THYROID DISEASE

Scope

- Interpretation of thyroid function tests
- Hyperthyroidism /Thyrotoxicosis
- Thyroid storm
- Hypothyroidism
- Single thyroid nodule
- Multinodular goiter
- Nonthyroidal illness (Sick euthyroid syndrome)

ภาวะที่มีผลต่อ thyroid binding globulin

Total hormone จะเพิ่มลดตาม TBG แต่ free hormone จะไม่ถูกรบกวน

เพิ่ม TBG	ลด TBG
Pregnancy	Hypoalbuminemia: NS, cirrhosis, malnutrition
Chronic active hepatitis	Active acromegaly
Drugs: estrogen, tamoxifen, methadone, heroin, perphenazine, 5-fluouracil, clofibrate, raloxifene, mitotane	Drugs: steroids, salicylate, androgens, danazol, L-asparaginase, slow-release niacin (nicotinic acid),phenylbutazone

ยาที่มีผลต่อ TFT

T_3, T_4	FT_3, FT_4	Drug	Note
ต่ำลง	ต่ำลง	Rifampicin, phenytoin, PHB, CBZ	ยาไปเร่งการทำลาย hormone ที่ตับ
ต่ำลง	สูงขึ้น	Heparin (ผ่าน FFA), furosemide (high dose), salicylates, certain NSAIDS	ยาไปแย่งจับกับ albumin
TSH ต่ำลง		Dobutamine, dopamine, steroids, octreotide	ลด TSH secretion

TSH	FT_4	FT_3	Common cause	Rare cause
N	N	N	Normal	
H	N	N	Subclinical hypothyroid	-Recovery phase of nonthyroidal illness
N/L	L	L	Central hypothyroidism	-Nonthyroidal illness -Drugs -Recently Rx of hyperthyroidism
H/N	H	H		-Central hyperthyroidism
L	N	N	Subclinical hyperthyroidism	Nonthyroidal illness
L	H/N	H/N	Thyrotoxicosis	-Thyroiditis -Gestational thyrotoxicosis -Molar pregnancy -Factitious thyrotoxicosis -Iodine induced

Thyrotoxicosis

- Thyrotoxicosis
  - ภาวะทางคลินิกและการตรวจพบthyroid hormoneสูงในร่างกาย เกิดได้จากหลายอย่างทั้งจากthyroid gland, drug หรือสร้างจากที่อื่น
- Hyperthyroidism
  - ภาวะทางคลินิกและการตรวจพบthyroid hormoneสูงในร่างกาย เกิดจากthyroid glandเองสร้างhormoneมากเกินไป

Clinical features

- Constitutional
  - Heat intolerance, fatigue
  - Increase intake, weight loss, flushing, sweating
- CVS
  - Palpitation, dyspnea on exertion
  - Tachycardia, AF, increase pulse pressure
- Local sign and symptom
  - Shortness of breath, hoarseness, dysphagia
  - Stridor, thyromegaly, Pemberton's sign

