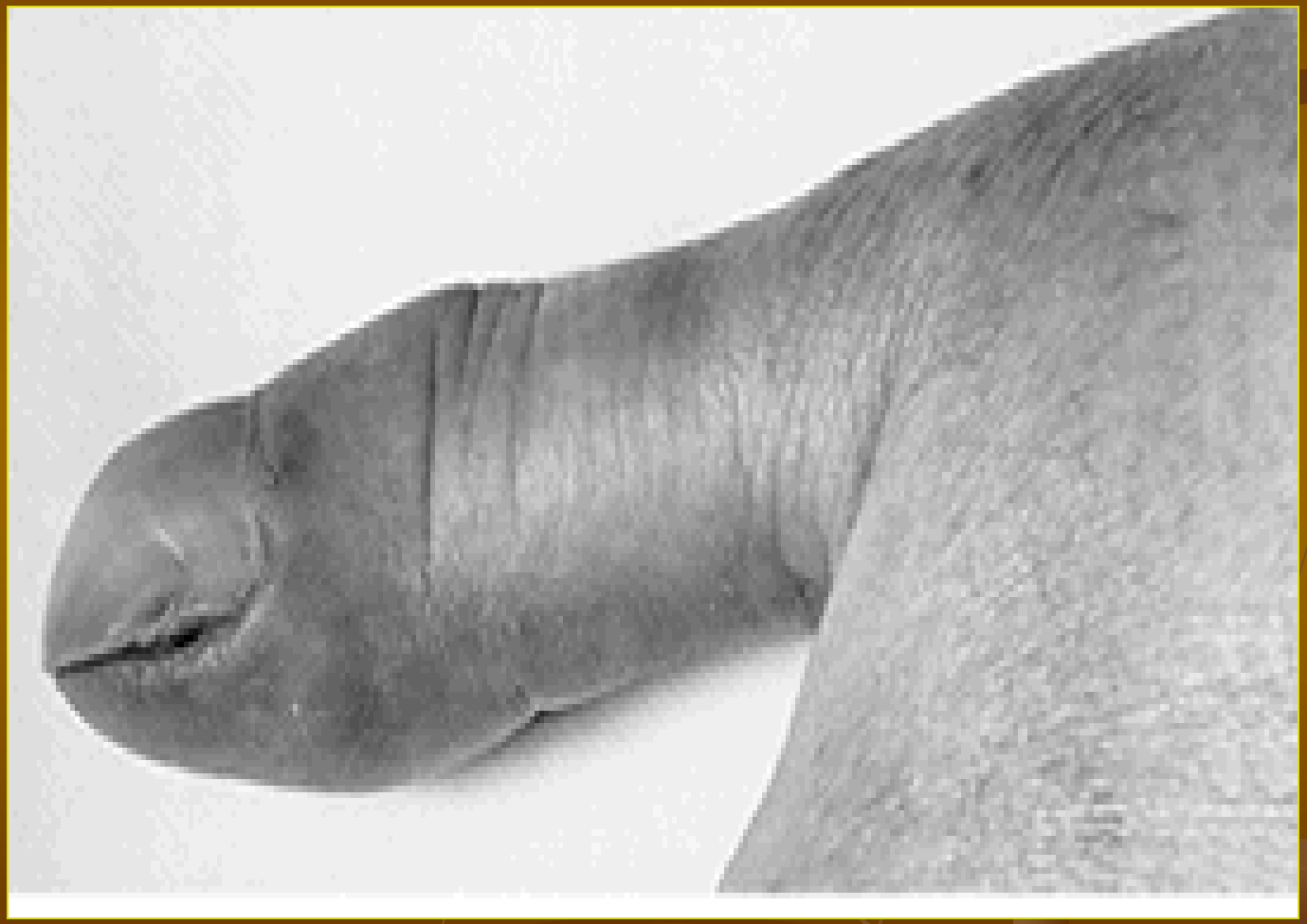
Clinical signs

- **GOITRE** : Smooth, Diffuse enlargement , Palpable Thrill , Bruit 5% normal Thyroid.
- **PRE-TRIBIAL MYXOEDEMA** :

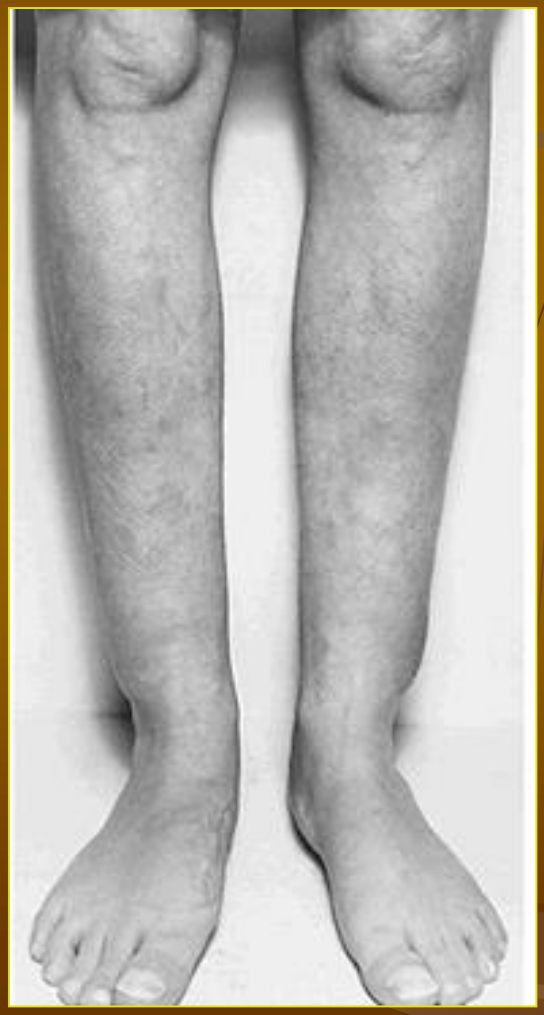
  Bilateral, Symmetrical Deposition of Mucopolysacharide. Lower 1/3 leg,

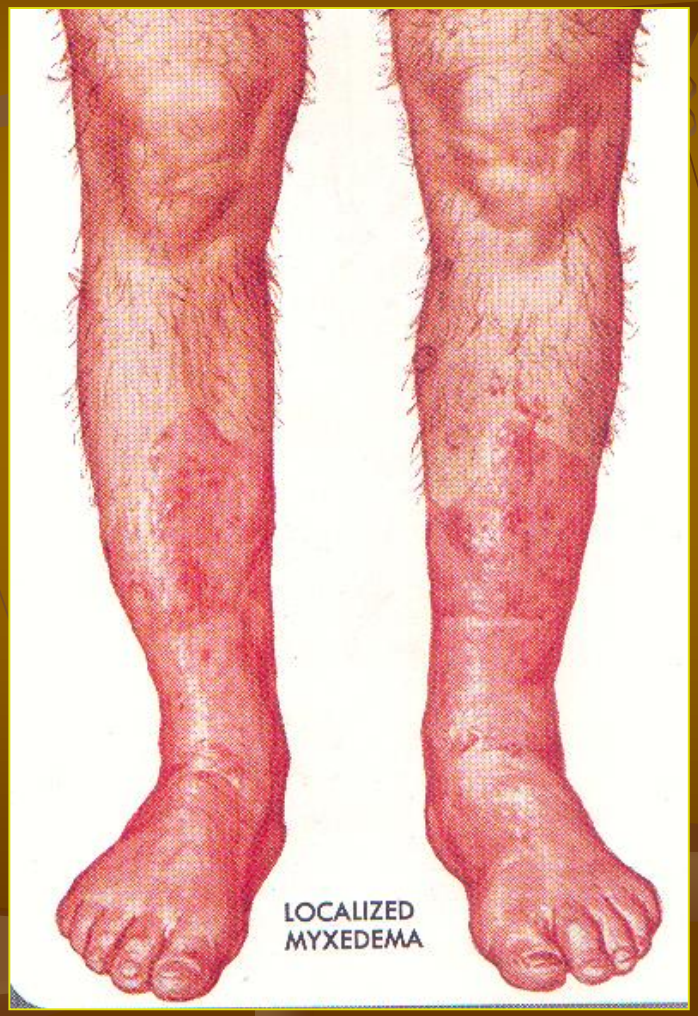
  above ankle – Hand, face, cheek
- **SKIN** : Thickened, Elastic Hair follicle stand out : pig skin
- **NAILS** : Brittle, soft, Thin
  Plummer Nails .Peeling of surface layers

