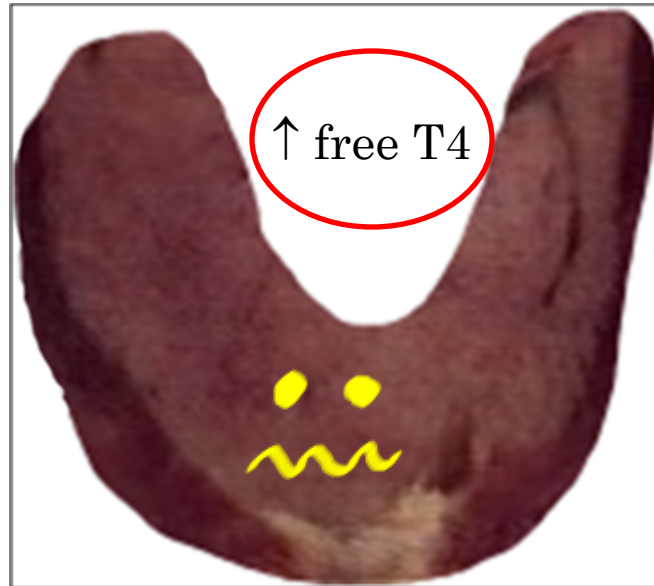


Hyperthyroidism, Inflammatory Disorders



Howard J. Sachs, MD

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Hyperthyroidism, Inflammatory Disorders



The total T4 may be elevated
in pregnancy and with OCP use

Graves



Thyroiditis

1. Lymphocytic
2. (Silent)
3. Postpartum

1. Granulomatous
2. (Painful)
3. Viral



Nodules, Hot

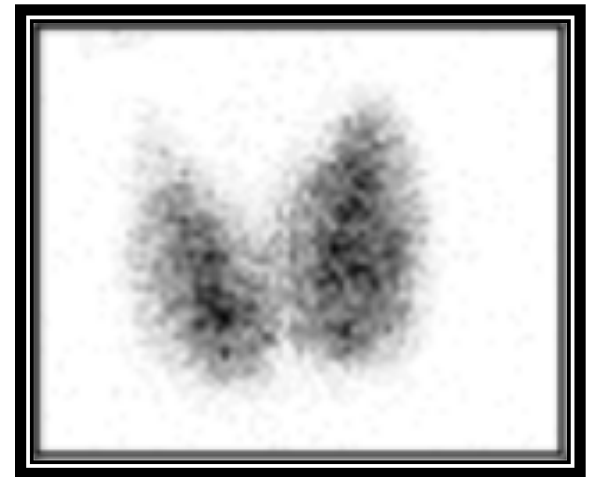
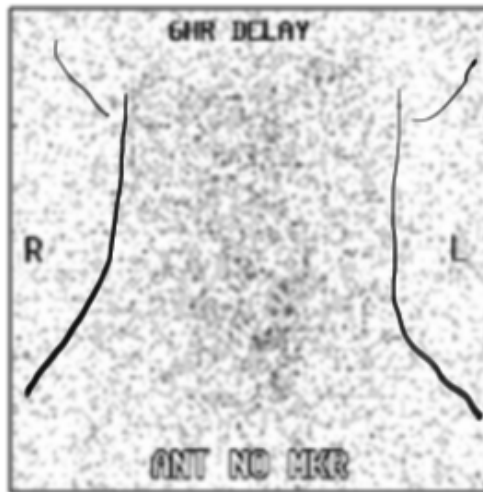


Thyroiditis

Graves



I¹²³



Key Point I

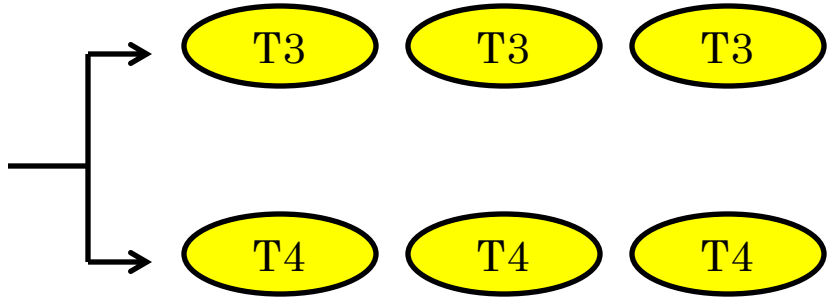
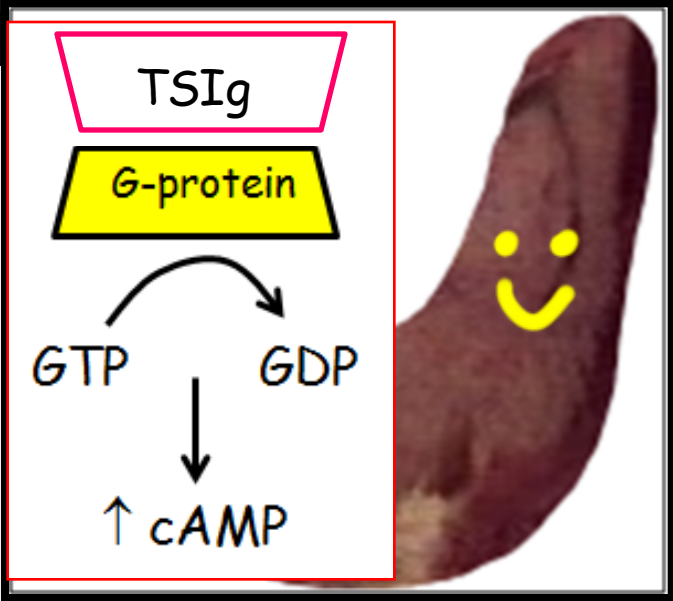
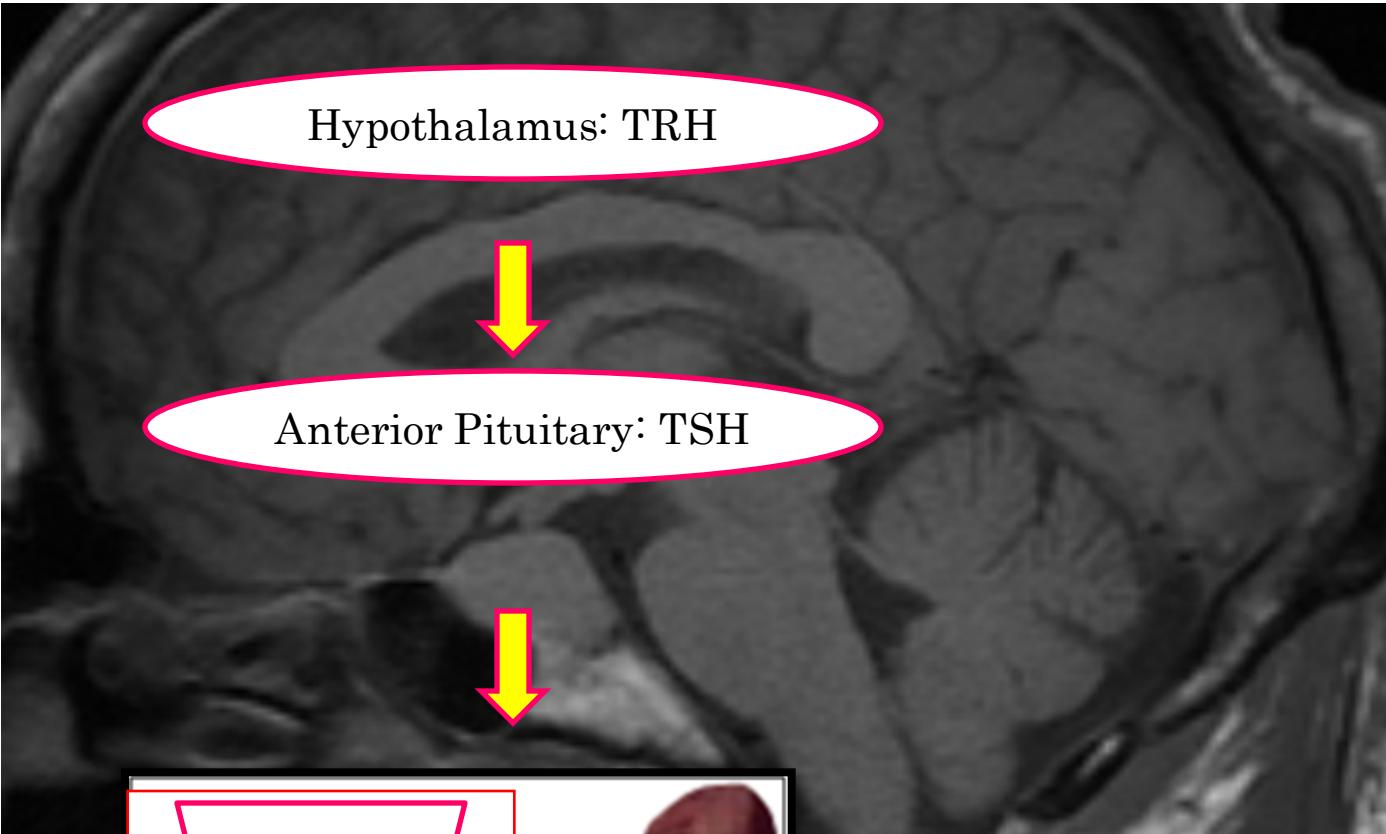
Language of hyperthyroidism