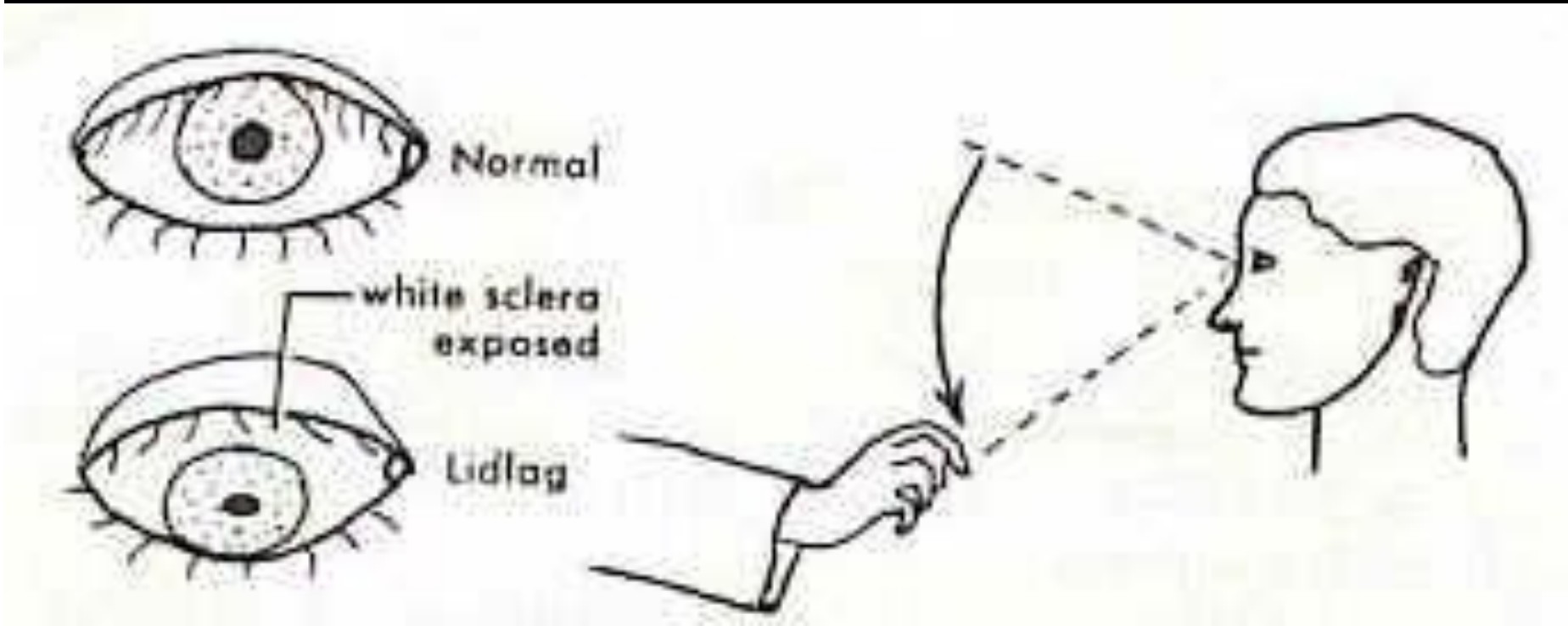
Clinical features

- Gastrointestinal
  - Diarrhea, jaundice
- Neuromuscular/psychiatric
  - Nervousness, poor attention span, weakness
  - Rapid fire speech, insomnia, dysphoric mood
  - Proximal muscle weakness, tremor
  - Brisk relaxation phase of DTR

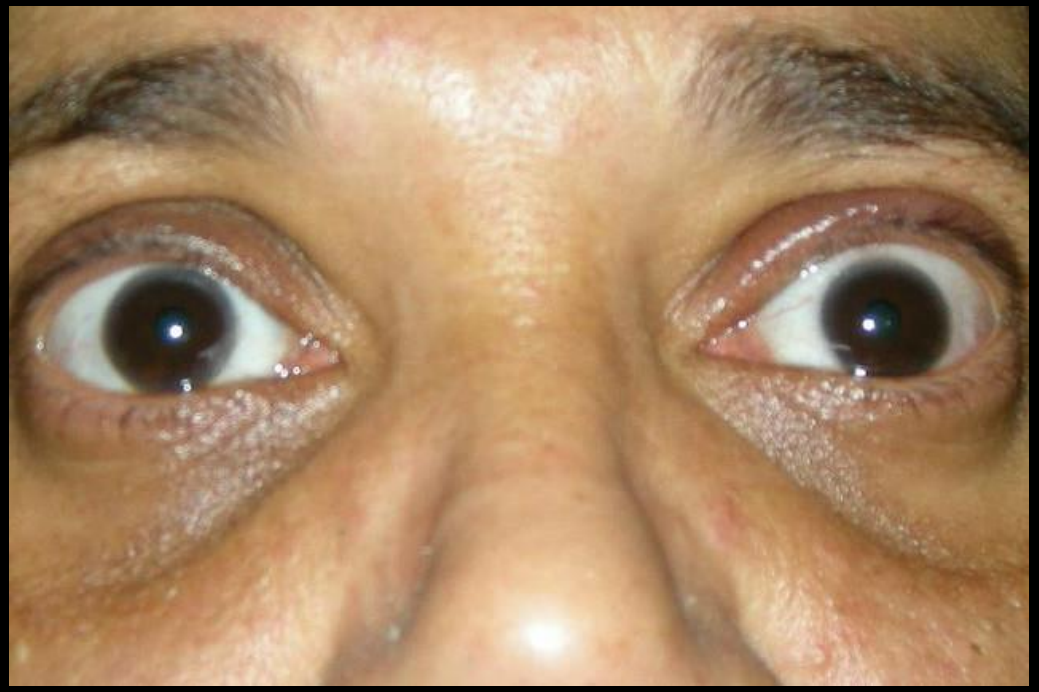
Clinical features

- Skin
  - Hair loss, warm moist skin
  - Fine and brittle hair, onycholysis
- Reproductive
  - Oligomenorrhea, infertility, gynecomastia
  - Loss of libido
- Metabolic derangement
  - Osteoporosis