Plummer nails

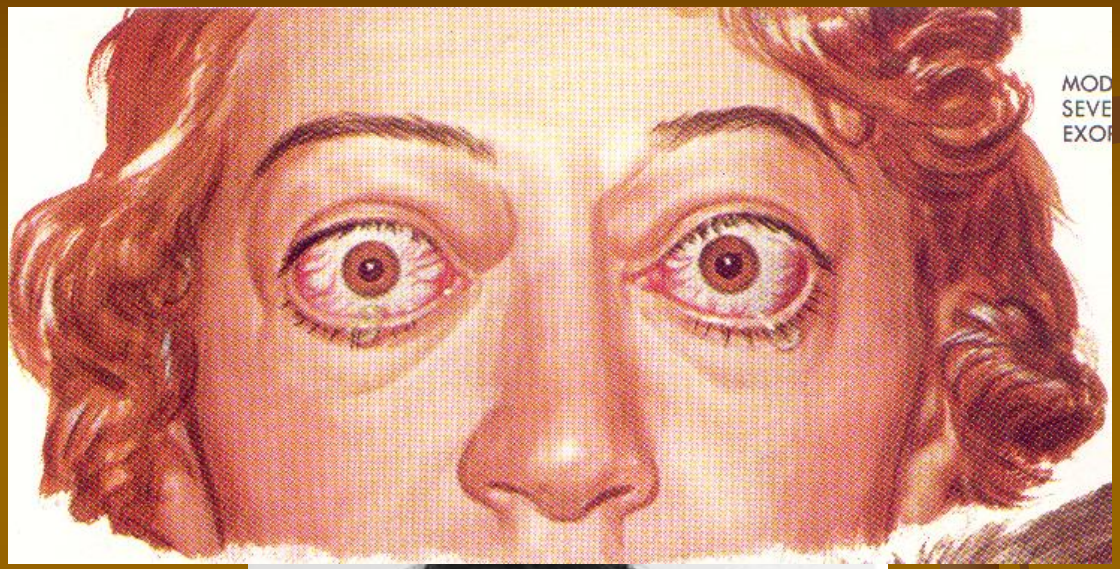


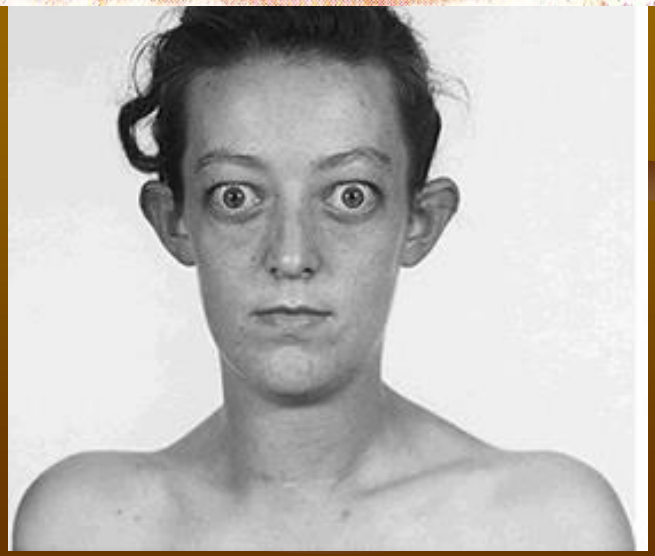
Thyroid Pachydermopathy
Pretibial lymph oedema





Exopthalamos





Normal position of eyelid

Upper eyelid covers the pupil from 11o clock to 1o clock.

Lower eyelid touches just below the lower limbus

EYE SIGNS OF THYROTOXICOSIS

- Phenomenon affecting lids
- Phenomenon affecting globe
- Forehead phenomenon
- Phenomenon affecting Conjunctiva

EYE SIGNS OF THYROTOXICOSIS

Phenomenon affecting lids

- Retraction of upper lid : DALRYMPLE'S SIGN
  (staring, frightened look)
- Accentuation of Retraction of upper lid During stare : KOCHER'S SIGN

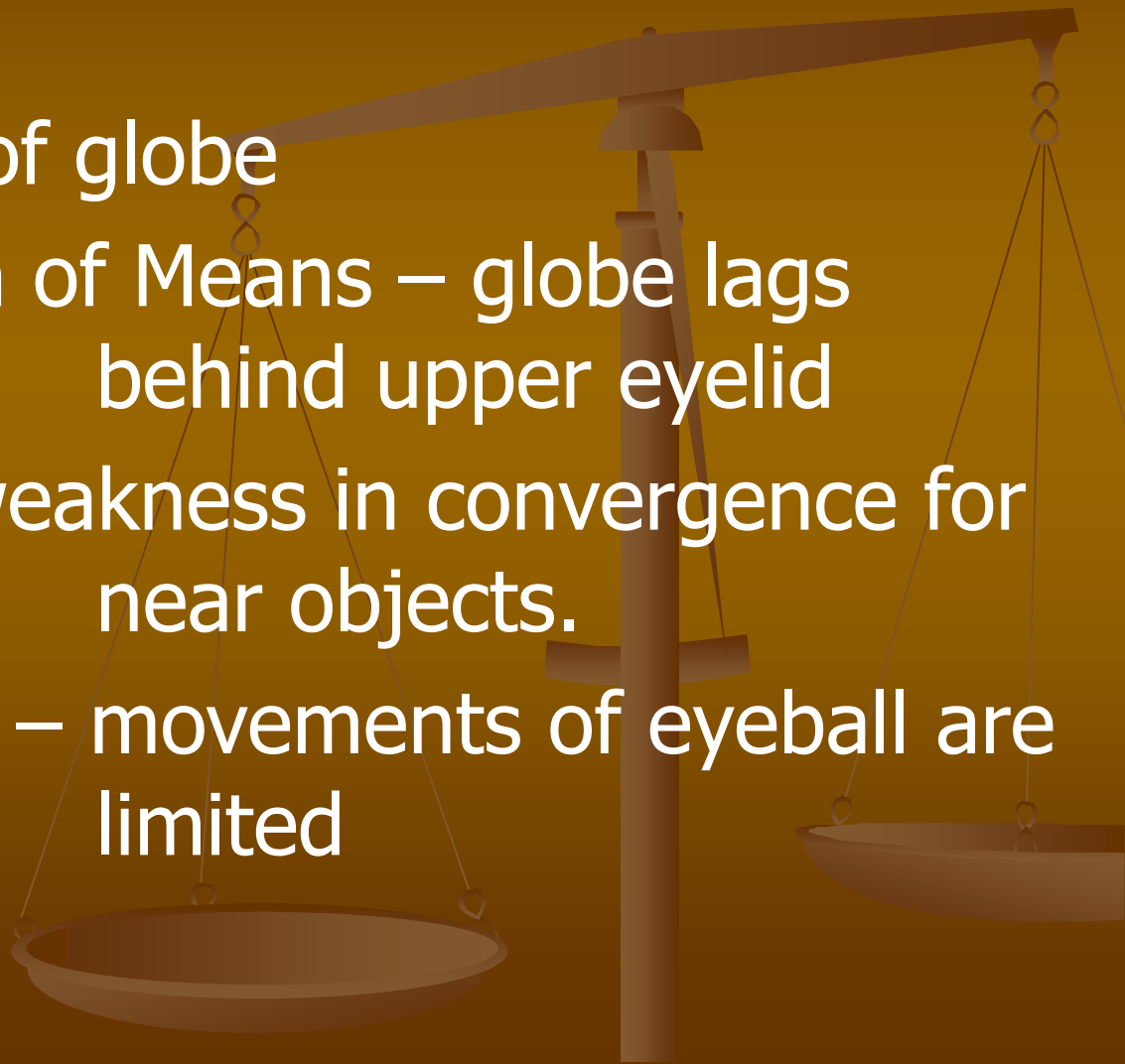
- Lid lag : VON-GRAFE'S SIGN
- Jerky lid movement : BOSTON'S SIGN
  (Upward, downward movement)
- Infrequency and incompleteness of blinking : STELLWAG'S SIGN

- Fullness of upper eyelid : ENROTH'S SIGN
- Difficulty in eversion of upper lid : GIFFORD'S SIGN
- Hyper pigmentation of lid : JELLINEK'S SIGN