Basal Metabolic Rate	Matrix	β -Adrenoreceptor
Heat Intolerance Weight Loss Hyperreflexia Diarrhea Anxiety	Ophthalmopathy Dermatopathy Sweaty skin Hair thinning	Lid lag Dysrhythmia Palpitation Tremor Osteoporosis

Key Point II

Ophthalmopathy = Graves





~~Hypothalamus: TRH~~

~~Anterior Pituitary: TSH~~

Low TSH

↑ T4

TsIg

G-protein

GTP

GDP

↑ cAMP

T3

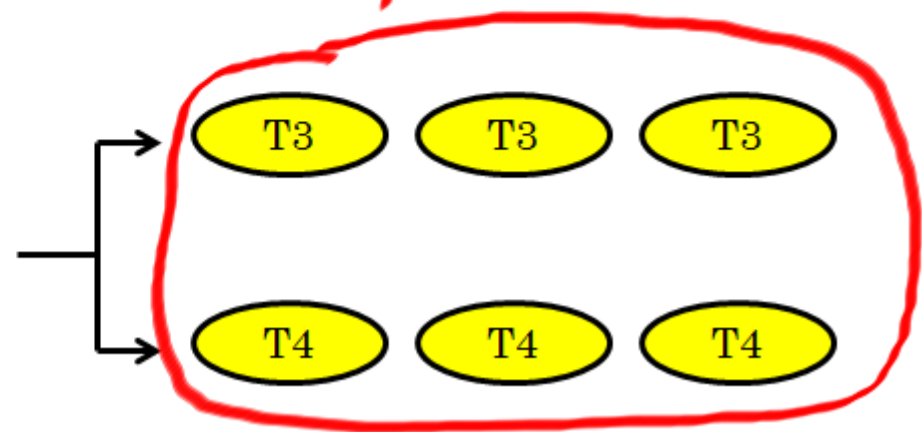
T3

T3

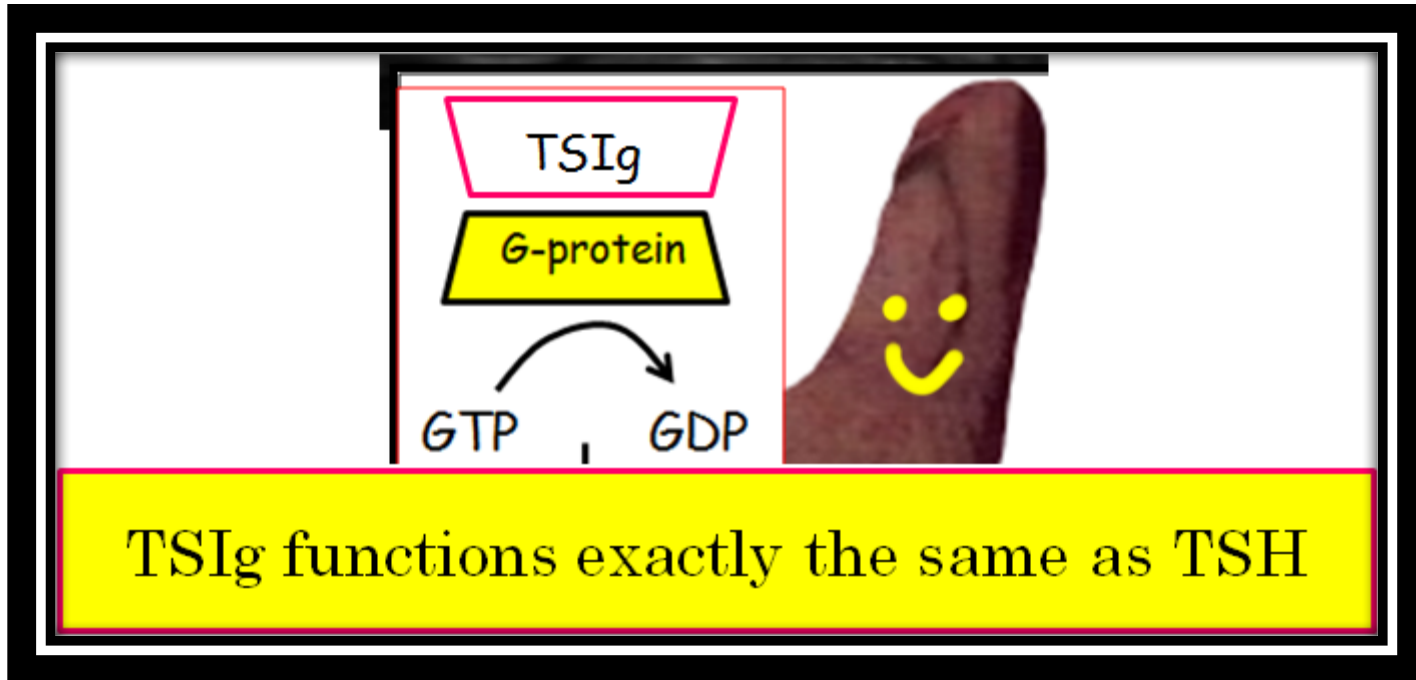
T4

T4

T4



Key Point III



Type II Hypersensitivity (against fixed tissue antigen)



Hypothalamus: TRH

Anterior Pituitary: TSH

Rare condition but nice to reason it out:

High fT4
High TSH
Low TRH

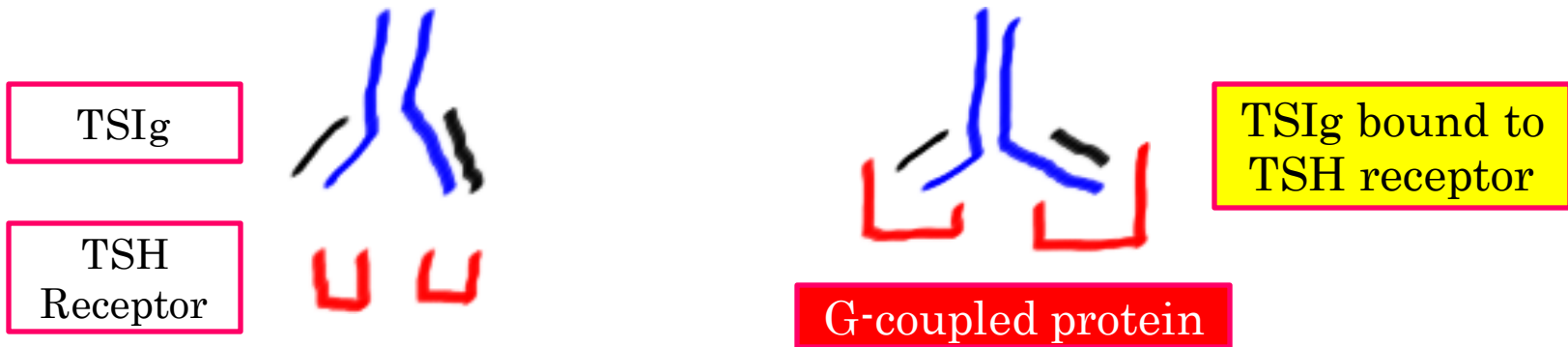
Secondary Hyperthyroidism, TSH secreting adenoma



