THYROID FUNCTION TESTS

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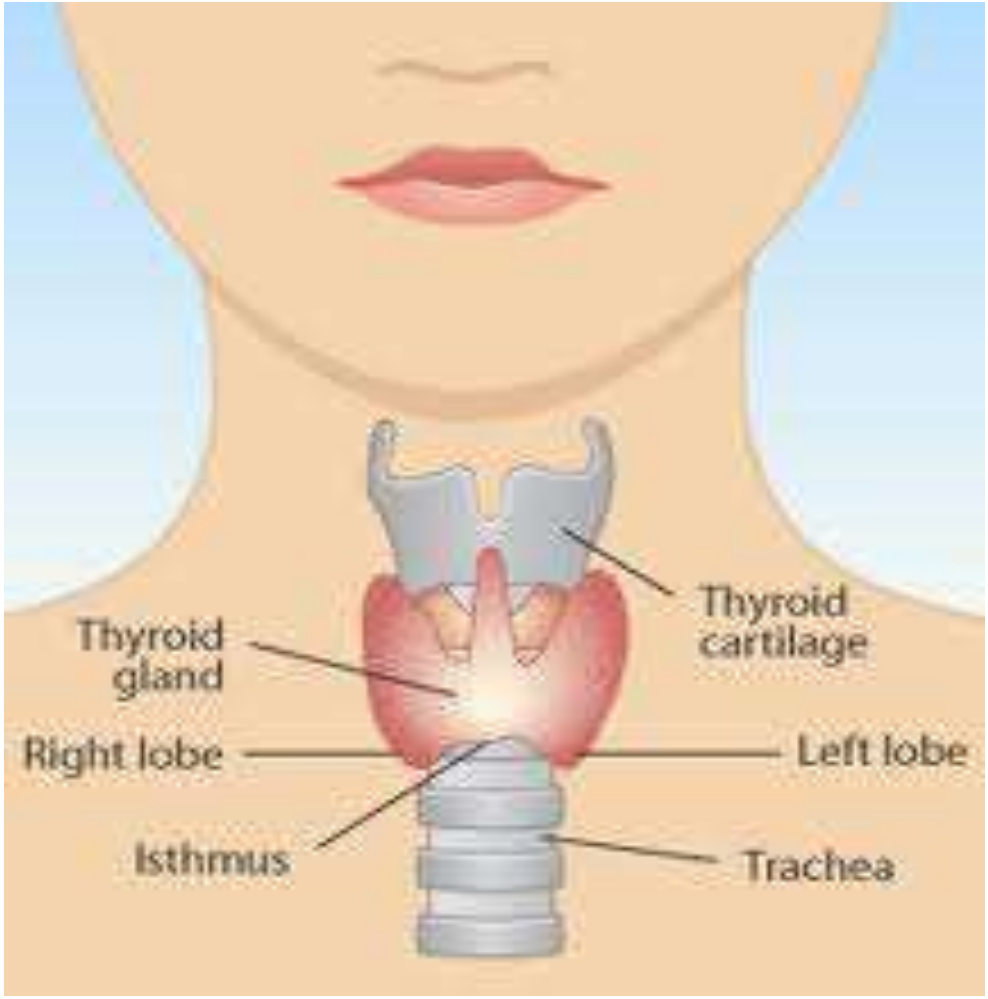
Objectives:

- To diagnose thyroid disorders in a person with symptoms
- To possibly evaluate the cause for the thyroid dysfunction
- To screen newborns for an underactive thyroid
- To monitor and follow up thyroid replacement therapy in hypothyroidism or antithyroid treatment in hyperthyroidism
- To diagnose and monitor female infertility problems
- To evaluate the function of the pituitary gland (occasionally)

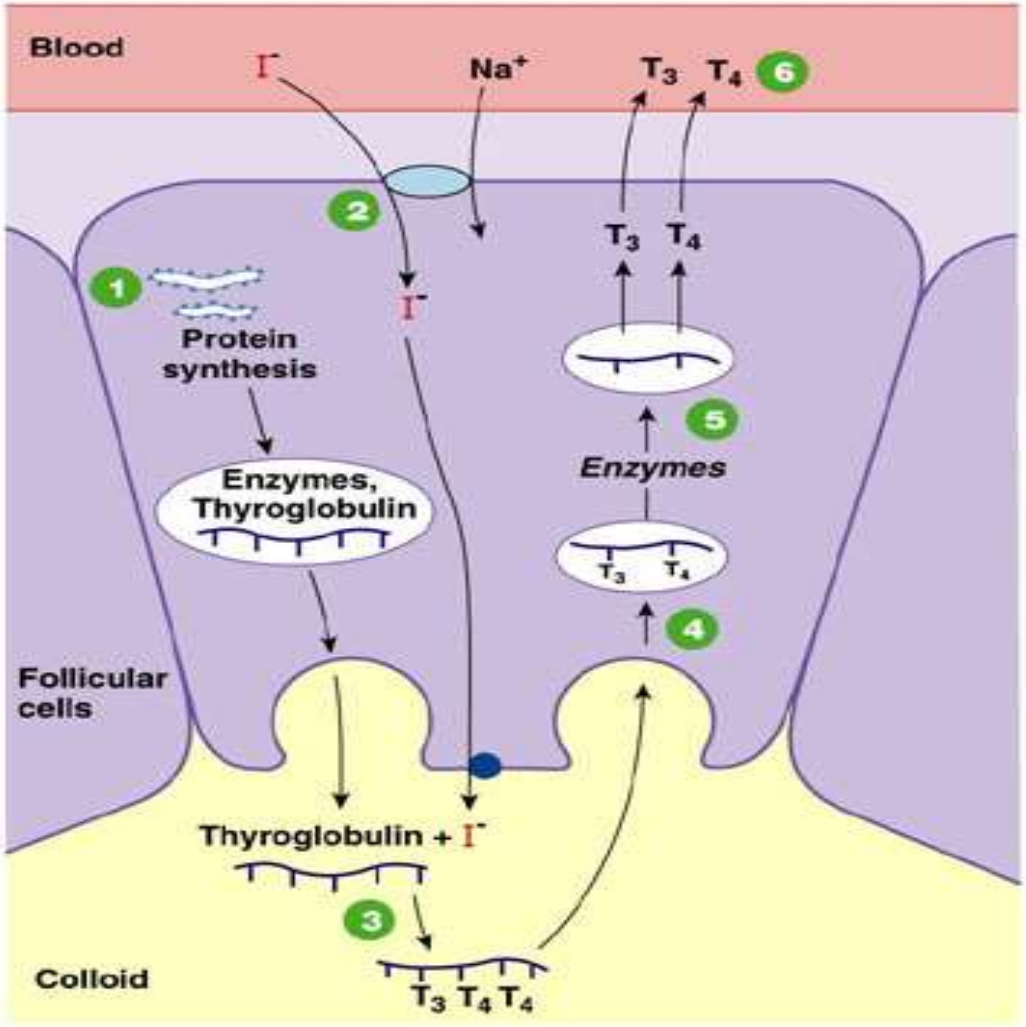
LIMITATIONS:

- A single thyroid function test is not absolute in diagnostic accuracy
- Non-thyroidal factors affect thyroid function tests
- Inherent pitfall's of the method of determination may lead to false positive or false negative results.

INTRODUCTION:



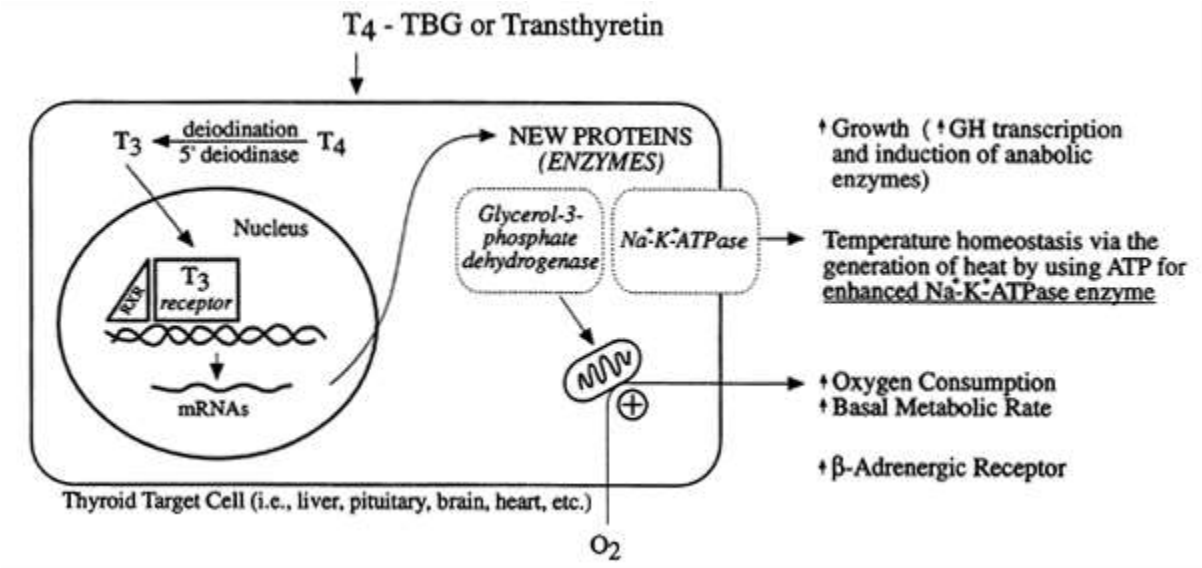
SYNTHESIS OF THYROID HORMONES:



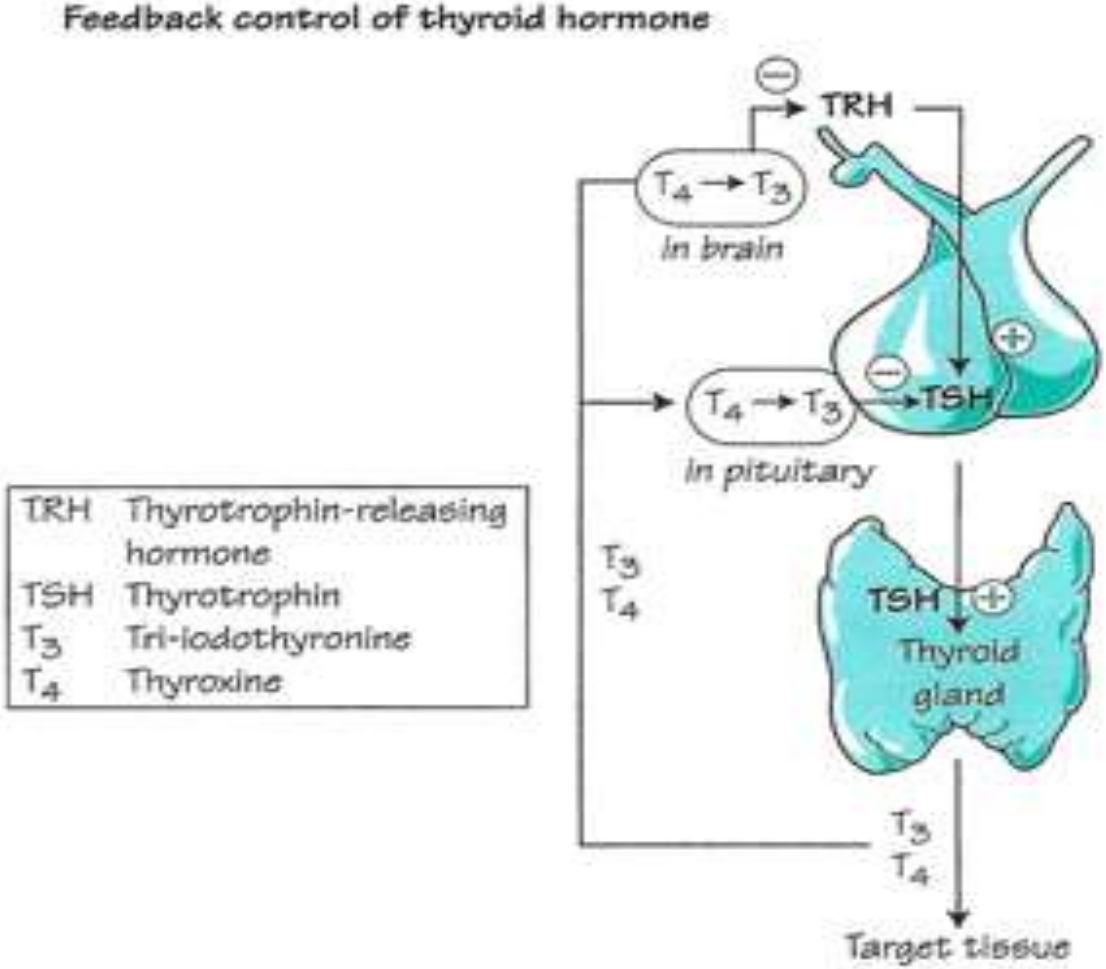
1. Follicular cell synthesizes enzymes and thyroglobulin for colloid.
2. I^- is co-transported into the cell with Na^+ and transported into colloid.
3. Enzymes add iodine to thyroglobulin to make T_3 and T_4.
4. Thyroglobulin is taken back into the cell.
5. Intracellular enzymes separate T_3 and T_4 from the protein.
6. Free T_3 and T_4 enter the circulation.