EYE SIGNS OF THYROTOXICOSIS

PHENOMENON AFFECTING GLOBE

- Exopthalamos
- Mobility defect of globe
- Globe – lag sign of Means – globe lags behind upper eyelid
- Mobius sign – weakness in convergence for near objects.
- Opthalmoplagia – movements of eyeball are limited



EYE SIGNS OF THYROTOXICOSIS

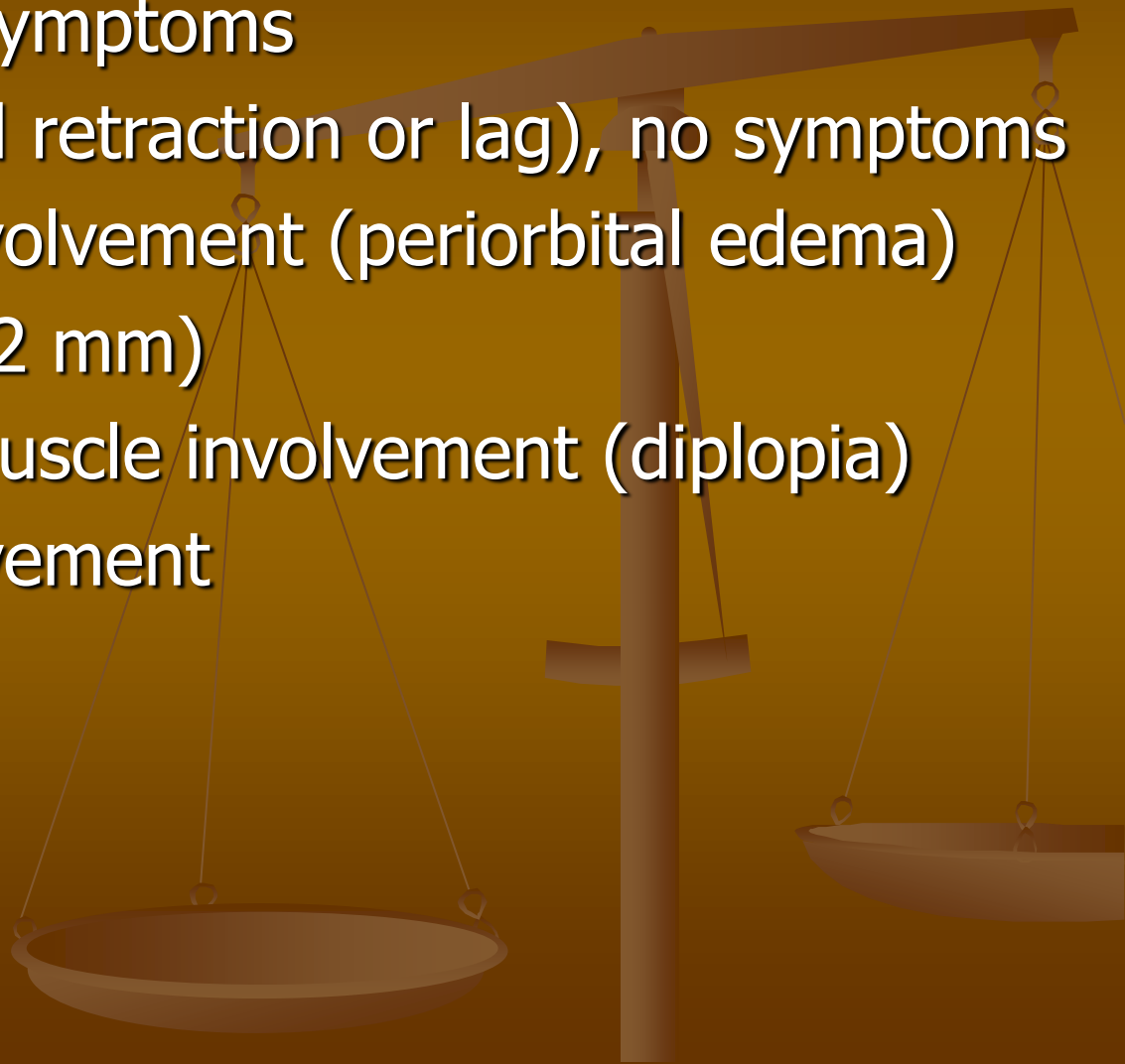
FOREHEAD PHENOMENON
JIFFROY'S SIGN :
Absence of wrinkling of forehead on looking upwards