Graves Disease

(Triad: thyroid, eye, skin)

- Background
 - Autoimmune disorder : Hallmark is the production of antibody against the TSH receptor (TSI – thyroid stimulating immunoglobulin)



Graves Disease

(Triad: thyroid, eye, skin)

- Pathogenesis
 - Autoantibody binds to and stimulates TSH receptor
 - Activated T cells secrete cytokines that stimulate fibroblast proliferation and synthesis of extracellular matrix proteins



Graves Disease

(Triad: thyroid, eye, skin)

Key Point IV

T cells secrete cytokines



Graves Disease

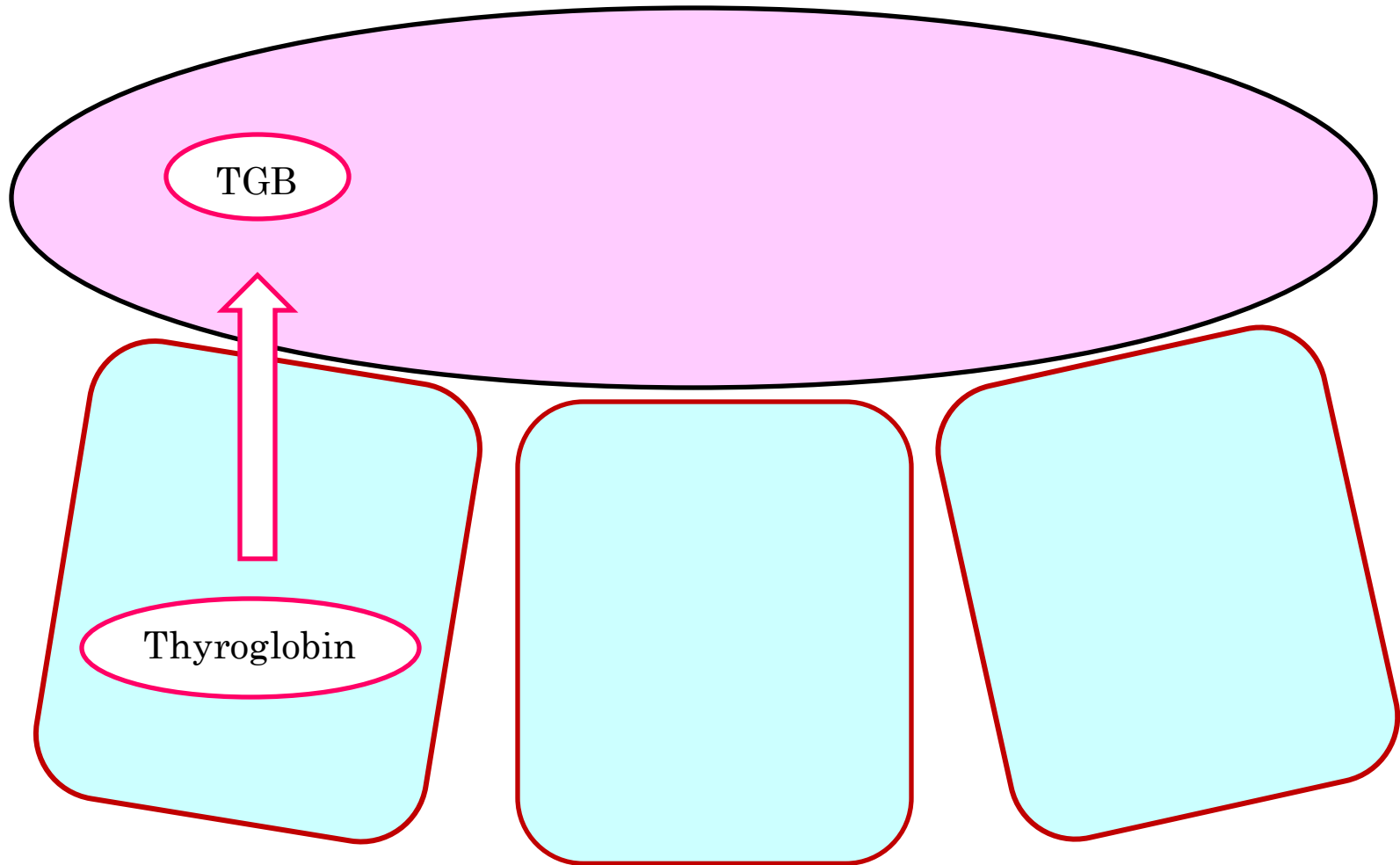
(**Triad**: thyroid, eye, skin)

- **Pathology**
 - Diffuse hypertrophy/-plasia of follicular epithelial cells with crowding of follicles

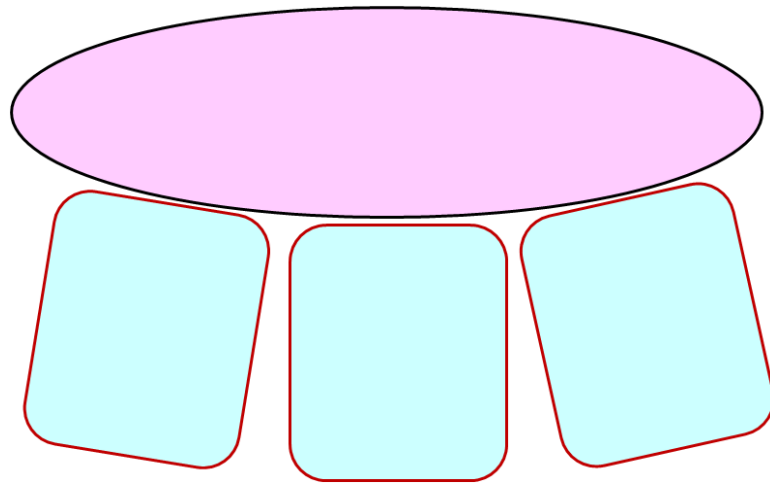
TSH is a **trophic** hormone.

Key Point V

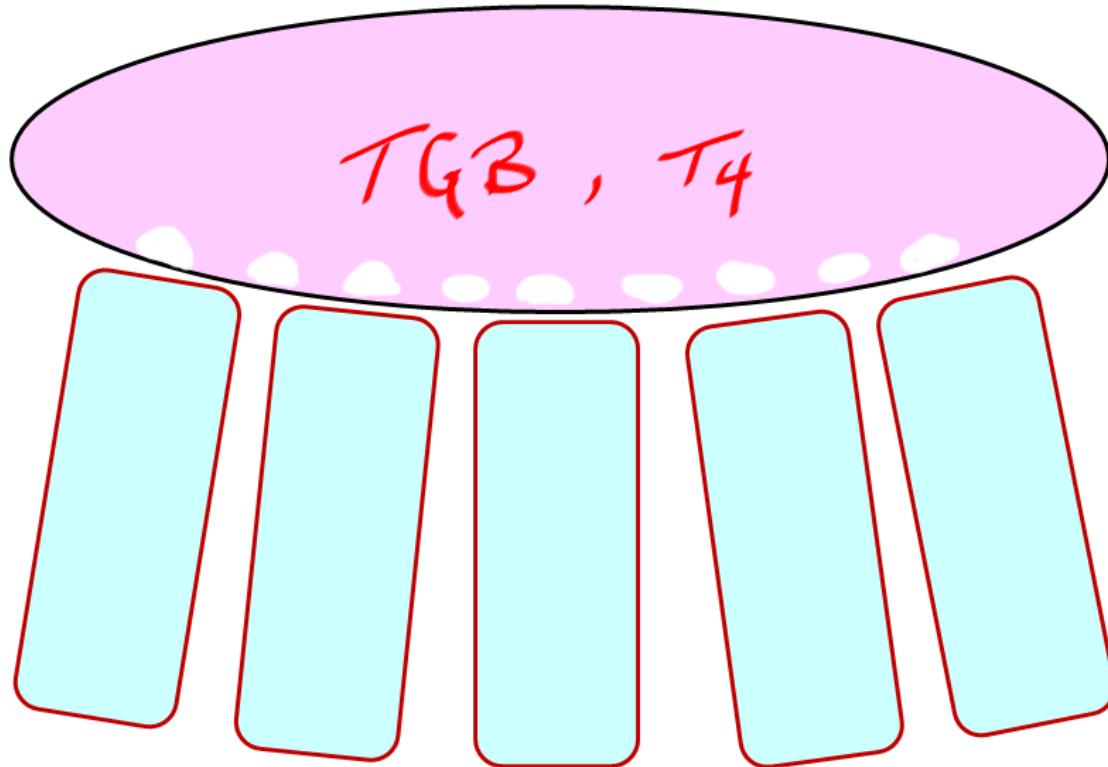
Thyroid follicular lumen filled with colloid