Lid lag

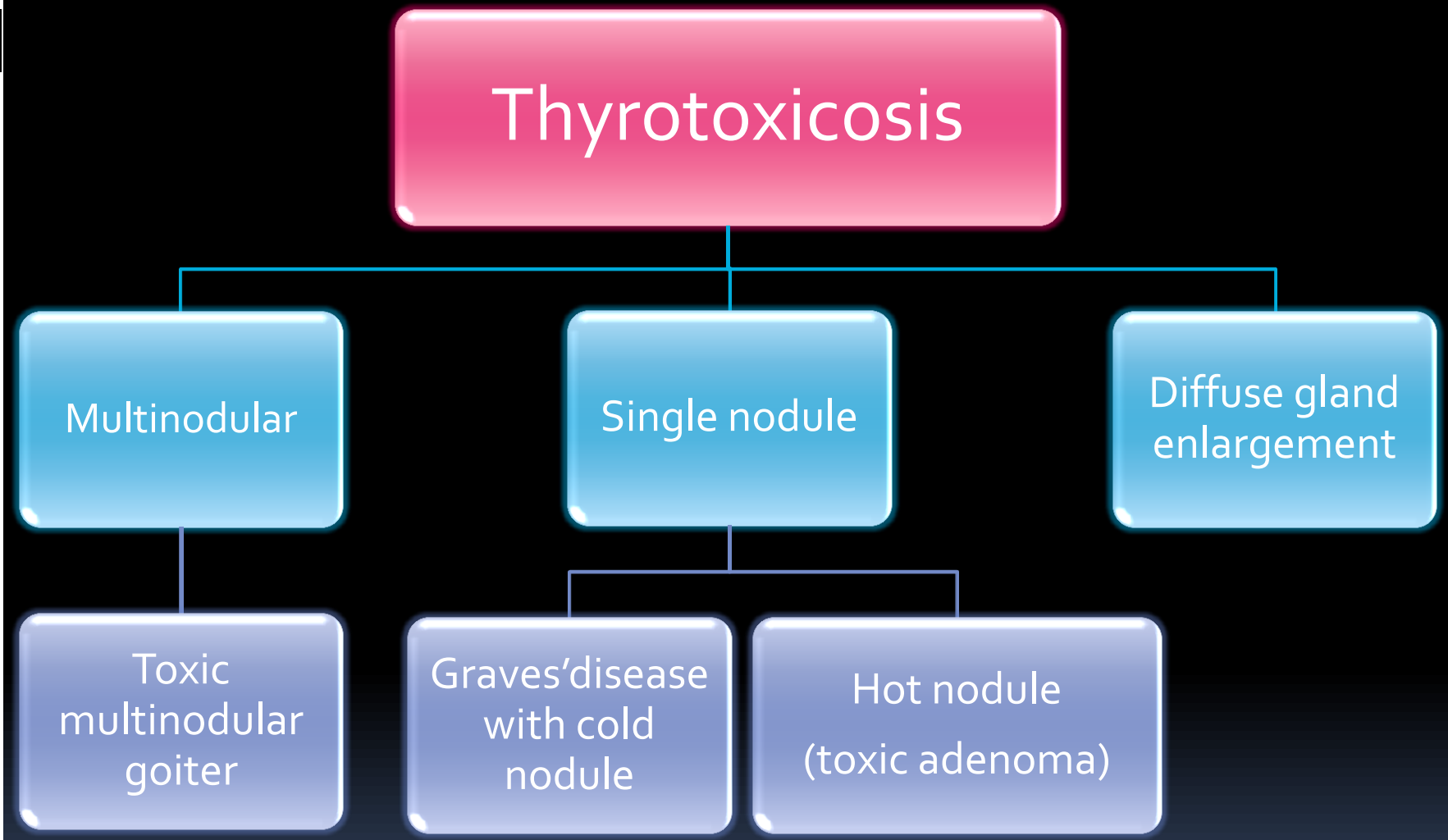


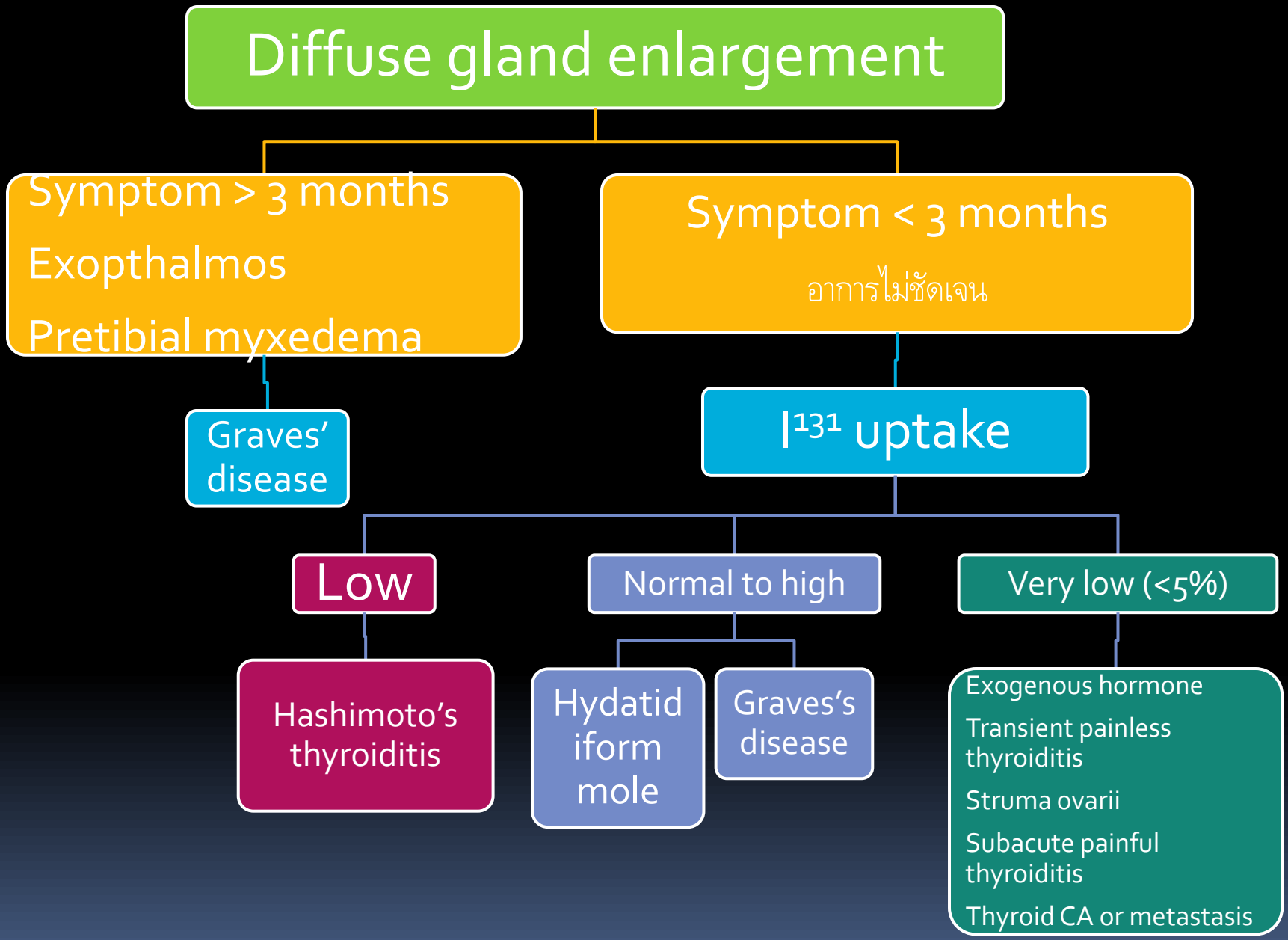
Lid retraction



Exophthalmos

Onycholysis : Plummer’s nail


Thyrotoxicosis
Multinodular
Single nodule
Diffuse gland enlargement
Toxic multinodular goiter
Graves'disease with cold nodule
Hot nodule (toxic adenoma)


Diffuse gland enlargement
Symptom > 3 months
Exopthalmos
Pretibial myxedema
Symptom < 3 months
อาการไม่ชัดเจน
Graves' disease
I131 uptake
Low
Normal to high
Very low (<5%)
Hashimoto's thyroiditis
Hydatid iform mole
Graves's disease
Exogenous hormone
Transient painless thyroiditis
Struma ovarii
Subacute painful thyroiditis
Thyroid CA or metastasis

Thyrotoxicosis associated with hyperthyroidism

- Production of abnormal thyroid stimulator (Graves' disease)
- Production of thyroid stimulator (HCG-mediated)
  - Hyperemesis gravidarum
  - Trophoblastic tumor
- Intrinsic thyroid autonomy
  - Toxic adenoma
  - Toxic multinodular goiter
  - Metastatic thyroid carcinoma
- Drug induced hyperthyroidism
  - Iodine, radiographic contrast agent

Thyrotoxicosis not associated with hyperthyroidism

- Inflammatory disease
  - Subacute thyroiditis