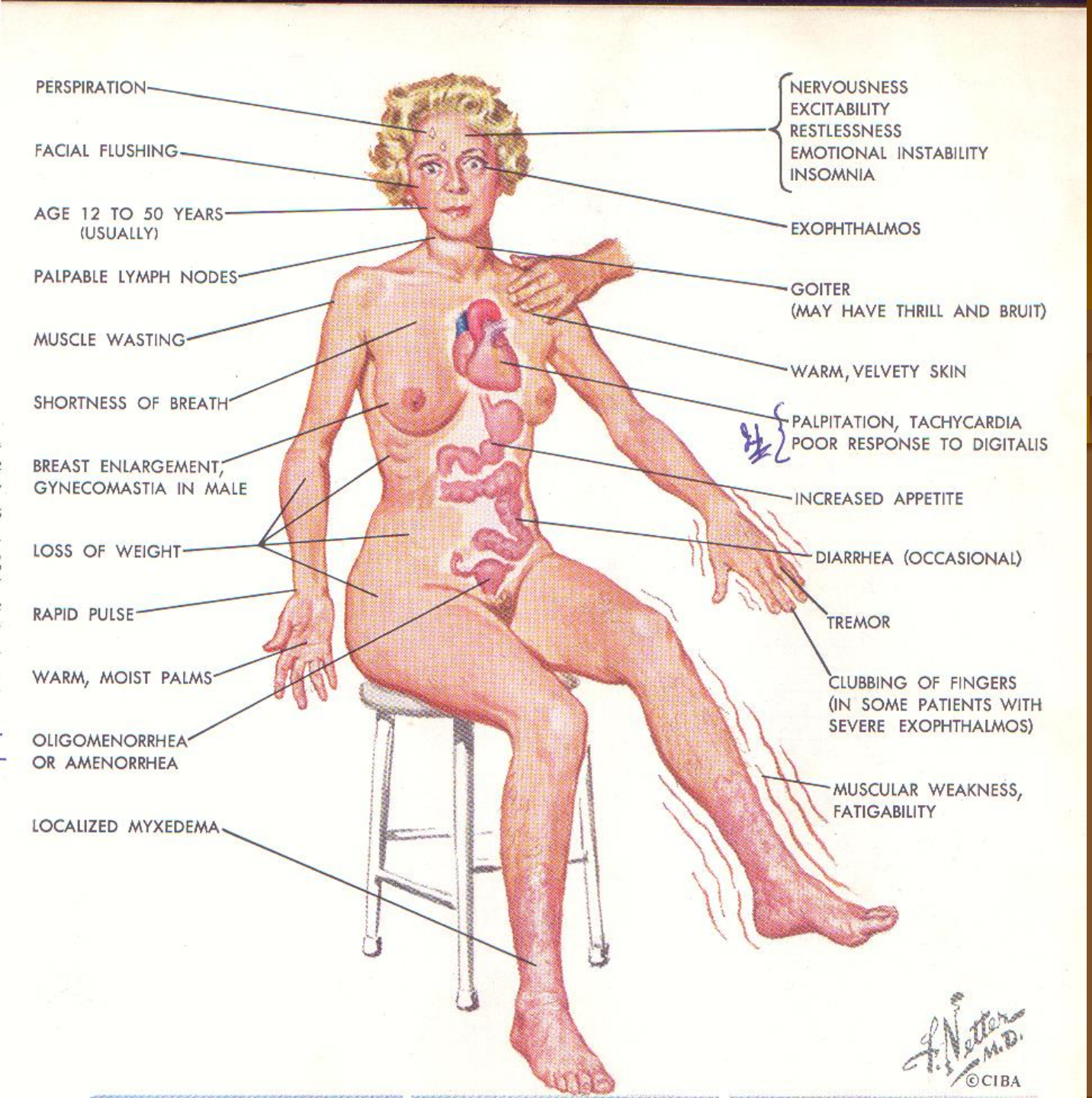
PHENOMENON AFFECTING CONJUNCTIVIA

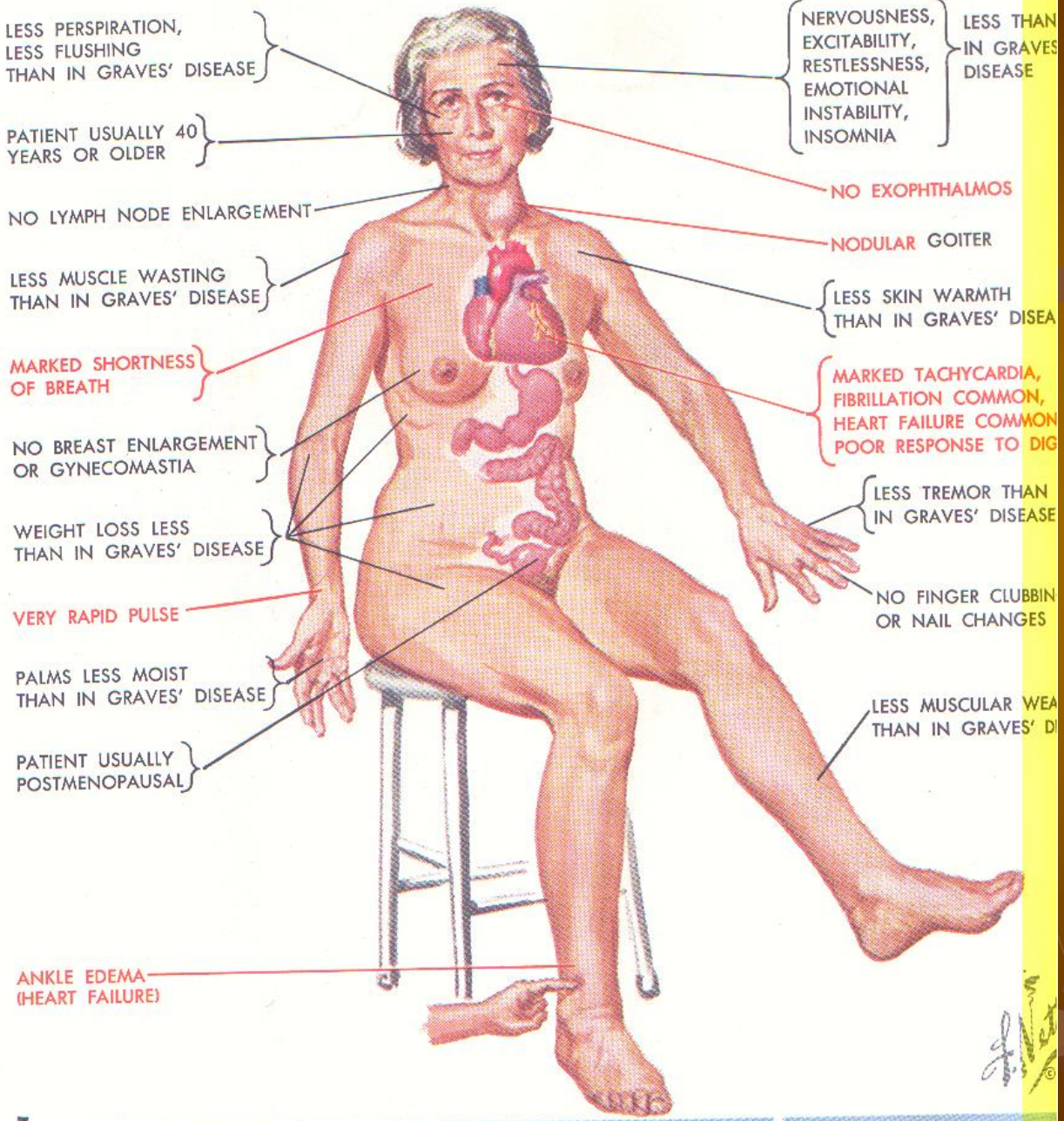
- Deep injection : dilation and engorgement of Conjunctival vessels
- Excessive lacrimation
- Chemosis ; Conjunctival edema
- Ulceration

Abridged classification of Eye changes in GRAVE'S DISEASE

- 0 = No signs or symptoms
- 1 = Only signs (lid retraction or lag), no symptoms
- 2 = Soft tissue involvement (periorbital edema)
- 3 = Proptosis (>22 mm)
- 4 = Extraocular muscle involvement (diplopia)
- 5 = Corneal involvement
- 6 = Sight loss




PERSPIRATION
FACIAL FLUSHING
AGE 12 TO 50 YEARS (USUALLY)
PALPABLE LYMPH NODES
MUSCLE WASTING
SHORTNESS OF BREATH
BREAST ENLARGEMENT, GYNECOMASTIA IN MALE
LOSS OF WEIGHT
RAPID PULSE
WARM, MOIST PALMS
OLIGOMENORRHEA OR AMENORRHEA
LOCALIZED MYXEDEMA
NERVOUSNESS
EXCITABILITY
RESTLESSNESS
EMOTIONAL INSTABILITY
INSOMNIA
EXOPHTHALMOS
GOITER (MAY HAVE THRILL AND BRUIT)
WARM, VELVETY SKIN
PALPITATION, TACHYCARDIA
POOR RESPONSE TO DIGITALIS
INCREASED APPETITE
DIARRHEA (OCCASIONAL)
TREMOR
CLUBBING OF FINGERS (IN SOME PATIENTS WITH SEVERE EXOPHTHALMOS)
MUSCULAR WEAKNESS, FATIGABILITY
F. Netter M.D.
©CIBA


LESS PERSPIRATION, LESS FLUSHING THAN IN GRAVES' DISEASE
PATIENT USUALLY 40 YEARS OR OLDER
NO LYMPH NODE ENLARGEMENT
LESS MUSCLE WASTING THAN IN GRAVES' DISEASE
MARKED SHORTNESS OF BREATH
NO BREAST ENLARGEMENT OR GYNECOMASTIA
WEIGHT LOSS LESS THAN IN GRAVES' DISEASE
VERY RAPID PULSE
PALMS LESS MOIST THAN IN GRAVES' DISEASE
PATIENT USUALLY POSTMENOPAUSAL
ANKLE EDEMA (HEART FAILURE)
NERVOUSNESS, EXCITABILITY, RESTLESSNESS, EMOTIONAL INSTABILITY, INSOMNIA
LESS THAN IN GRAVES DISEASE
NO EXOPHTHALMOS
NODULAR GOITER
LESS SKIN WARMTH THAN IN GRAVES' DISEA
MARKED TACHYCARDIA, FIBRILLATION COMMON, HEART FAILURE COMMON POOR RESPONSE TO DIG
LESS TREMOR THAN IN GRAVES' DISEASE
NO FINGER CLUBBIN OR NAIL CHANGES
LESS MUSCULAR WEA THAN IN GRAVES' D

Primary (Graves)	Secondary (Parry's Disease)
In Normal Gland	In abnormal Gland
Aetiology Psychosomatic Idiopathic	Pituitary
Maybe Course Progressive with remission	Course Progressive, no Remission
Onset sudden or insidious	Onset deceptive,gradual requiring several yrs.
Psychic stress +	Psychic stress negative
Weight loss present	weight loss Marked
appetite Voracious	Poor appetite
Neurogenic CNS affected	CVS Affected
Exopthalamos, Pretibial lymphodema Present Plummer's Nails	absent
BMR raised	Not raised
Response to Iodides, Good	Minimal or lacking
Response ATT Good	Large dosages required
Response to Radioactive Iodine, Good	LESS EFFECTIVE
Treatment medicine	Surgery

Graves	TNG	Toxic Nodule
Clinically apart in young patient	> 50 yrs of age	20 to 40 yrs
M: F - 1:6	F > M	
Emotional Neurogenic, Mypathic Manifestation more marked	Less marked	Less marked
Calorigenesis more marked	Less obviously	