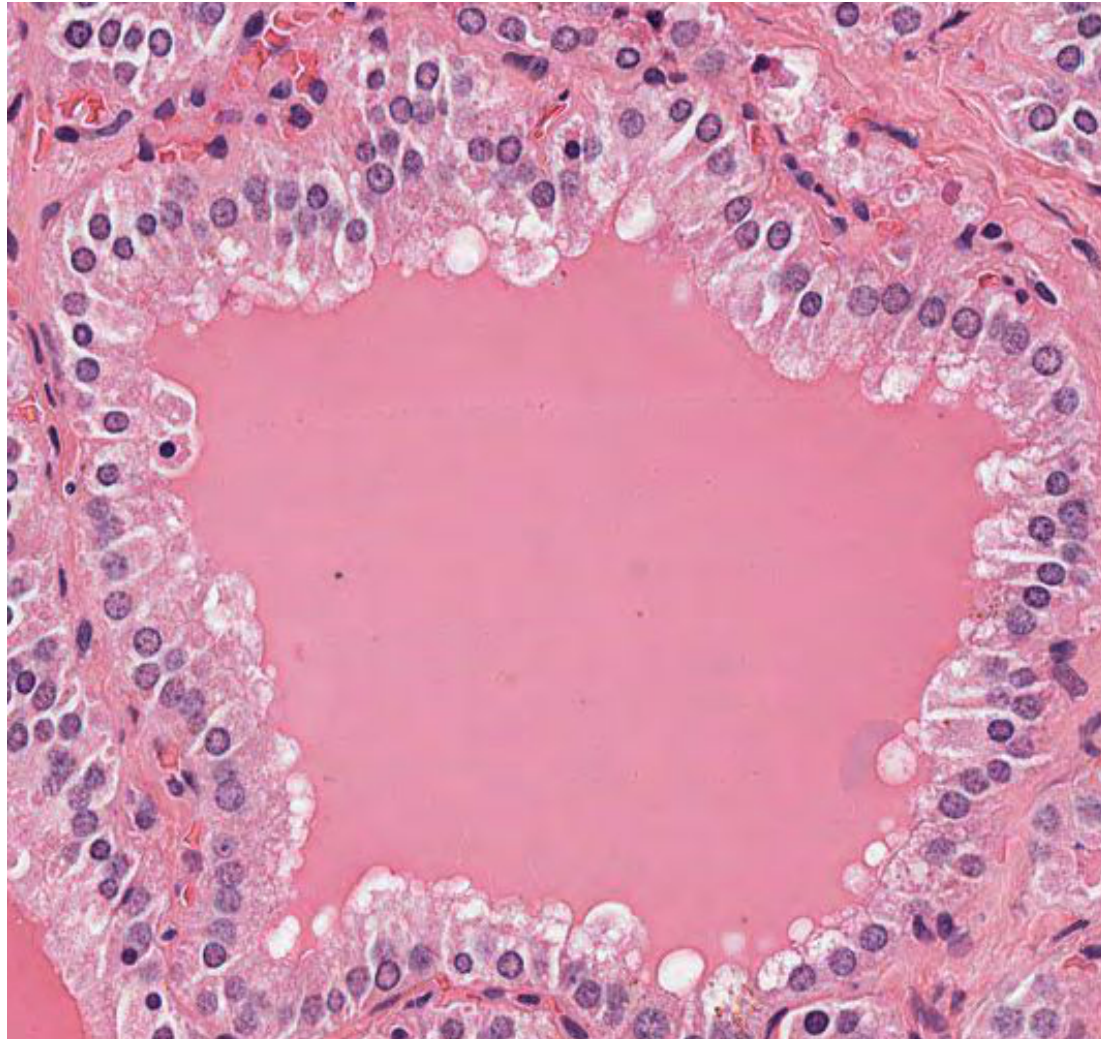


Healthy, cuboidal epithelium



Follicular crowding, hyperplasia, 'scalloping'





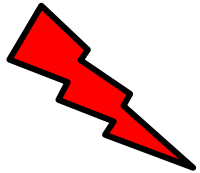
Follicular Crowding
Epithelial hyperplasia
Scalloping

Graves Disease

(Triad: thyroid, eye, skin)

- Pathology

– Ophthalmopathy, **infiltration** by:



Cytokines



Cytokines

Graves Disease

(**Triad**: thyroid, eye, skin)

- Pathology

- T-cell infiltrate PLUS **B-cells/plasma cells**
 - **Germinal centers** are common.

Germinal Centers: **Hashimoto**/Lymphocytic and Graves

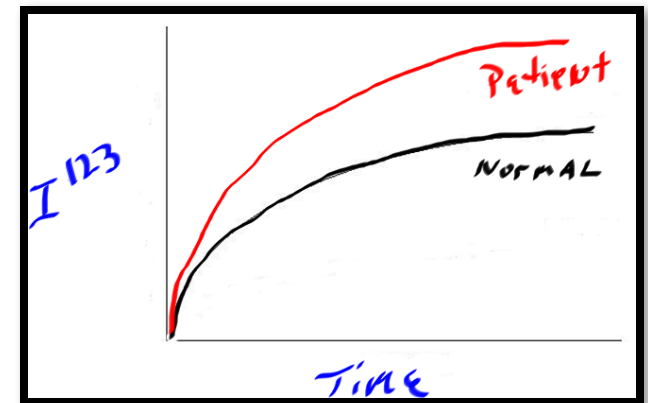
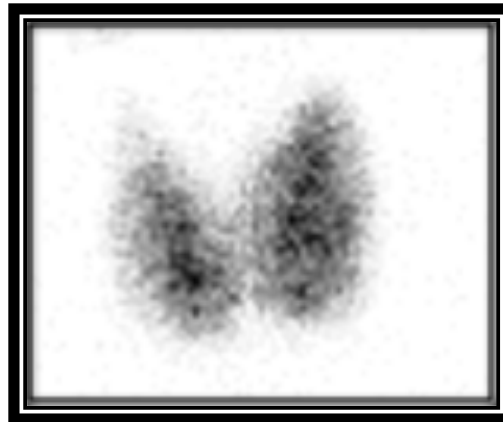
Graves Disease

- Clinical: s/s \uparrow T₄
 - Diffuse glandular enlargement (bruit?)
 - **Exophthalmos**
 - **Dermatopathy**: pretibial myxedema

Graves Disease

- Clinical: s/s \uparrow T₄
 - Diffuse glandular enlargement (bruit?)
 - Exophthalmos
 - Dermopathy: pretibial myxedema
- Diagnostics
 - TSH (low), free T₄ (elevated), Thyroglobulin (elevated)
 - TSIg (+)
 - Nuclear scan: diffuse uptake (excluding the dx of thyroiditis)