  - Postpartum thyroiditis
  - Drug induced thyroiditis
  - Radiation thyroiditis
- Extrathyroidal source of hormone
  - Exogenous hormone

Graves' disease

- Most common cause
- Autoantibodies against the TSH receptor
- Diffuse goiter (smooth and firm) with opthalmopathy, dermopathy (pretibial myxedema)

Pretibial myxedema

Acropachy

Diffuse goiter

Graves' disease : investigation

- Anti-TSH receptor antibody =

TSH Receptor-Stimulating Immunoglobulins (TSIs)

Graves' disease : investigation

- Antithyroglobulin and Antimicrosomal (antiperoxidase) Ab
  - Autoimmune thyroid disease
  - Modestly increased titers, positive 70%
  - Not specific to Graves' disease
- Radioactive iodine uptake
  - High uptake, >30%(10-25%)
- Thyroid ultrasonography
  - Increased blood flow

Graves' disease : management

- Antithyroid drugs
- Radioactive iodine
- Surgery

Antithyroid drugs

- Thionamides
  - Inhibit thyroid hormone synthesis
  - Indication
    - First line therapy for pregnant, children and adolescents
    - Pretreatment before RAI for severe cases, or preoperation
  - Disadvantages
    - Adverse drug reactions
    - Low cure rate (40-50%)
    - Drug compliance