INVESTIGATION

- SLEEPING PULSE RATE ; > 90

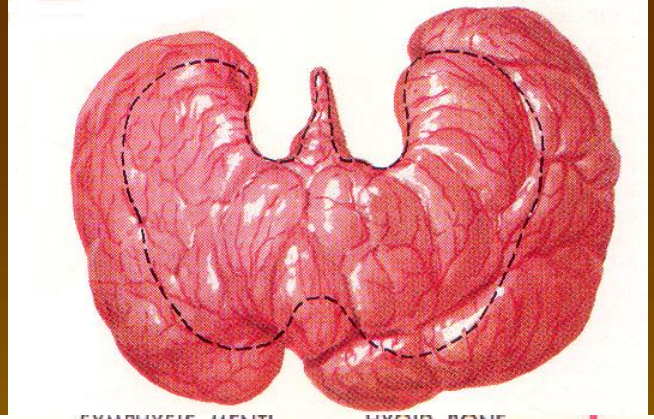
PBI > 7 microgm B.E.I > 5 micr gm
Serum T 3 70 to 200 ng/di
Serum T 4 5.5. To 13.5 mic g/dl
Serum T S H 0 – 9 microunit/ml

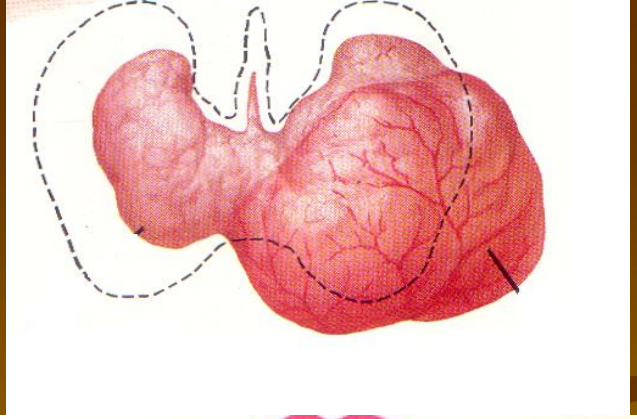
SERUM CHOLESTEROL < 200 mg%
SERUM CREATININE > 1.5 mg%

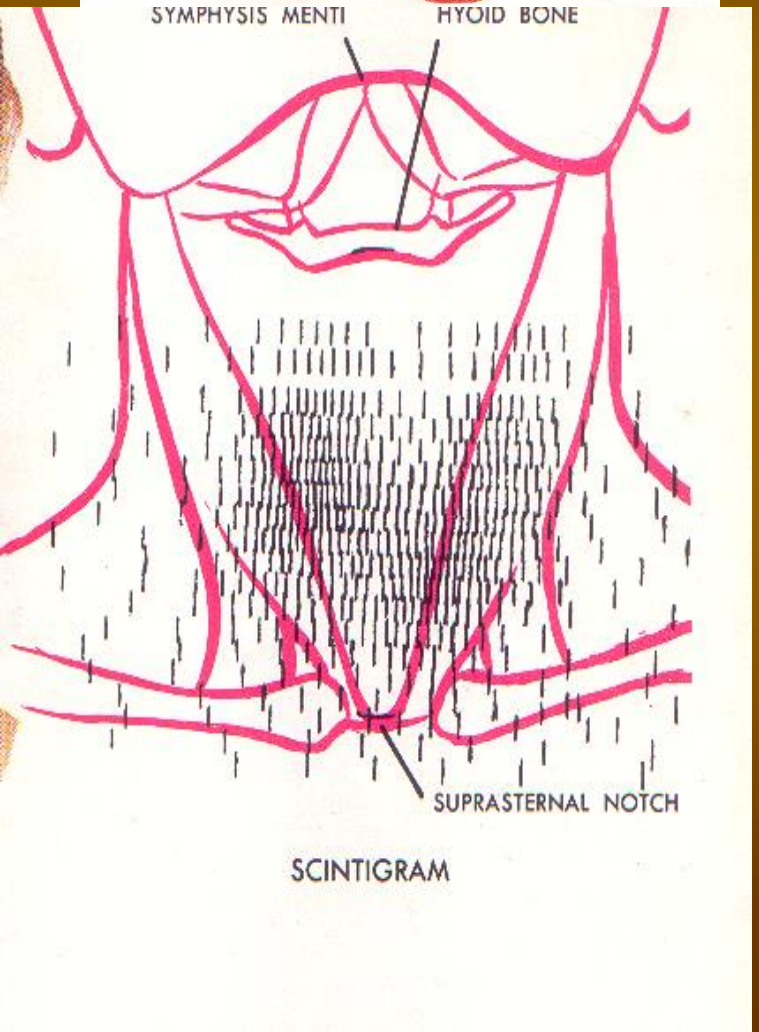
THYROID SCAN TOXIC NODULE
THYROID Tsab/TRAB levels

T3 UPTAKE TEST > 85 %
F T I = Serum T4 x 100 2.25 to 7 > 7
T3 uptake

I 131 uptake Rapid uptake
Rapid Turnover
No excretion
TSH SUP. TEST 10 to 20% decrease
T R H test



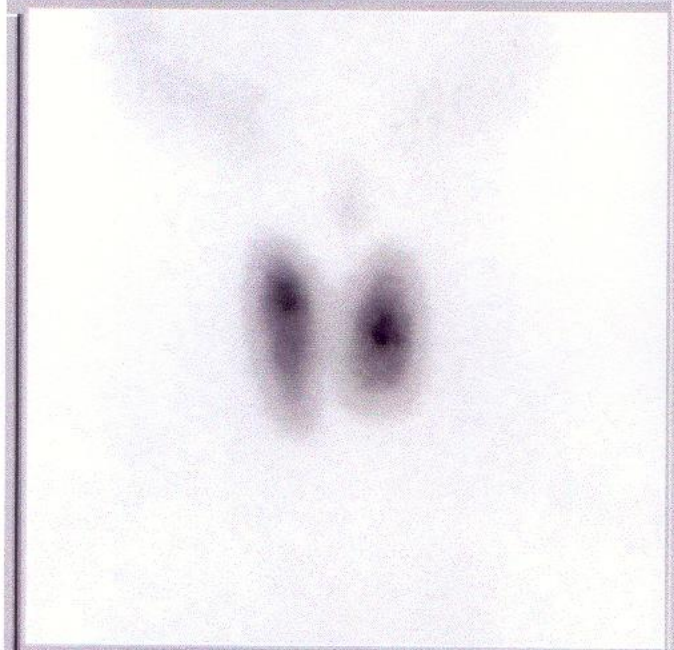




SCINTIGRAM

SCINTIGRAM

NAME : WADIA RN 55F
RUBY HALL CLINIC
THY/654/00

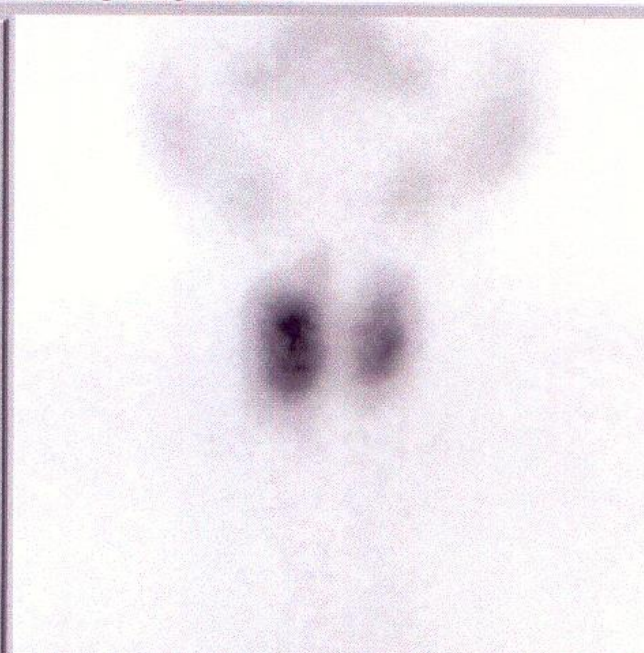


RIGHT LEFT

ISOTOPE : Tc-99m
REFER.ACT.: 242.6 MBq

	TOTAL	RIGHT	LEFT
UPTAKE (%):	7.1	3.4	3.7
CTS.(kcts):	108.6	52.1	56.5
SIZE(cm^2):	12.5	5.6	6.9

NAME : SHITOLE P. 42F
RUBY HALL CLINIC
THY/56/2001



RIGHT LEFT

ISOTOPE : Tc-99m
REFER.ACT.: 111.7 MBq

	TOTAL	RIGHT	LEF
UPTAKE (%):	4.0	2.6	1.
CTS.(kcts):	83.9	54.2	29.
SIZE(cm^2):	15.3	8.4	6.