Radiolabeled I¹²³



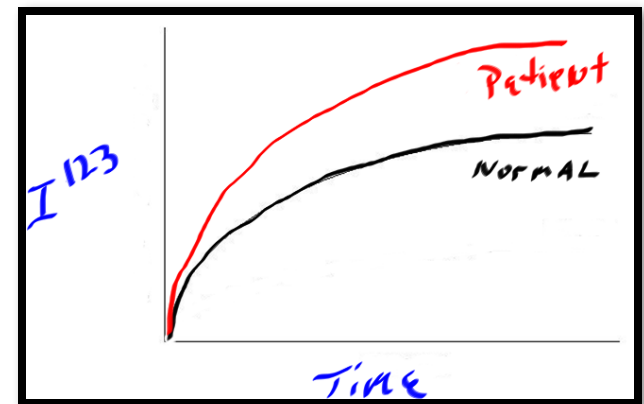
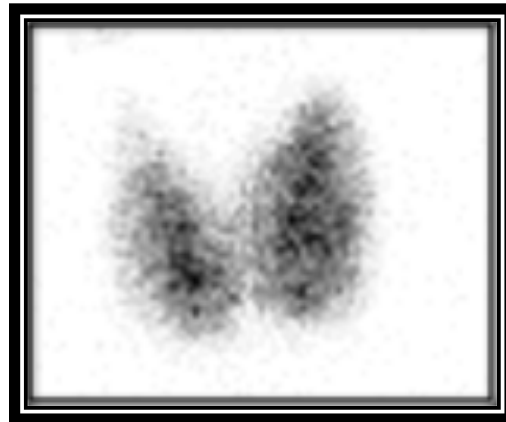
Graves Disease

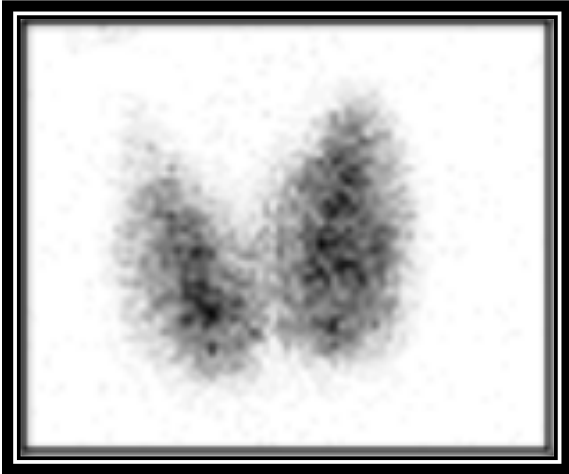
Diagnostics

- TSH (low), free T4 (elevated), Thyroglobulin (elevated)
- TSIg (+)
- Nuclear scan: diffuse uptake (c/w thyroiditis)

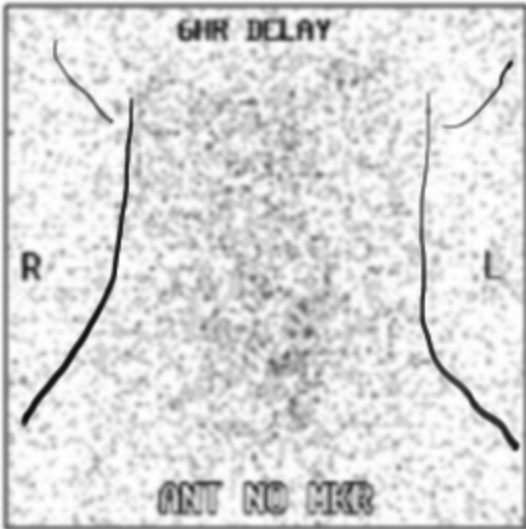
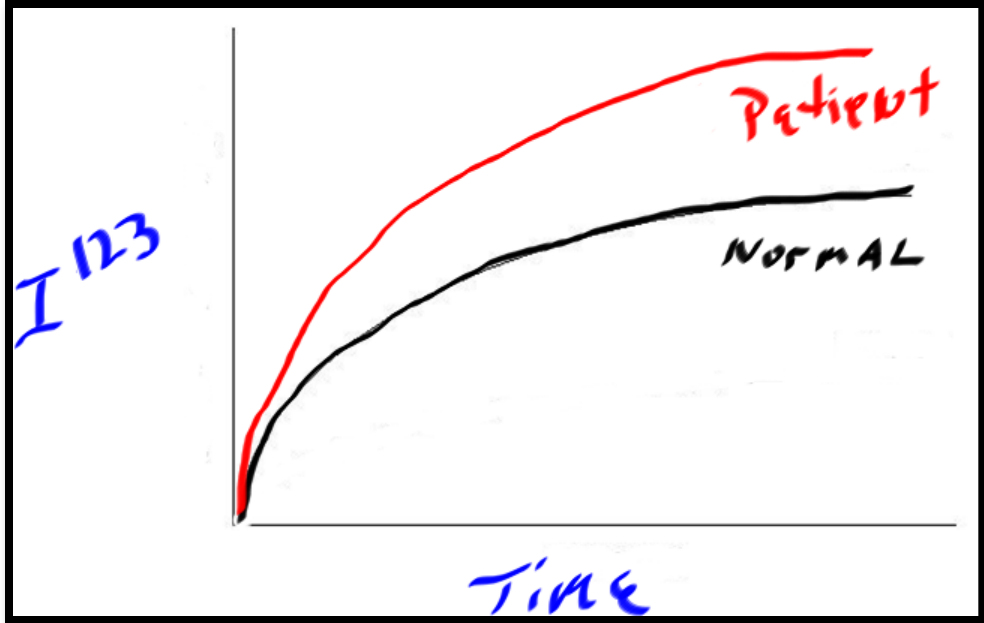
Key Point VI

Radiolabeled I^{123}





c/w Thyroiditis



Graves Disease

- Treatment
 - Meds: Thionamines – PTU, Methimazole; **BETA-BLOCKERS**
 - Radiation: I^{131}
 - Surgery (if compressive)
 - Eyes: Glucocorticoids (thionamines don't work)

T cells secrete cytokines



Pop Quiz: Great Question!

Key **pathologic** similarities and differences between Graves and a TSH secreting adenoma?

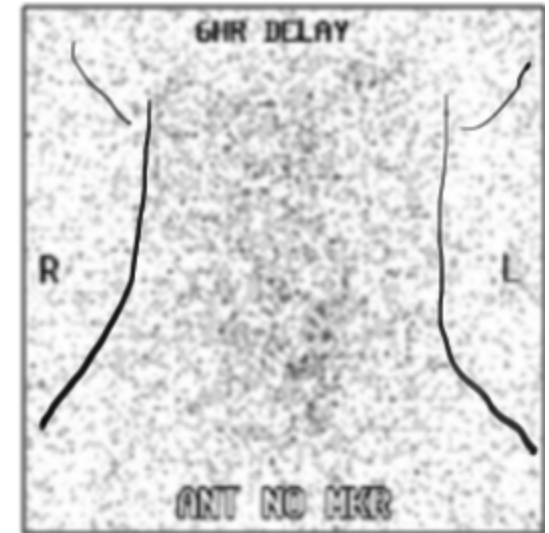
Similar: Both exhibit changes of trophism (hypertrophy, hyperplasia, scalloping)

Difference: adenoma does not elaborate cytokines so no infiltrative or inflammatory pathology.