Fig. 23-9

Mechanism of action and functions of thyroid hormones:



REGULATION:


Feedback control of thyroid hormone
TRH
$T_4 \rightarrow T_3$
in brain
$T_4 \rightarrow T_3$
TSH
in pituitary
T_3
T_4
TSH
Thyroid gland
T_3
T_4
Target tissue
TRH Thyrotrophin-releasing hormone
TSH Thyrotrophin
T_3 Tri-iodothyronine
T_4 Thyroxine

Classification of thyroid function tests:

- **Direct tests of thyroid function :**

  - Radioactive Iodine Uptake Studies

- **Based on circulating thyroid hormonal levels:**

  - Total T_4 and Total T_3
  - Free T_4 and Free T_3

Classification of thyroid function tests (Cont.)

- **Based on metabolic functions of thyroid hormones**

- BMR
- Serum Cholesterol
- Serum Creatine
- Serum Uric acid
- Serum Creatine-kinase
- Plasma Tyrosine level

Classification of thyroid function tests (Cont.)

- **Based on homeostatic control of thyroid hormones:**
  - TRH - Stimulation test
  - Serum TSH
- **Miscellaneous Tests:**
  - Immunological tests
  - Thyroid scan
  - Thyroid Ultrasound
  - Fine Needle Aspiration

Radioactive Iodine Uptake Studies:

- Iodine-131, localized by thyroid tissue and is metabolized in the same manner as stable iodine.
- RAIU – reflects the iodine trapping ability.
- Normal range – 15 to 35%
- Interpretation :

- Abnormally high RAIU- Hyperthyroidism
- Abnormally low RAIU- Hypothyroidism

Total T_4 and Total T_3 :

- T4 or T3 bound to protein (mainly thyroid binding

  globulin) + Free T4 or T3

- Normal range -

- T4 : 4.5 -12 µg/dl
- T3 : 0.79 -1.49 ng/ml

- Can be affected by binding protein levels

Free T_4 and Free T_3 :

- Biologically active forms of thyroid hormones
- Not affected by binding protein levels
- More accurate reflection of thyroid hormone function
- Normal range:

- F T4: 0.8 -1.6 ng/dl
- F T3: 1.4- 4.2 pg/ml

TRH-STIMULATION TEST:

- Principle: If TRH administered then

  TSH ↑
- Hypothyroidism:already TSH

  TRH given = TSH ↑↑
- Hyperthyroidism: blunted response

Serum TSH:

- Ultrasensitive (IRMA) TSH methods are available
- Normal level 0.49 -4.67 µIU / ml
- Increased TSH –Primary Hypothyroidism
- Low to high or normal TSH –Secondary hypothyroidism
- Suppressed TSH- Hyperthyroidism

TESTS OF METABOLIC FUNCTIONS:

- BMR
  - NORMAL BMR: 5% TO 20%
  - EUTHYROID STATE: (-10%) TO 10%
  - HYPOTHYROIDISM: (<20%)
    (-30% TO -60%)
  - HYPERTHYROIDISM: 50% TO 75%
- Serum cholesterol:

Hypothyroidism	Hyperthyroidism
Decrease cholesterol	Increase cholesterol

Tests of metabolic functions:

- Serum Creatine

Hyperthyroidism	Hypothyroidism
Creatine(>0.6mg%)	creatine(<0.6mg%)

- Uric acid inc in myxoedematous state
- Serum C-K level raises in hyperthyroidism
- Hyperthyroidism increases blood calcium due to exaggerated osteoclastic activity

IMMUNOLOGICAL TESTS:

- Observed in 1)autoimmune thyroiditis
  2)malignancies
- Common Abs Detected :

- Tg Ab
- Thyroid peroxidase TPOAb (Antimicrosomal Ab)
- TSH receptor (TSI)

Thyroid Scan:

- Study the distribution of radioactive iodine
- Advantages:

- distinguishes diffuse glandular activity from the patchy pattern of nodular goiter from normal
- functionally classifies hot areas, cold areas
- information about size, shape and position
- detects functioning thyroid tissues in lungs, bones

  in cases like ectopic thyroid, metastatic conditions of thyroid

- Thyroid Ultrasound:

- differentiate between different types of nodules of the thyroid gland
- Monitoring nodule size
- For guiding FNA biopsies
- For the aspiration of cystic leisons
- Evaluation of recurrent thyroid cancer

- FNAC:

- For this test a small needle is inserted into the thyroid gland in order to get a sample of thyroid tissue , usually from a nodule
- The tissue is then observed under a microscope to look for any signs of cancer

Thyroid Dysfunction:

- Hypothyroidism
- Hyerthyroidism

Hypothyroidism:

- **Primary (Goitrous) Hypothyroidism**
- Hashimoto's thyroiditis
- Endemic iodine deficiency
- Subacute thyroiditis
- Defects in hormone synthesis
- Drug-induced

- **Primary (Nongoitrous) Hypothyroidism**
- Spontaneous thyroid atrophy
- Radioactive iodine therapy
- Surgical ablation
- External radiation

Hypothyroidism

- **Secondary Hypothyroidism**
  - Pituitory disease
  - Hypothalamic disease

Symptoms of Hypothyroidism:

- Weight gain
- Easy fatigue
- Dry skin
- Constipation
- Hair loss
- Cold intolerance
- Frequent menstrual peroids

Hyperthyroidism:

- **Associated with Thyroid Hyperfunction**
- Graves's disease
- Plummer's disease
- Solitary toxic adenoma
- TSH - secreting pituitory tumor
- HCG – secreting trophoblastic tumor
- Iodine – induced Hyperthyroidism
- Hyperemesis gravidarum

Hyperthyroidism (cont.):

- **Non Associated with Thyroid Hyperfunction**
- Subacute thyroiditis
- Silent lymphocytic thyroiditis
- Thyrotoxicosis facticia
- Drug-induced thyrotoxicosis
- Struma ovarii
- Hyperfunctioning metastatic thyroid carcinoma

Symptoms of Hyperthyroidism:

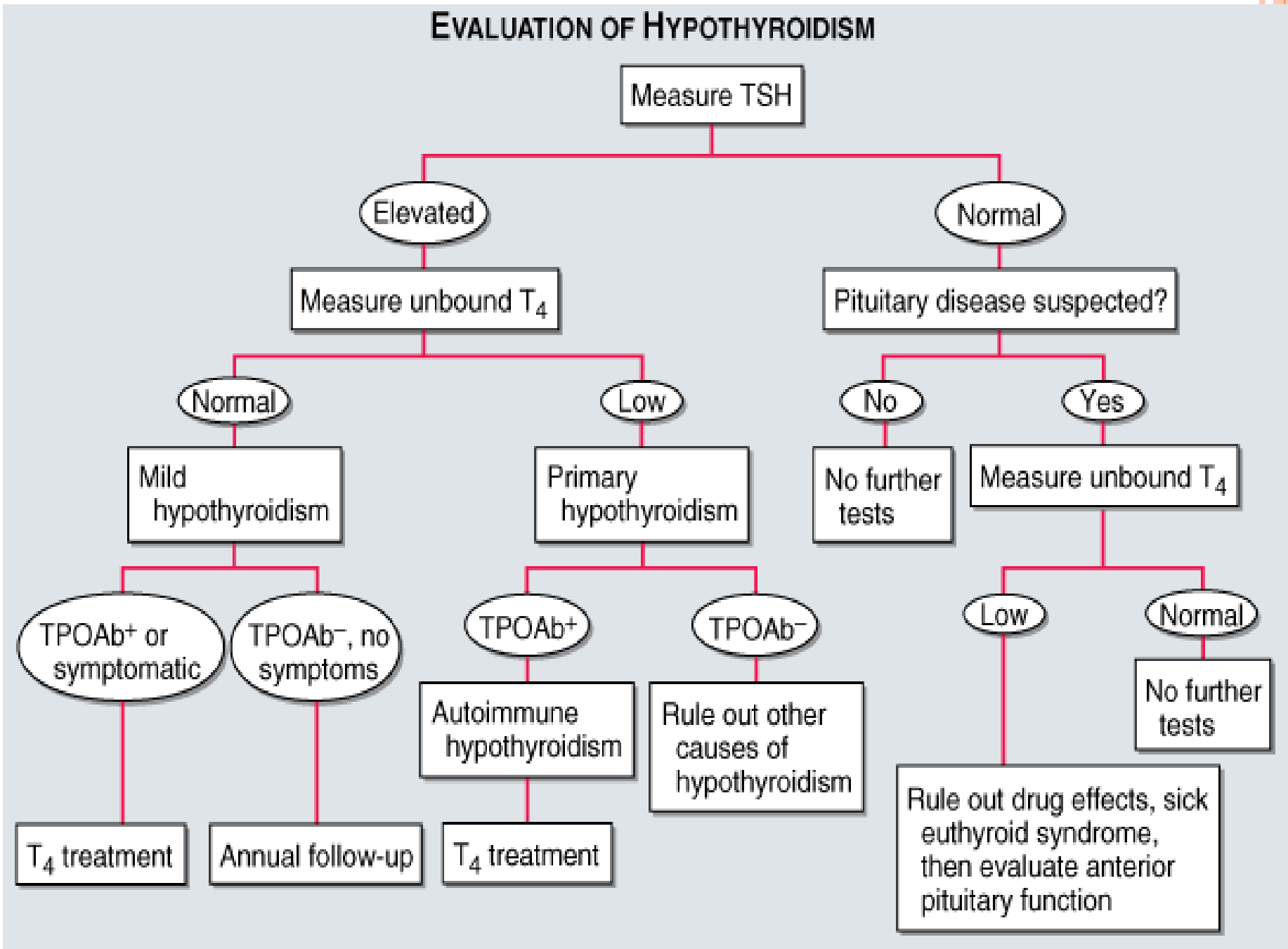
- Tiredness
- Weight loss
- Heat intolerance
- Sweating
- Irritability
- Anxiety
- Exophthalmos
- Muscle weakness
- Thyroid enlargement