GRAVE'S DISEASE

SELF LIMITING DISEASE

NATURAL HISTORY : HAS EXACERBATION AND REMISSION

CONTROLE WITH ATT IN PHASE OF EXACERBATION

WHEN REMISSION IS OBTAINED

MAINTAINENCE AT LOW DOSE

6 MONTHS Rx - 40% LONG LASTING REM

Grading of Toxicity

- Grading of toxicity is to be done before any management protocol is started
- Grading of toxicity is done on sleeping pulse rate
- Mild <90 per min
- Moderate 90-110 per minute.
- Severe > 110 per minute

Anti - Thyroid DRUGS

Advantages
- Easy to administer
- No Surgery
- No Radio-active Iodine

Disadvantages
- Unpredictable
- High failure Rate 50%
- Long Term Treatment : 2 years
- High relapse rate ever after long treatment
- Some goiters increase in size
- -Dangerous for some site.
- Toxicity
  - 0.3% agranulocytosis,
  - aplastic anaemia 3 to 12%
  - skin rash,Polyarteritis ,
  - peripheral Neuritis
- Constant Medical Supervision required
- Exopthalamos might worsen

INDICATION
- Mild Thyrotoxicosis
- To control before surgery
- As ancillary to Radio-active Iodine Therapy
- Recurrence after surgery
- Children and Young patients
- High pre-op Thyroid ab
- Ist Trimester of Pregnancy

Mechanism of Action

- Biochemical action

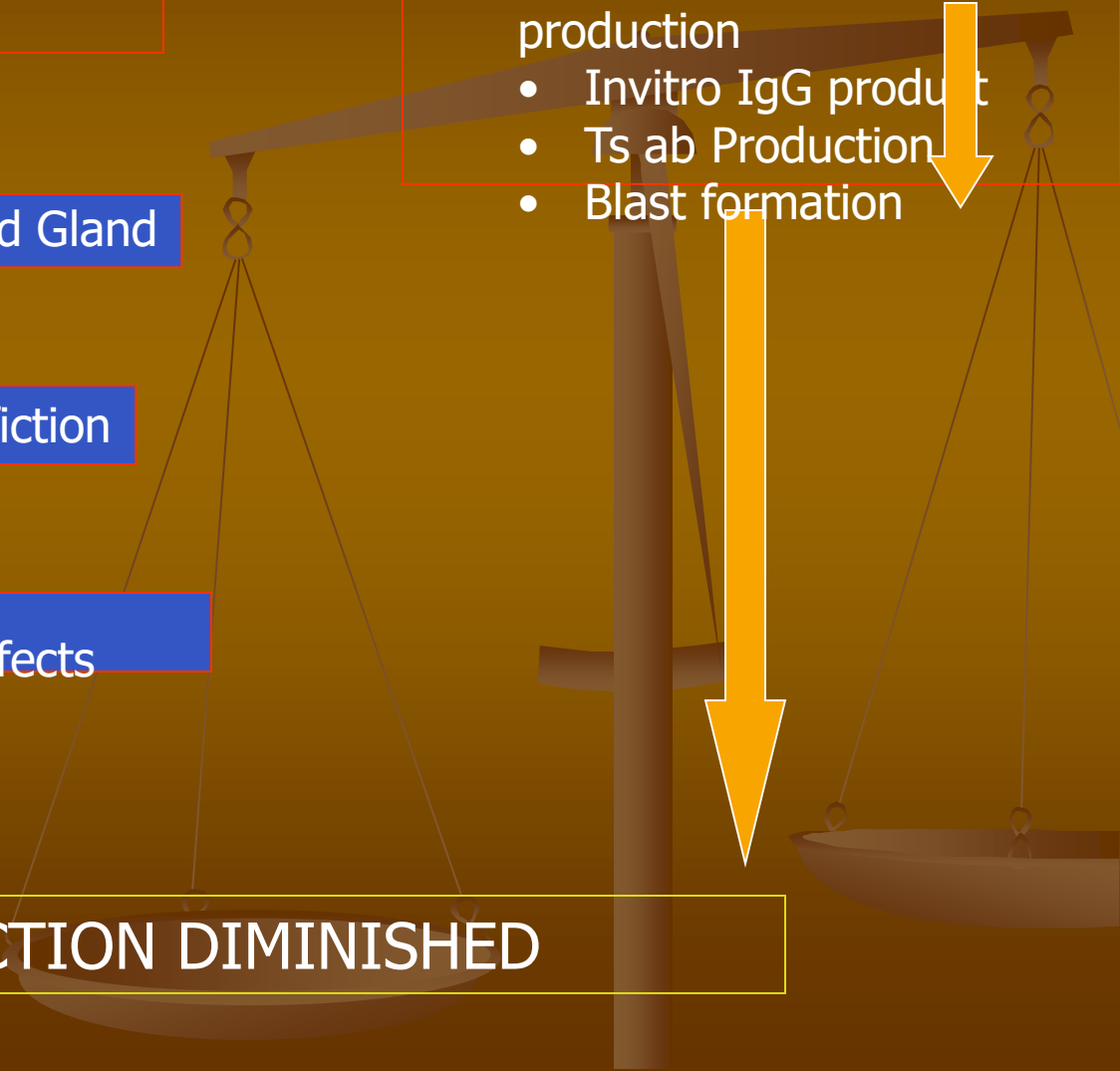
Immunological action

- Microsomal ab production
- Invitro IgG product
- Ts ab Production
- Blast formation

- Get concentrated into Thyroid Gland
- Inhibit intrathyroidal organifiction

Local immunosuppressive effects

TS AB PRODUCTION DIMINISHED



ANTI THYROID DRUGS REGIME

- Carbamizole 5 mg TDS
- Propylthio uracil 300 mg /day

Carbimazole 10- mg QID
Propylithio uracil 750 mg/day

ESCALATION

MONITORING CLINICALLY

Maintainence Dose
Controlled (6weeks)

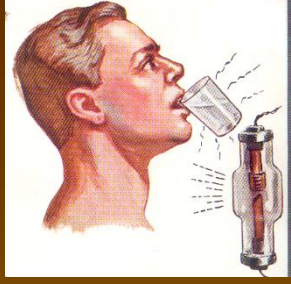
Clinically controlled
but Tachycardia
Beta blockers

Combine Eltroxine 20 mg /day
Thyroid extract 30 mg /day

MONITORING TOXICITY,(Bone marrow depression)

Radio-active Iodine Therapy
INDICATIONS

- Adults –non pregnant female ,
  > 45 years of age
- Recurrent Thyrotoxicosis
- High risk Thyro -cardiac
- Diffuse glandular enlargement
- complication

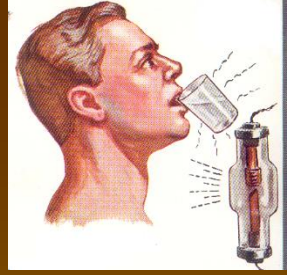


Radio-active Iodine Therapy

Mode of action

- Selective destruction of acini of thyroid
- Radiation induced destruction of lymphocytes that produce Ts Ab
- Ts ab level increases for 3 months and decreases afterwards

Radio-active Iodine Therapy



ADVANTAGES -
- Easy to administer
- single dose treatment, > 1 dose 20 to 30%
- Selective action

- Disadvantages :
- Radiation hazards to fetus, children
- Not suitable for multinodular goiter
- Slow response rate ; 3 month A T T Required
- Long term follow up essential
- Needs Radio-Isotope facility
- Large goiters may not shrink
- Increasing Hypothyroidism 20% after 2 years
- 2 to 3 % per year 43% at end of 10 years

Radio-active Iodine Therapy
Dose regime

- Dose 150 micro curie/per estimated gm of thyroid tissue

$$= \frac{\text{Estimated wt of Thyroid} \times 150}{\text{24 hours 131 uptake}}$$

- DTG 7 t 9 milli curie
- TNG 12 to 15 milli curie

SURGERY

Mech. Of action

- Source of T3,T4 production increased
- Lymphocytes producing Ts ab eliminated
- Both Target organ and bullets removed