Thyroiditis

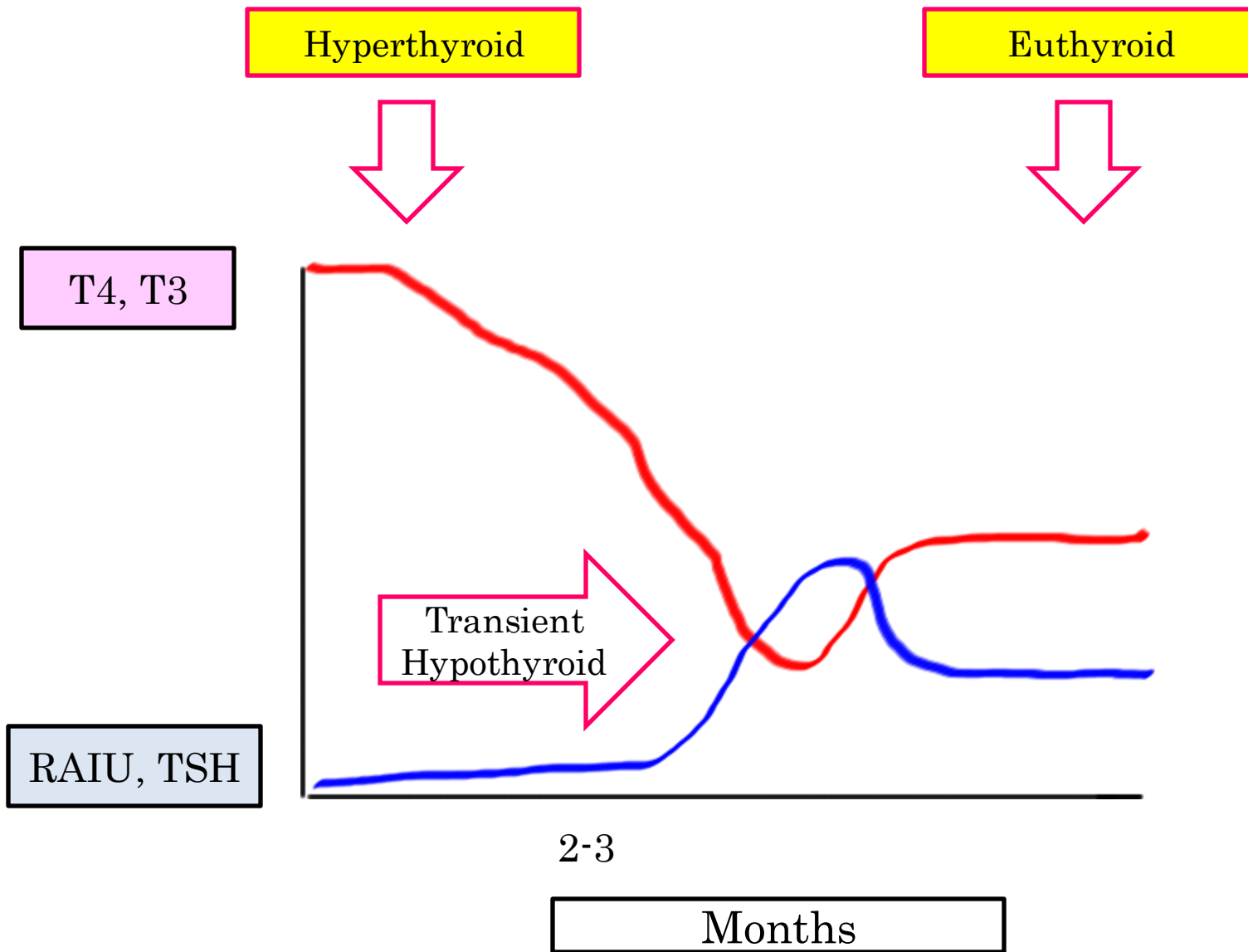
1. Lymphocytic
2. (Silent)
3. Postpartum

1. Granulomatous
2. (Painful)
3. Viral



Capillary

Capillary



Hyperthyroid



Euthyroid



T4, T3

Key Point VII

The patient with granulomatous (viral) thyroiditis recovers and the story ends.

The patient with lymphocytic thyroiditis **may** have recurrent pattern of injury and go on to develop hypothyroidism. These patients are identified by the presence of autoantibodies.

Lymphocytic (Painless/Silent) Thyroiditis

Disclaimer:

- A relatively indistinct entity (not listed in First Aid).
- Included as an autoimmune thyroid disorder that has overlapping features with Hashimoto's (Hashitoxicosis) and Postpartum Thyroiditis.
- No excitement compared with Graves and Granulomatous

Lymphocytic (Painless/Silent) Thyroiditis

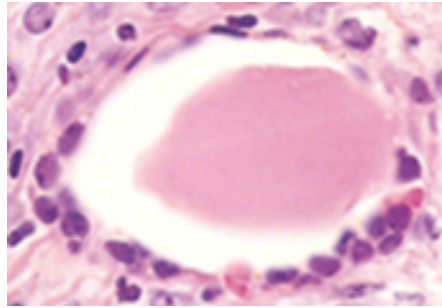
- Background
 - Present as hyperthyroidism BUT can progress to hypothyroidism
- Pathogenesis
 - Considered a variant of Hashimoto's [i.e. pathologic and serologic (autoantibody) similarities].
- Pathology
 - May resemble Hashimoto's w/ lymphocytic infiltration and large germinal centers
 - No fibrosis or Hurthle cell metaplasia

Lymphocytic (Painless/Silent) Thyroiditis

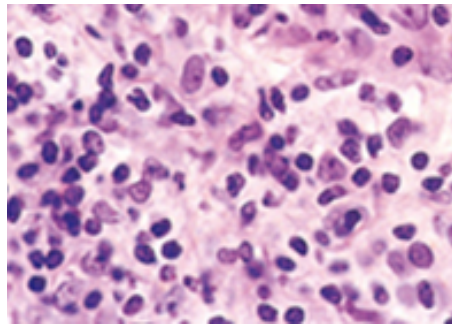
- Clinical
 - s/s thyroid dysfunction (mild)
 - Mild glandular enlargement may be present prompting serologic testing.
- Diagnostics
 - Mild hyperthyroidism (TSH suppressed, T4 elevated)
 - Autoantibodies present (TPO, TGB)

Granulomatous (Painful, DeQuervain) Thyroiditis

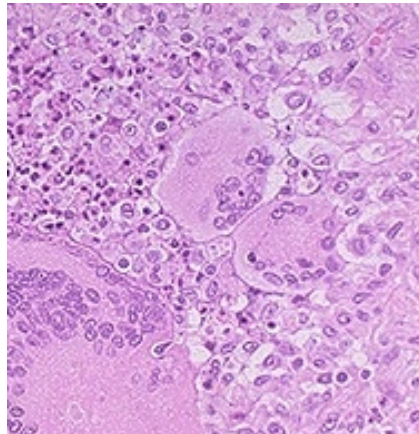
- Background
 - “Doc, I have a sore throat.” On exam, the soreness is observed in the form of a large, focally tender thyroid gland.
- Pathogenesis
 - Triggered by an antecedent viral infection with stimulation of cytotoxic T cells against thyroid antigens
 - Since it is initiated by a viral infection, it is NOT progressive (i.e. self limited)
- Pathology
 - Early: PMN, microabscesses
 - Late: lymphocytic infiltrate, activated MΦ (Giant Cells), and follicle loss with limited fibrosis