Antithyroid drugs

- Propylthiouracil
  - High dose PTU : inhibit peripheral deiodination $T_4 \rightarrow T_3$
  - Half-life 1-2 h
  - Use in pregnant woman, thyroid storm, minor drug reaction to MMI
  - Starting dose 150-300 mg/day (3 times)
- Methimazole
  - Half-life 4-6 h
  - Starting dose 15-30 mg/day (once a day)

Antithyroid drugs : side effect

- Minor 1-5%
  - Rash, arthralgia, itching
  - Rx : Antihistamine, switch to others thionamide
- Major
  - Agranulocytosis (PMN < 500 ตัว/mm^3)
    - 0.3%
    - PTU : idiosyncratic, MMI : dose dependent
    - Most occur in 3 months after Rx
    - แนะนำอาการไข้สูง เจ็บคอ ให้หยุดยา
    - Rx: broad-spectrum ATB & supportive Rx
    - Absolute contraindication

Antithyroid drugs : side effect

- Hepatotoxicity 0.2%
  - PTU : hepatocellular degeneration (most in 3 months)
  - MMI : cholestatic jaundice
  - สามารถใช้ยาอีกตัวหนึ่งทดแทนได้
- Vasculitis
  - PTU > MMI
  - Drug induced lupus
  - Arthritis, fever, hemoptysis, glomerular disease
  - ANCA positive 20%
  - Absolute contraindication

- Beta adrenergic blockers
  - Reduce palpitation, tachycardia
  - Propranolol : inhibit peripheral conversion
  - Atenolol ได้ผลไม่ต่างจาก propranolol
  - Contraindication : asthma, heart failure, heart block

Follow up

- F/U TFT q 6-8 weeks (in first 6 months)
- TSH เจาะตรวจ 6 เดือนหลังการรักษา
- Hormone decrease to normal level in 6-12 weeks
- ปรับยาลดลงตามอาการและผลเลือด
- Maintenance dose
  - PTU 50-100 mg/day
  - MMI 5-10 mg/day
- Duration 12-18 months (remission rate 40-60%)
- Relapse 50-60% in first 3-6 months

Radioactive iodine ablation

- Indication
  - Thyrotoxicosis esp. elderly patients
  - Adverse effect from antithyroid drugs, relapse, poor compliance
- Contraindication
  - Absolute CI: Pregnancy, breast feeding
  - Relative CI: Uncontrolled hyperthyroidism, active thyroid orbitopathy
  - Age < 20 yr

Radioactive iodine ablation

- Side effect
  - Hypothyroidism (most common) incidence increase 2-3%/year after treatment
  - Postradiation thyroiditis
  - Graves' ophthalmopathy worsening

Preparing for ^{131}I treatment

(1) Stop MMI/PTU ≥ 3-7 days

(2) Avoid seafood, iodized salt ≥ 1-2 wks

(3) Avoid drugs which contain iodine (cough syrup, Lugol's soln, potassium iodide, amiodarone) ≥ 2-3 wks

- After ^{131}I resume MMI/PTU after 3-7 days.
- If still hyperthyroid after 6 mo, consider repeating RAI or use other Rx options.

Surgery

- Subtotal thyroidectomy
- Indication
  - มี cold thyroid nodule อาจเป็นมะเร็ง
  - Not response to antithyroid drugs esp. pregnant woman (2^{nd} Trimester)
  - Thyroid gland enlargement > 70 g and compressive symptoms
  - Adverse effect from drugs and deny iodine ablation
  - Severe ophthalmopathy

Thyroid storm

Etiology

- Most common : Graves' disease
- Less common : toxic adenoma, toxic multinodular goiter
- Rare : hypersecretory thyroid adenoma, TSH-oma, struma ovarii/teratoma, hCG-secreting hydatidiform mole
- After use IFN-alpha, IL-2, radiocontrast media, amiodarone administration

Precipitating factors

1. Systemic insults : surgery, trauma, AMI, pulmonary thromboembolism, DKA, parturition, severe infection, pregnancy
2. Treatment relation :
   - Discontinuation of antithyroid drugs
   - Excessive ingestion or intravenous administration of iodine (ex. Radiocontrast dyes, amiodarone), radioiodine therapy,
   - Excessive pseudoephedrine and salicylate use

Symptoms

- General symptom
- Cardiorespiratory
- GI symptom
- Neurologic symptom

Fever
Profuse sweating
Poor feeding
Weight loss
Fatigue (more common in elderly)

Palpitation
Dyspnea
Chest pain

Nausea and vomitting
Abdominal pain
Jaundice
Diarrhea

Anxiety (more common in elderly)
Confusion
Seizure, coma

Signs

- Fever
  - Temperature consistently exceeds 38.5 c
- Excessive sweating
- Neurologic signs
  - Agitation & confusion
  - Hyperreflexia & transient pyramidal sign
  - tremors, seizures, coma
- Cardiovascular
  - HT with wide PP
  - Hypotension in later stages with shock
  - Tachycardia with disproportionate to fever
  - Sign of high output HF
  - Cardiac arrythmia
- Signs of thyrotoxicosis
  - Exophthalmos, diffuse goiter