Advantages

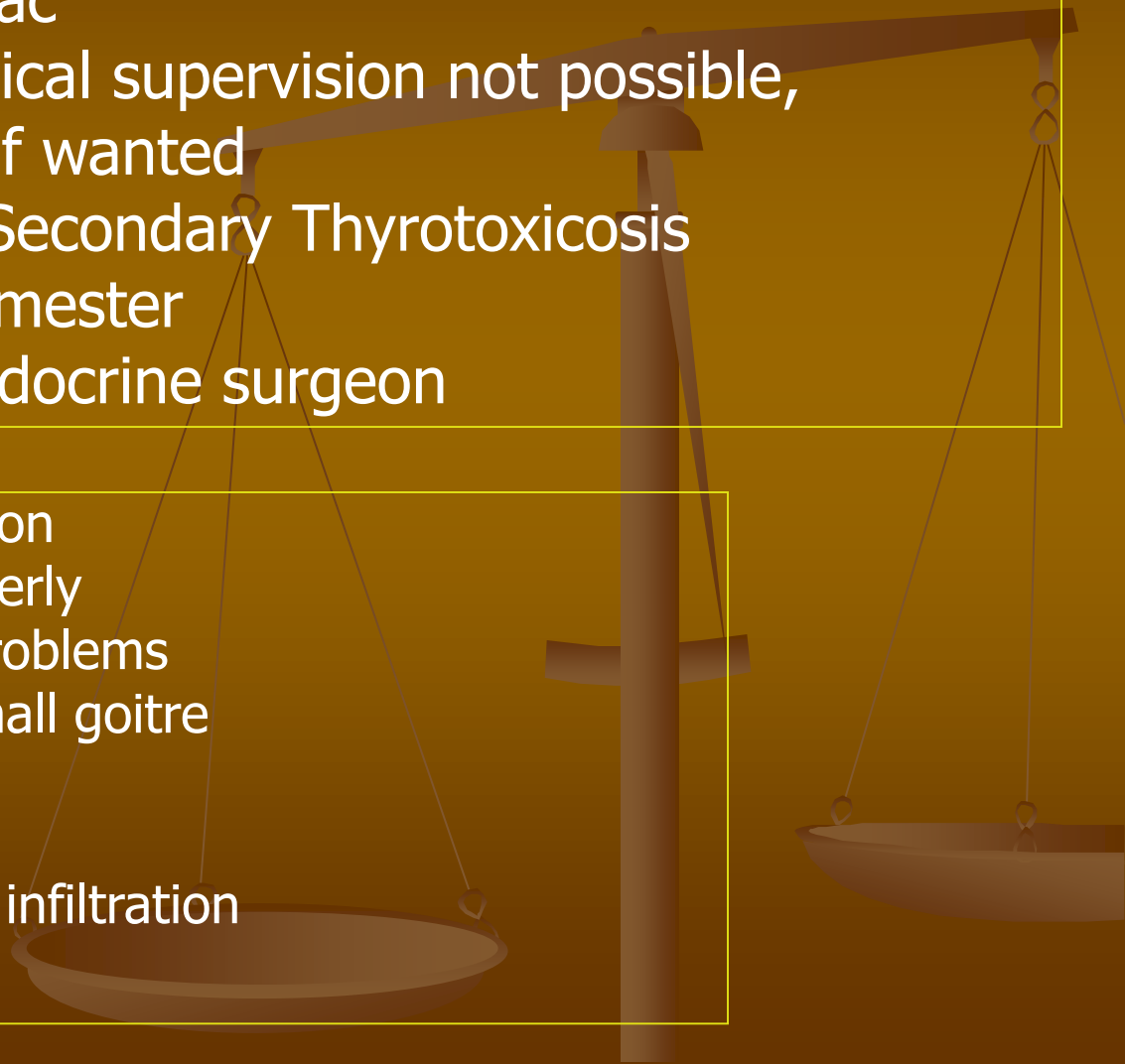
- Cure is rapid,
- Predictable
- Adequate surgery
  High cure rate

Disadvantages

- High mortality Rate even in experienced hand
- Recurrence 5 %
- Hypothyroidism 15 to 25 %
- Recurrent Laryngeal Nerve palsy 0.6 %
- Hypoparathyroidism
- Expensive

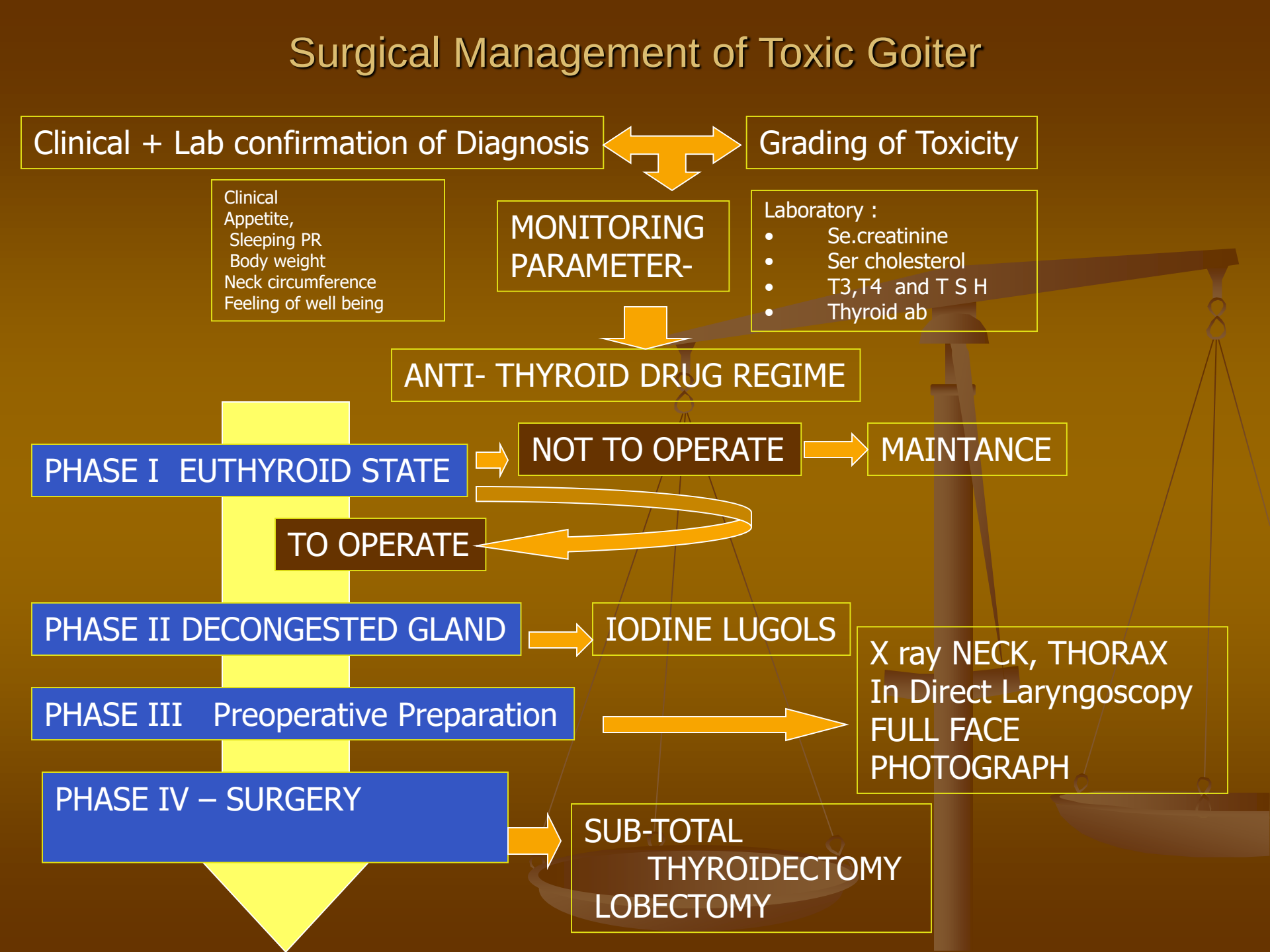
INDICATIONS for surgery

- Bulky nodular Gland with pressure symptoms
- Controlled Thyrocardiac
- When Long term Medical supervision not possible, immediate Relief wanted
- Relapse after A TT, Secondary Thyrotoxicosis
- Pregnancy second Trimester
- Available of skilled endocrine surgeon