Follicular atrophy



Inflammatory
Infiltrate



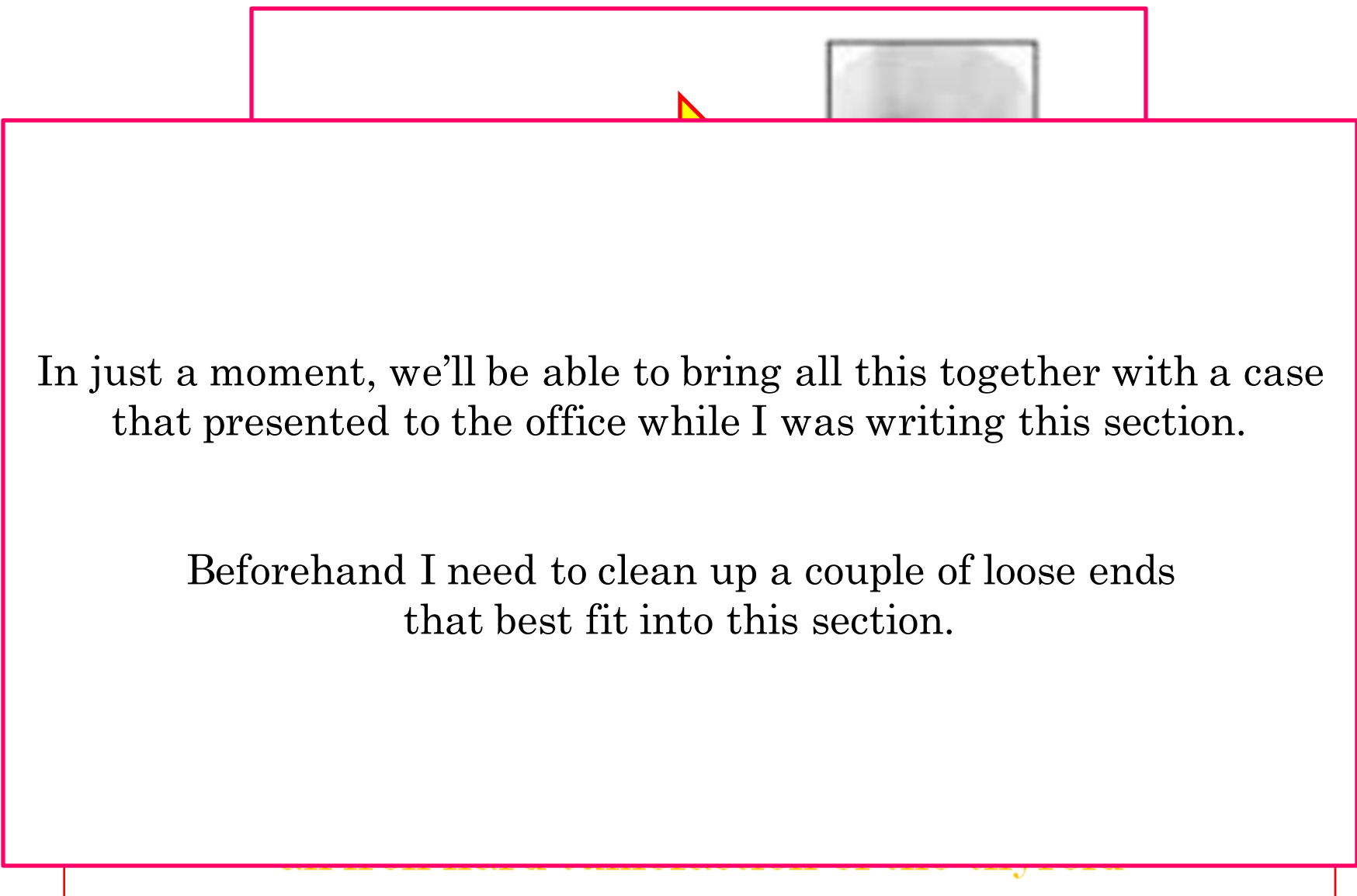
Multinucleate
Giant Cell

Key Point VIII

Granulomatous (Painful, DeQuervain) Thyroiditis

- Clinical
 - s/s of hyperthyroidism; they might express a viral prodrome
 - PE: Enlarged, tender gland
 - Inflamed phase is **transient** (2-6 weeks)
- Diagnostics
 - Initial hyperthyroid (low TSH, hi T4)
 - Radionuclide scan: **decreased uptake**
 - Elevated **ESR**
- Treatment
 - ASA/NSAIDs
 - Beta-blocker if necessary

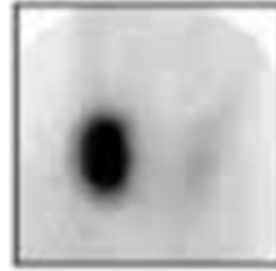
Viral Infection: no abx (TSI, TPO)



In just a moment, we'll be able to bring all this together with a case that presented to the office while I was writing this section.

Beforehand I need to clean up a couple of loose ends that best fit into this section.

Hot Nodule



Low TSH, high T4; (+) Nodule; (+) RAIU scan

Riedel's Thyroiditis

‘an iron hard tumefaction of the thyroid’

Riedel's Thyroiditis

'an iron hard tumefaction of the thyroid'

Disclaimer:

Rarely a question; commonly pathology included as a distractor

Riedel's Thyroiditis

‘an iron hard tumefaction of the thyroid’

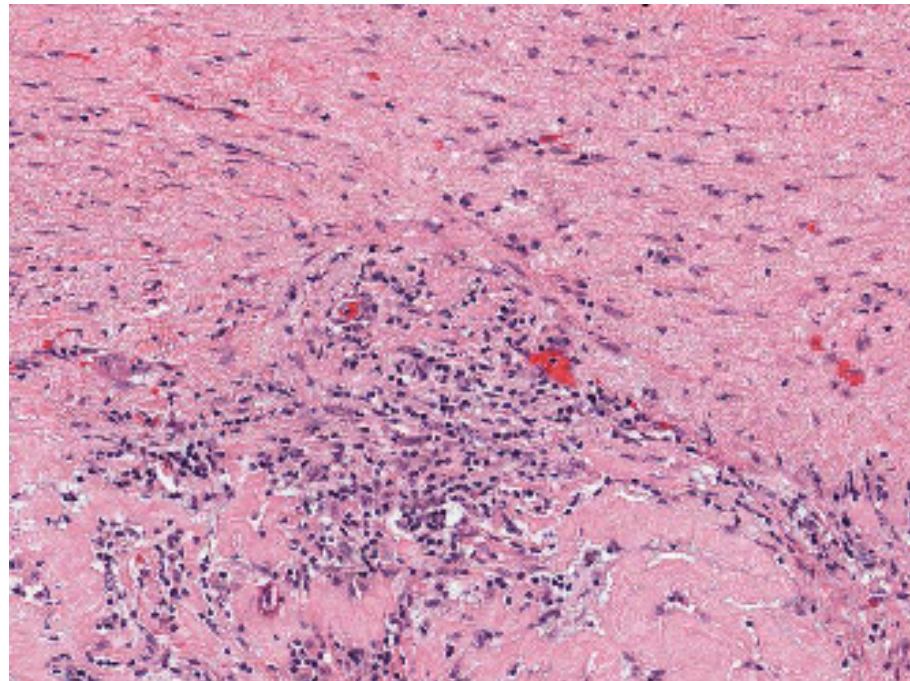
- Background
 - Characterized by painless yet **extensive fibrosis** involving the neck AND surrounding structures
 - Can be so extensive as to cause hypoparathyroidism
 - Given the firmness, Riedel's will mimic malignancy
- Pathogenesis - FYI
 - IgG4-related disease
 - Fibrosis and tissue infiltration by plasma cells producing IgG4
 - May be associated with other sclerosing conditions
 - Retroperitoneum, mediastinum

Riedel's Thyroiditis

'an iron hard tumefaction of the thyroid'

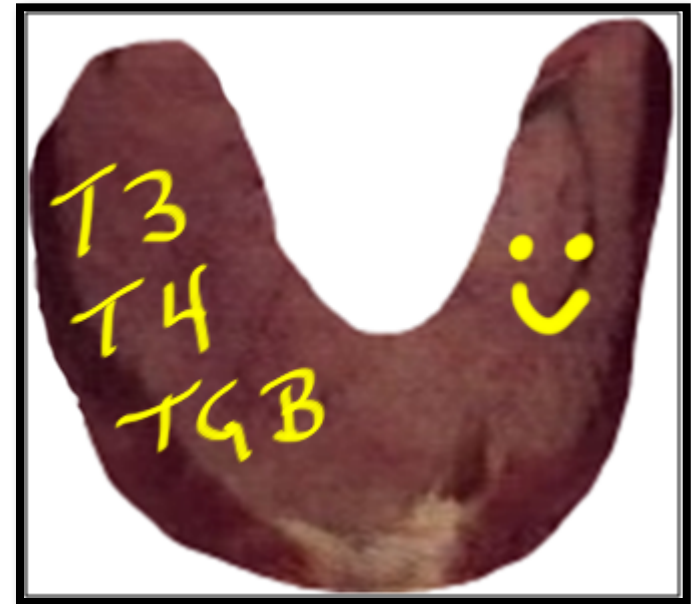
- Pathology

- Dense collagenous fibrous tissue with mononuclear inflammatory infiltrate
- Extends beyond capsule



Key Material Covered

- ✓ Physiology
 - ✓ TSH, TSIg
- ✓ Pathology
 - ✓ Graves
 - ✓ Granulomatous thyroiditis
 - ✓ Germinal Centers
 - ✓ Riedel's
- ✓ Clinical
 - ✓ Progressive v self-limited
- ✓ Diagnostics
 - ✓ RAIU scan
 - ✓ Thyroglobulin
- ✓ Language
 - ✓ Ophthalmopathy v Lid Lag

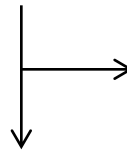


Patient presents with involuntary weight loss, loose stools and tremulousness. No viral prodrome reported.