Burch Wartofsky Score

Diagnostic parameters	Scoring points
Thermoregulatory dysfunction	
Temperature °F (°C)	
99–99.9 (37.2-37.7)	5
100–100.9 (37.8-38.2)	10
101–101.9 (38.3-38.8)	15
102–102.9 (38.9-39.2)	20
103–103.9 (39.3-39.9)	25
>/= 10	
Centr	
Absen	
Mild (	
Mode	
Sever	
Gastrointestinal-hepatic dysfunction	
Absent	0
Moderate (diarrhea, nausea/vomiting, abdominal pain)	10
Severe (unexplained jaundice)	20

Cardiovascular dysfunction	
Tachycardia (beats/minute)	
90–109	5
110–119	10
120–129	15
>/= 140	25
Congestive heart failure	
Present	10
Precipitating event	
Absent	0
Present	10

Score ≥ 45 : highly suggestive storm

Score 25-44 : suggestive of impending storm

Score < 25 : unlikely to represent thyroid storm

Management

- Specific treatment : Acute management
  - Treat underlying cause
  - Multidrug approach for multiple targets

1. Stopping synthesis of new hormone within the thyroid gland
2. Halting the release of stored thyroid hormone from the thyroid gland
3. Preventing conversion of T4 → T3
4. Controlling the adrenergic symptoms associated with thyrotoxicosis

1. Inhibition of new hormone production

- Propythiouracil 1200 mg/day
  - 200-400 mg po q 6-8 h, or per rectal + น้ำ 90 ml สวนเก็บ
  - Decrease T4→ T3 conversion ด้วย
  - First line therapy
- Methimazole
  - 20-25 mg po q 4-6 h

If contraindication to both drugs & normal renal function >> Lithium carbonate 300 mg po q 8 h, keep drug level 0.6-1 mEq/L

2. Inhibition of thyroid hormone release

- Lugol's solution 1 0 drops [20 drops/ml, 8mg iodine/drop] po q 8 h
- Potassium iodide, SSKI 5 drops [20 drops/ml, 38 mg iodide/drop] po q 6 hr

-Administer at least 1 h after thionamide

-Escape from the Wolff-Chaikoff effect (ลด organification & release) after 2-3 weeks of iodine administration

3. Preventing conversion of T4→ T3

- Propythiouracil
- Dexa 1-2 mg IV q 6 hr
- Hydrocortisone
  - 100 mg iv q 8h
  - Use when patient hypotensive to treat possible concomitant adrenal insufficiency

Thai guideline : Dexamethasone 8-12 mg/day or other steroids for 3-4 days in any patient with thyroid crisis

4. Controlling adrenergic symptoms

- Beta-adrenergic blockade
- Propranolol
  - 60-80 mg po q 4-6 h
  - Reactive airway disease: metoprolol, atenolol (β1 selective) แต่ยังต้องระวัง
  - Severe asthma / B-blocker contraindicated: CCB เช่น diltiazem 30 mg po q 8 hr
  - Caution in CHF, long standing hyperthyroidism

5.Supportive treatment

- Antipyretics : acetaminophen is preferable
- External cooling
- Rehydration
- Look for concealed infection, not use empirical antimicrobial

Subacute painful thyroiditis

- Painful, tender goiter
- Fever, malaise, myalgia and history of upper respiratory tract infection
- Transient hyperthyroidism followed by transient hypothyroidism
- Ix : low RAIU, increase ESR
- Rx : NSAIDs, steroid (in severe case)

Painless lymphocytic thyroiditis (postpartum thyroiditis)

- Self-limiting disease
- Most common in postpartum period
- Classically presents with triphasic pattern of thyroid function
  - Initial hyperthyroid phase
  - Hypothyroid phase
  - Recovery of normal thyroid function
- Rx
  - Hyperthyroid phase : beta-blocker
  - Hypothyroid phase : temporary thyroid hormone replacement

Hypothyroidism

- Congenital
- Acquired hypothyroidism
  - Acquired primary hypothyroid
    - Hashimoto's thyroiditis
    - Post iodine ablation, surgery
    - Iodine deficiency
    - Infiltration : hemochromatosis, amyloidosis
  - Acquired secondary hypothyroid

Clinical features

- Symptoms
  - Diminished sweating
  - Constipation
  - Paresthesia
  - Hoarseness
  - Weight increase
  - Dry skin
- Signs
  - Slow movement
  - Periorbital puffiness
  - Delayed ankle reflex
  - Coarse skin,Cold skin
  - Thyroid gland

Atypical manifestration
-Hypothermia
-heart failure
-pleural effusion
-ileus, pseudoobstruction
-neuro: depression, psychosis, ataxia, seizure, coma, dementia

Laboratory

- Hypercholesterolemia
- Hyponatremia
- Anemia : normochromic normocytic anemia, pernicious anemia
- Hyperprolactinemia
- Hypoglycemia
- Elevated CPK
- Hyperhomocysteinemia