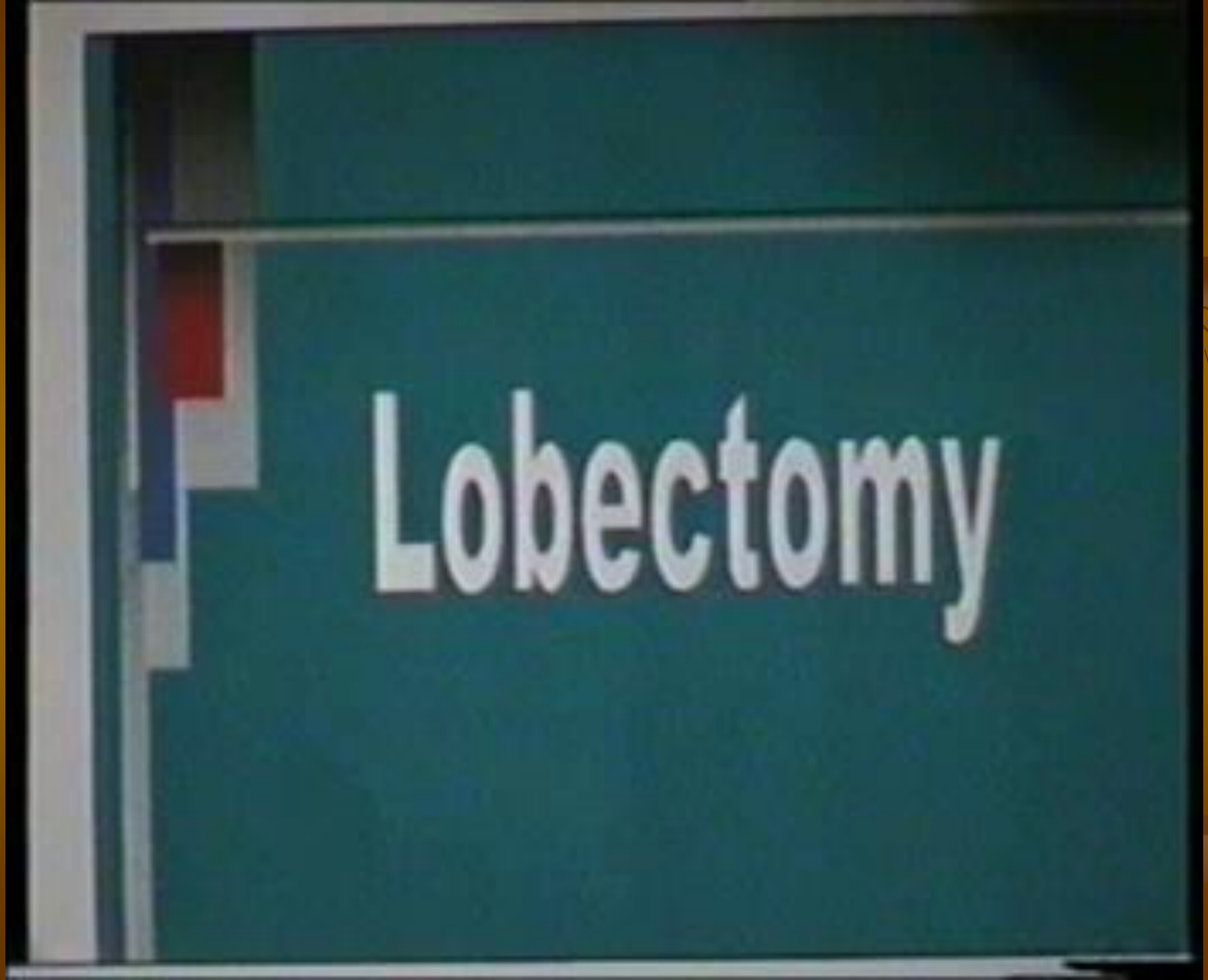
- Relative contraindication
- Age < 16 years Elderly
- Co-existent Medical problems
- Previous surgery small goitre
- Severe eye problem
- Remnant size
- Histological Lymphoid infiltration
- High Ts ab level

Surgical Management of Toxic Goiter



Opertive Surgery

Surgery of Thyroid


Lobectomy

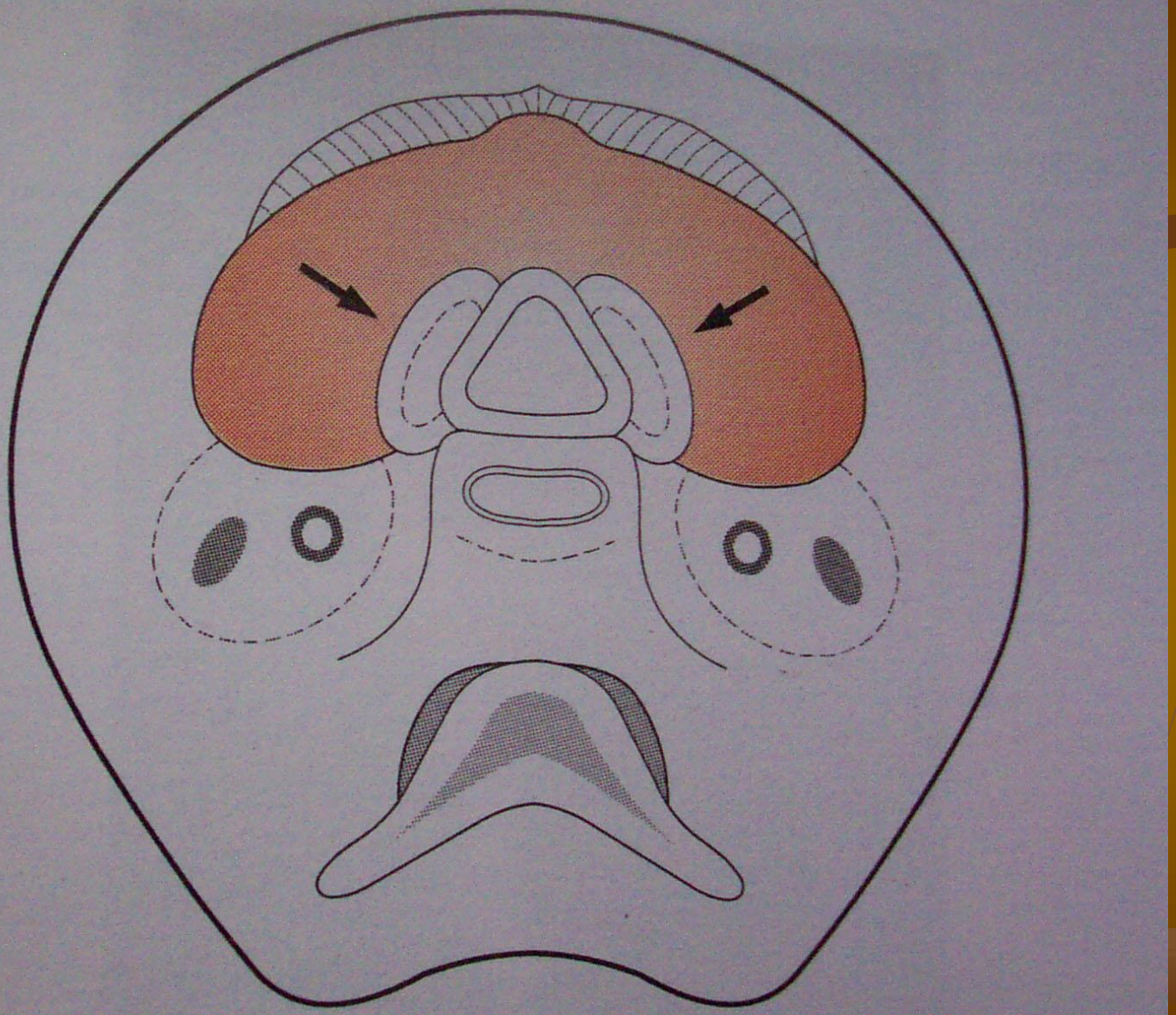
Postoperative Complications

1.Wound Comp. : a. Haematoma
b. Abcess
c. Fistula, Sinus
d.Lymphedema
e. Scar, Keloid formation

2. Hemorrhage
a. early – Tension Hematoma – Primary, Reactionary H'age
b. Delayed : Secondary H'age

3. Respiratory obstruction – cyanosis
1. Laryngeal edema : Intubation Injury
2. Tension Hematoma – Evacuation, Intubation, steroids Tracheotomy
3. Collapse or kinking of trachea
4. Recurrent laryngeal nerve palsy

d. Recuurent Lary N Palsy Transient occurs in 3% 3 week to 3 months



Tension haematoma deep to pretracheal muscles