PE: HR 108 and regular; (+) lid lag; 4 (+) reflexes;

Thyroid – nontender, mildly enlarged

Test	Result	Flag	Reference
Free T4	3.21 ng/dL	H	0.58-1.64
Thyroid Stimulating Hormone	0.14 uIU/mL	L	0.28-3.89

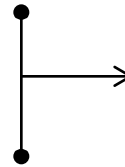


Labs: TSI, anti-TGB, anti-TPO, Thyroglobulin (quantitative)

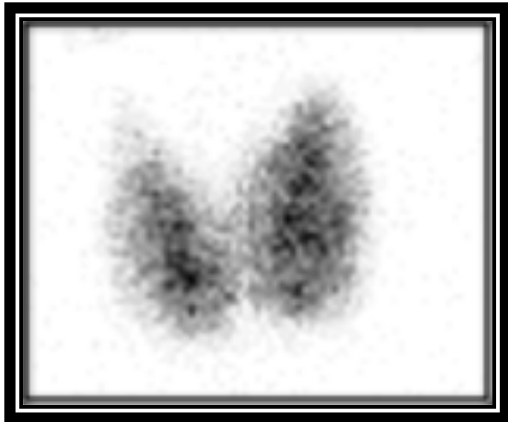
Propranolol LA 60 mg daily

Radioactive Iodide Uptake is Ordered

Test	Result	Flag	Reference
Free T4	3.21 ng/dL	H	0.58-1.64
Thyroid Stimulating Hormone	0.14 uIU/mL	L	0.28-3.89



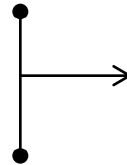
Labs: TSI, anti-TGB, anti-TPO, Thyroglobulin (quantitative)



Graves

Test	Result	Flag	Reference
Ordering Physician: SACHS, HOWARD			
THYROID STIMULATING IMMUNOGLOB	376	H	<140

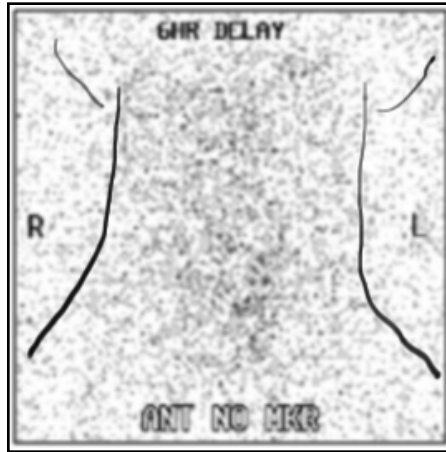
Test	Result	Flag	Reference
Free T4	3.21 ng/dL	H	0.58-1.64
Thyroid Stimulating Hormone	0.14 uIU/mL	L	0.28-3.89



Labs: TSI, anti-TGB, anti-TPO, Thyroglobulin (quantitative)

Aby (-), TGB

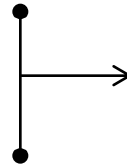
Granulomatous



Aby (+), TGB

Lymphocytic

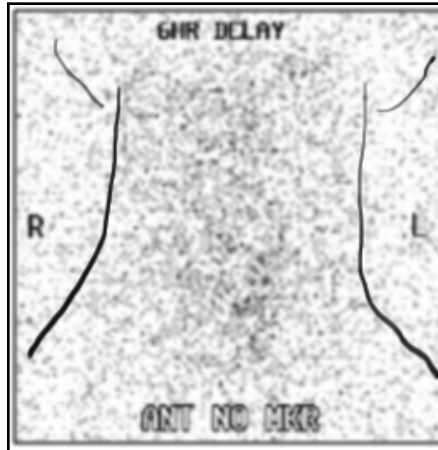
Test	Result	Flag	Reference
Free T4	3.21 ng/dL	H	0.58-1.64
Thyroid Stimulating Hormone	0.14 uIU/mL	L	0.28-3.89



Labs: TSI, anti-TGB, anti-TPO, Thyroglobulin (quantitative)

Aby (-), TGB

Granulomatous



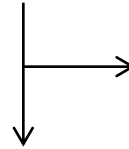
Aby (+), TGB

Lymphocytic

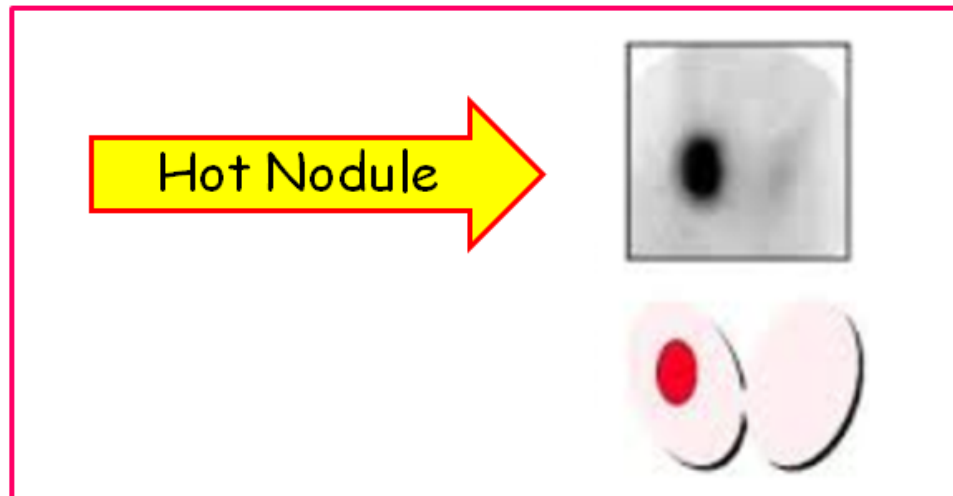
Aby (-), TGB (-)

Exogenous

Test	Result	Flag	Reference
Free T4	3.21 ng/dL	H	0.58-1.64
Thyroid Stimulating Hormone	0.14 uIU/mL	L	0.28-3.89

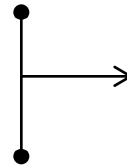


Labs: TSI, anti-TGB, anti-TPO,
Thyroglobulin (quantitative)

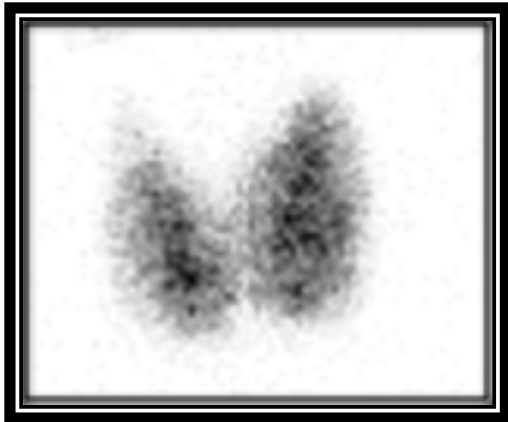


Low TSH, high T4; (+) Nodule; (+) RAIU scan

Test	Result	Flag	Reference
Free T4	3.21 ng/dL	H	0.58-1.64
Thyroid Stimulating Hormone	0.14 uIU/mL	L	0.28-3.89



Labs: TSI, anti-TGB, anti-TPO,
Thyroglobulin (quantitative)



Graves

Treatment of choice for
ocular involvement?

Glucocorticoids

Hyperthyroidism, Inflammatory Disorders

Graves

Lymphocytic

Granulomatous



Exogenous

Riedel's

Nodule, Hot

Howard J. Sachs, MD

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