Hashimoto's thyroiditis

- Most T cell lymphocyte → apoptosis
- Transient thyrotoxicosis → hypothyroidism (Hashitoxicosis)
- May be associated with polyendocrine failure syndrome ex. Adrenal insufficiency, type 1 DM
- Associated with other autoimmune : vitiligo, atrophic gastritis, pernicious anemia, systemic sclerosis, Sjogren's syndrome

Hashimoto's thyroiditis : investigation

- Antithyroglobulin and Antimicrosomal (antiperoxidase) Ab
  - Autoimmune thyroid disease
  - High titer positive, 90%

Hypothyroidism : management

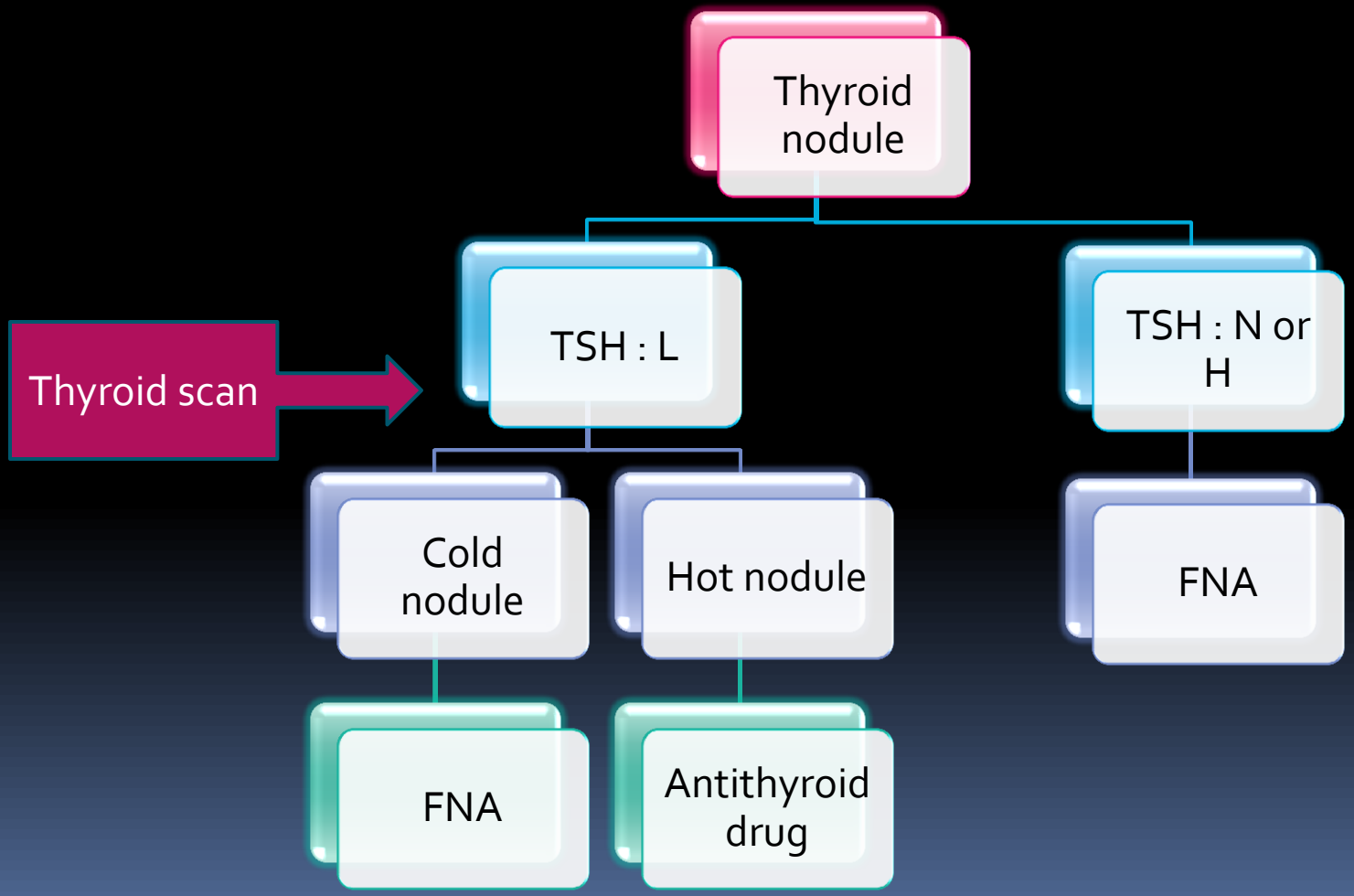
- Subclinical hypothyroidism
  - If TSH 5-10 (no symptom) : follow up
  - If TSH 5-10 (symptom) or > 10 : start levothyroxine
- Hypothyroidism
  - Start levothyroxine
- Target : keep normal FT_4 and TSH < 5
- Starting dose
  - Elderly, CAD, severe hypothyroid : 12.5-25 ug/day
  - Young : 25-50 ug/day