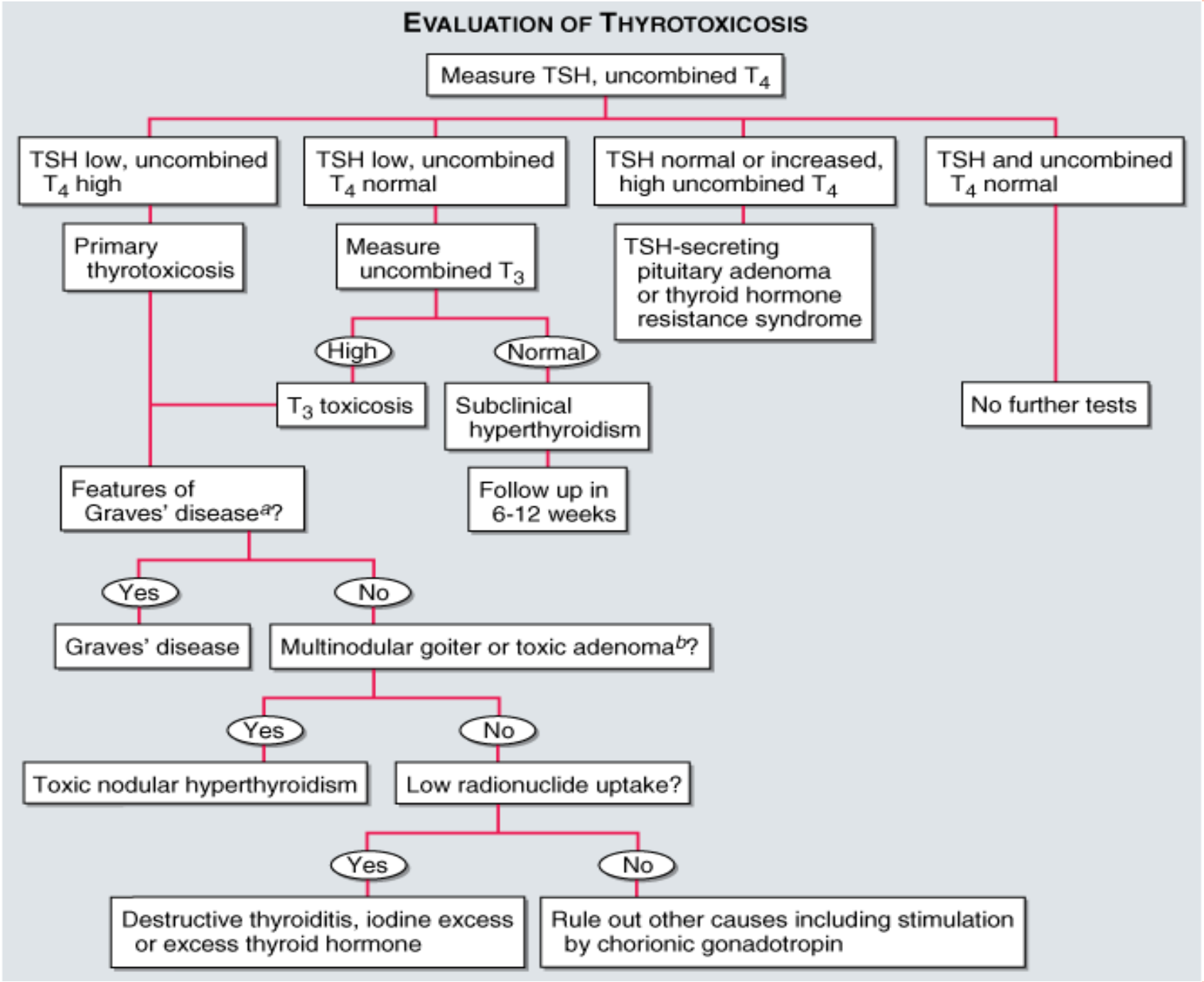
DIAGNOSIS OF THYROID DYSFUNCTION

- IN PAST THE THYROID TEST WERE PErFORMED STEP WISE:-

1. TOTAL SERUM T4 WAS MEASURED FOLLOWED BY
2. FT4 (FREE THYROXINE ESTIMATION)

- FT4 PROVIDES MORE RELIABLE INFORMATION THAN TOTAL T4 TEST
- BUT T4 & FT4E ARE NOT IDEAL INDICATORS OF THYROID STATUS & T3 IS PRIMARY ACTIVE THYROID HORMONE
- SO MEASURING T3 IS BETTER.
- T3 LEVEL FLUCTUATES RAPIDLY DUE TO NONTHYROIDAL FACTORS SO T3 IS ALSO NOT A GOOD GENERAL TEST
- MEASURMENT OF TSH IS MORE RELIABLE.