Single thyroid nodule

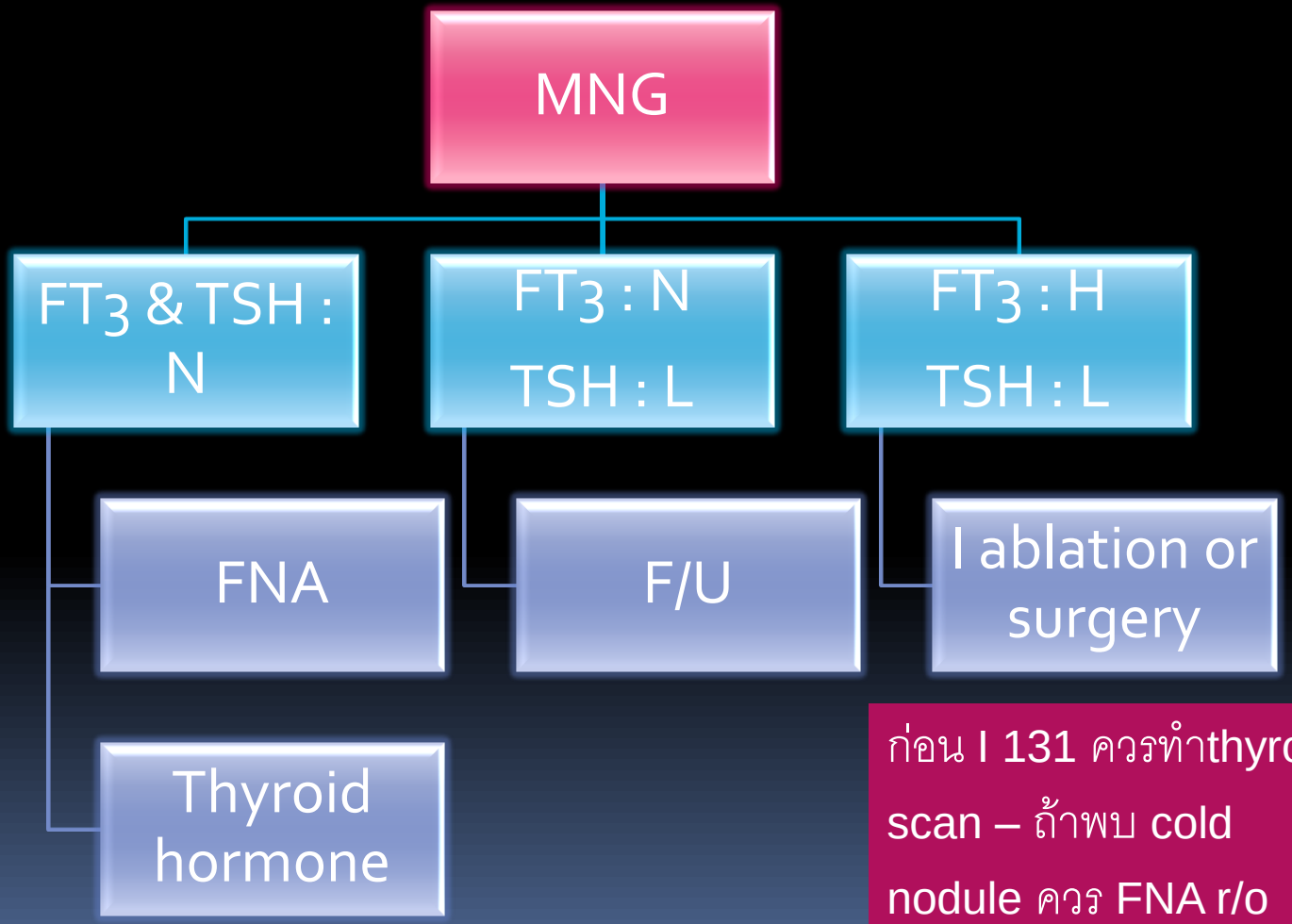
- Evaluation : malignancy?
  - History : ก้อนโตเร็ว กดอวัยวะข้างเคียง
  - Physical examination : แข็งมาก ติดอวัยวะข้างเคียง ต่อมน้ำเหลืองที่คอโต
  - Risk
    - Age < 20y, >60y
    - Male
    - History of radiation at head and neck area
    - Positive family history thyroid cancer

Single thyroid nodule

Thyroid nodule ควรทำ Ultrasound thyroid ทุกราย



Multinodular goiter



ก่อน I 131 ควรทำthyroid scan – ถ้าพบ cold nodule ควร FNA r/o malignancy ก่อน

Nonthyroidal illness

FT_3	FT_4	TSH	Note
ต่ำ	สูง		Early or mild illness
ต่ำ	ปกติ		Most common
	ต่ำ	ต่ำ	Severe illness
	ต่ำ	สูง (มักไม่เกิน 20)	Recovery phase

- Any acute, severe illness
- Absence of thyroid disease
- Rx: observe, repeat TFT after recovery from illness → normalization