EVALUATION OF HYPOTHYROIDISM
Measure TSH
Elevated
Normal
Measure unbound T_4
Pituitary disease suspected?
Normal
Low
No
Yes
Mild hypothyroidism
Primary hypothyroidism
No further tests
Measure unbound T_4
TPOAb+ or symptomatic
TPOAb−, no symptoms
TPOAb+
TPOAb−
Low
Normal
Autoimmune hypothyroidism
Rule out other causes of hypothyroidism
No further tests
T_4 treatment
Annual follow-up
T_4 treatment
Rule out drug effects, sick euthyroid syndrome, then evaluate anterior pituitary function

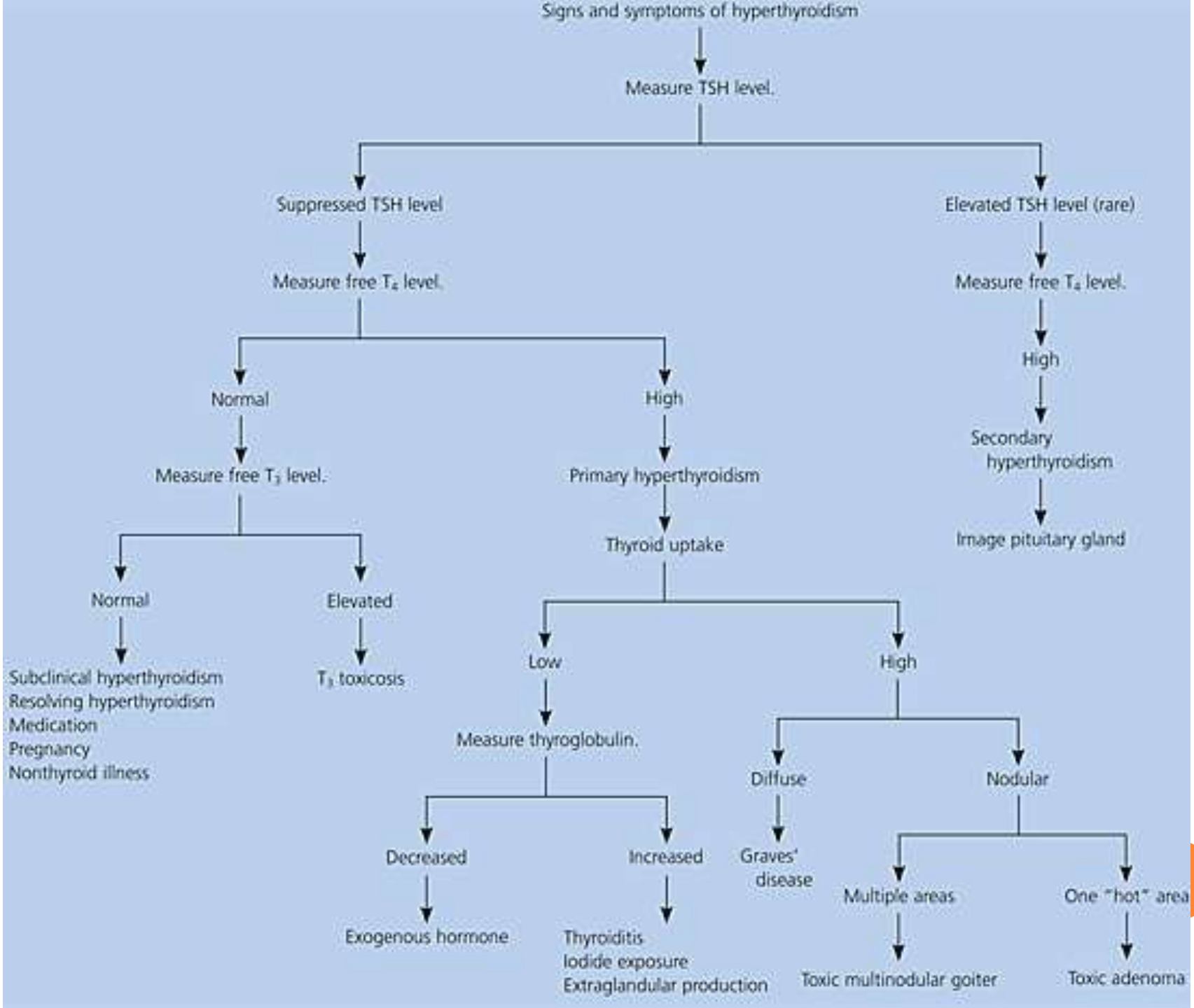

EVALUATION OF THYROTOXICOSIS
Measure TSH, uncombined T_4
TSH low, uncombined T_4 high
TSH low, uncombined T_4 normal
TSH normal or increased, high uncombined T_4
TSH and uncombined T_4 normal
Primary thyrotoxicosis
Measure uncombined T_3
TSH-secreting pituitary adenoma or thyroid hormone resistance syndrome
High
Normal
T_3 toxicosis
Subclinical hyperthyroidism
No further tests
Features of Graves' disease[a]?
Follow up in 6-12 weeks
Yes
No
Graves' disease
Multinodular goiter or toxic adenoma[b]?
Yes
No
Toxic nodular hyperthyroidism
Low radionuclide uptake?
Yes
No
Destructive thyroiditis, iodine excess or excess thyroid hormone
Rule out other causes including stimulation by chorionic gonadotropin

Outline of Treatment in hypothyroidism:

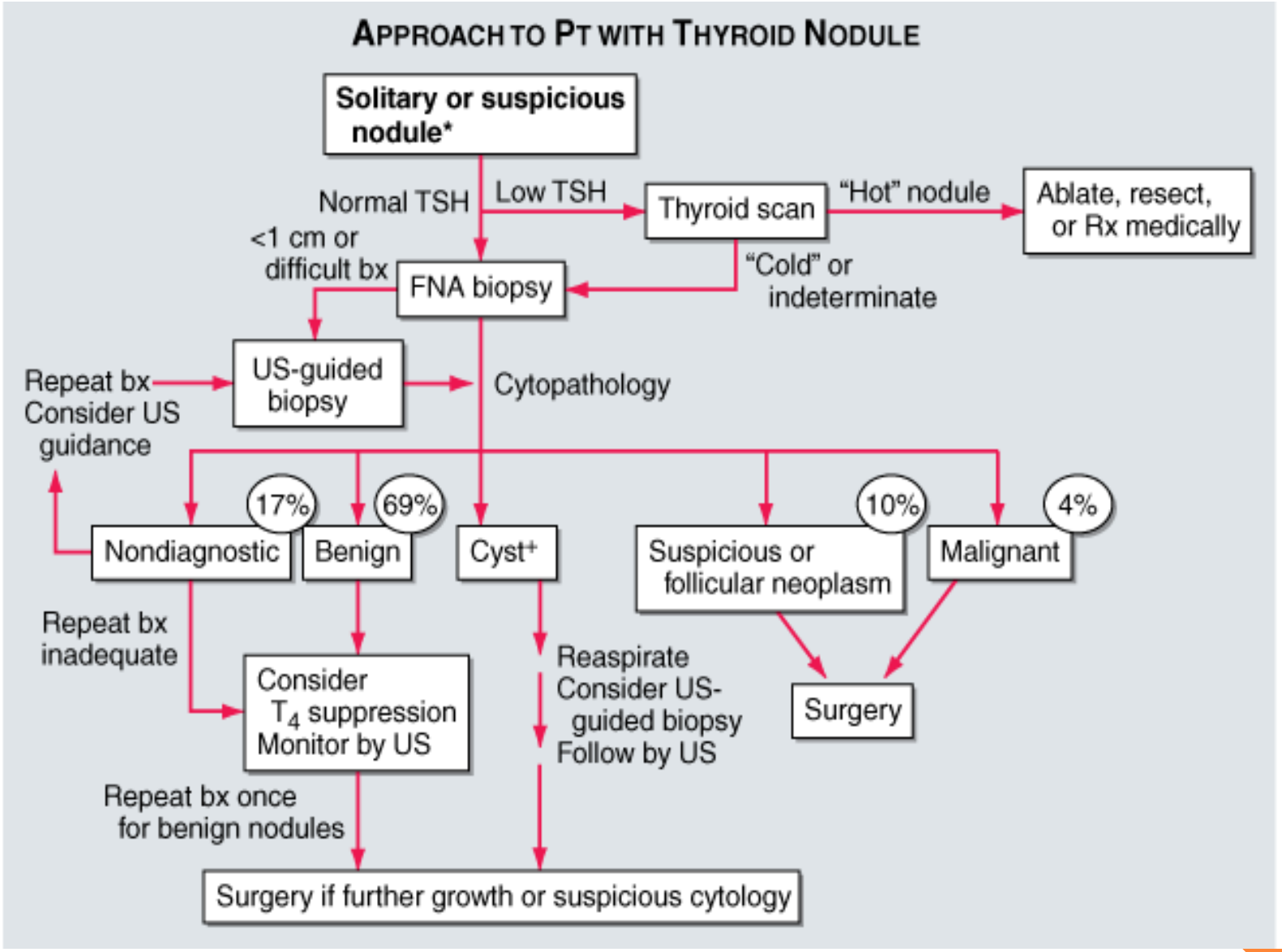
- Levothyroxine alone
- Levothyroxine combined with liothyronine

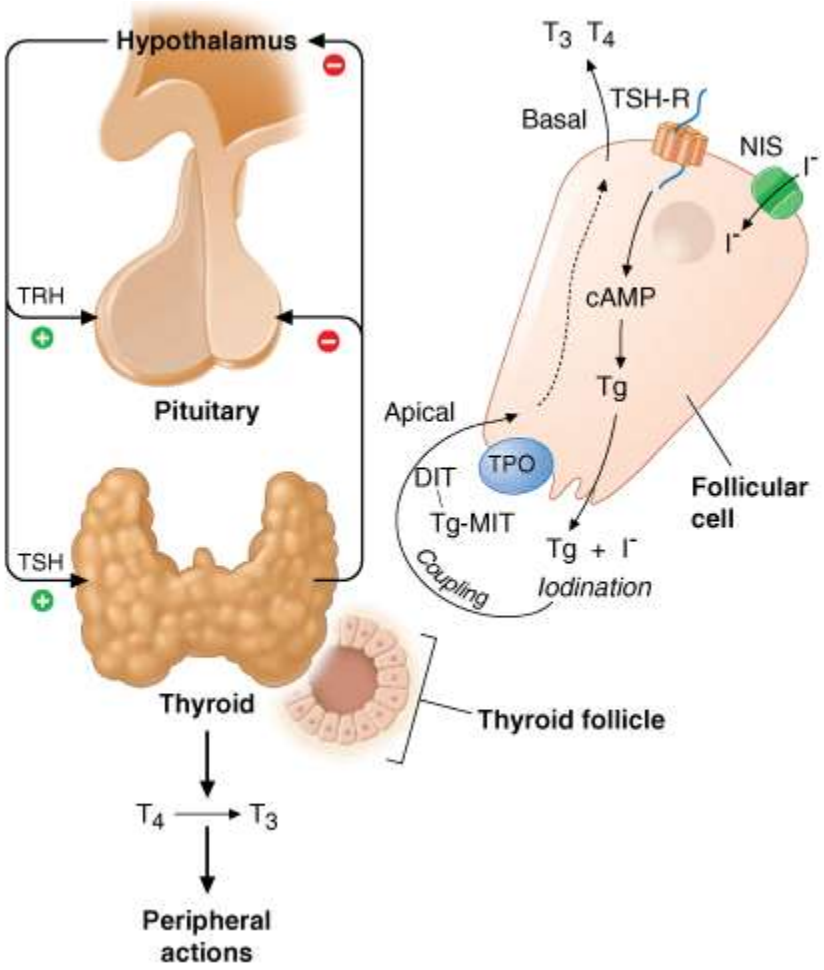
Outline of Treatment in hyperthyroidism:

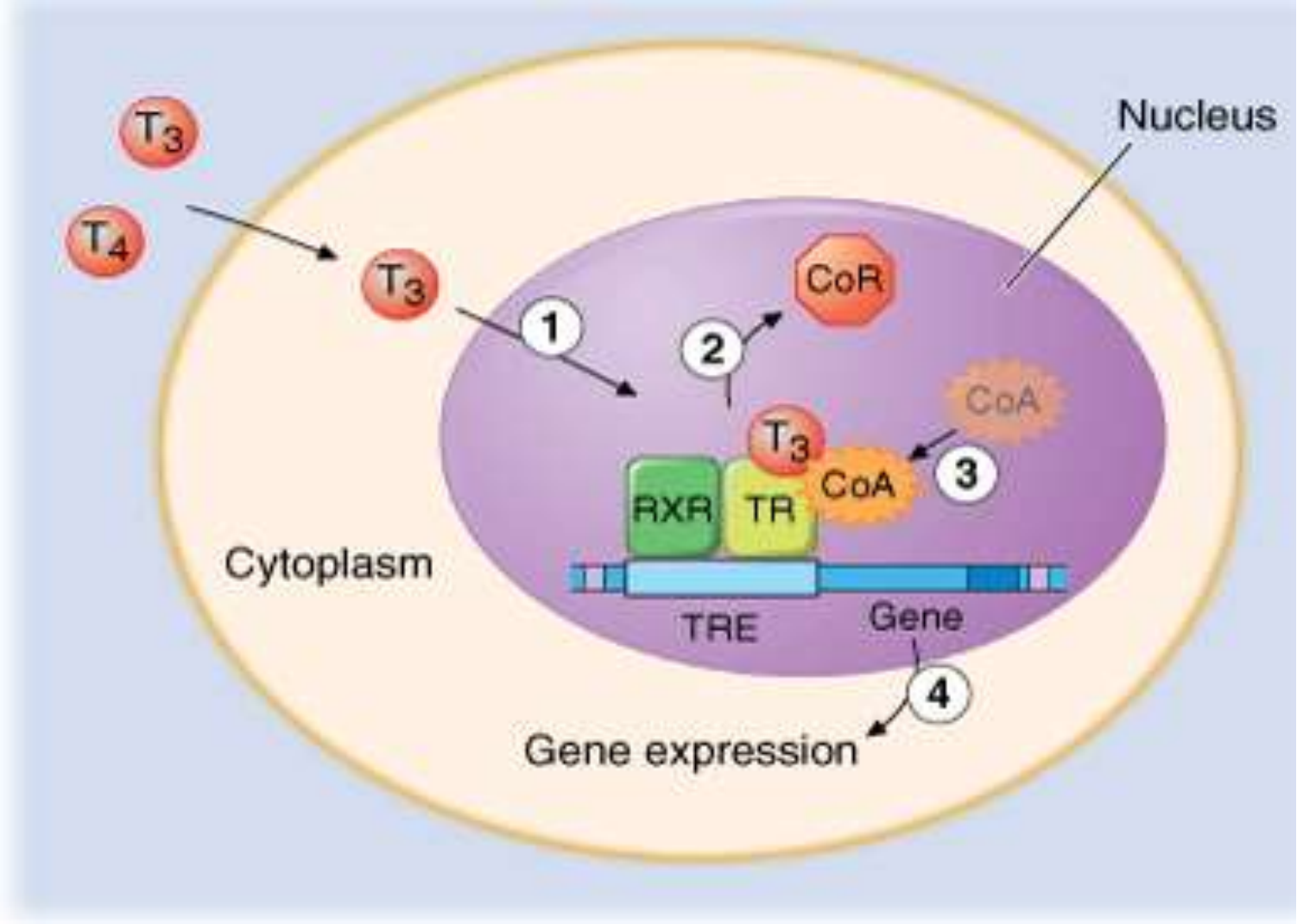
- Antithyroid drugs
- Radioiodine ^{131}I
- Beta-blockers
- Subtotal Thyroidectomy


Signs and symptoms of hyperthyroidism
Measure TSH level.
Suppressed TSH level
Elevated TSH level (rare)
Measure free T_4 level.
Measure free T_4 level.
High
Secondary hyperthyroidism
Image pituitary gland
Normal
High
Measure free T_3 level.
Primary hyperthyroidism
Thyroid uptake
Normal
Elevated
Subclinical hyperthyroidism
Resolving hyperthyroidism
Medication
Pregnancy
Nonthyroid illness
T_3 toxicosis
Low
High
Measure thyroglobulin.
Diffuse
Nodular
Decreased
Increased
Graves' disease
Multiple areas
One "hot" area
Exogenous hormone
Thyroiditis
Iodide exposure
Extraglandular production
Toxic multinodular goiter
Toxic adenoma

*


APPROACH TO PT WITH THYROID NODULE
Solitary or suspicious nodule*
Normal TSH
Low TSH
Thyroid scan
"Hot" nodule
Ablate, resect, or Rx medically
<1 cm or difficult bx
FNA biopsy
"Cold" or indeterminate
Repeat bx Consider US guidance
US-guided biopsy
Cytopathology
17%
69%
10%
4%
Nondiagnostic
Benign
Cyst+
Suspicious or follicular neoplasm
Malignant
Repeat bx inadequate
Consider T_4 suppression Monitor by US
Reaspirate Consider US-guided biopsy Follow by US
Surgery
Repeat bx once for benign nodules
Surgery if further growth or suspicious cytology


Hypothalamus
TRH
Pituitary
TSH
Thyroid
T4 → T3
Peripheral actions
T3 T4
Basal
TSH-R
NIS
I-
I-
cAMP
Tg
Apical
TPO
DIT
Tg-MIT
Coupling
Tg + I-
Iodination
Follicular cell
Thyroid follicle


Nucleus
T3
T4
T3
1
2
CoR
CoA
T3
CoA
3
RXR
TR
Cytoplasm
TRE
Gene
4
Gene expression

- Free Thyroxine(FT4)

- Active form of thyroxine
- More accurate reflection of thyroid hormone function
- Newer test that is not affected by protein levels
- Normal range:0.8-2.4 ng/dL

THANK YOU