

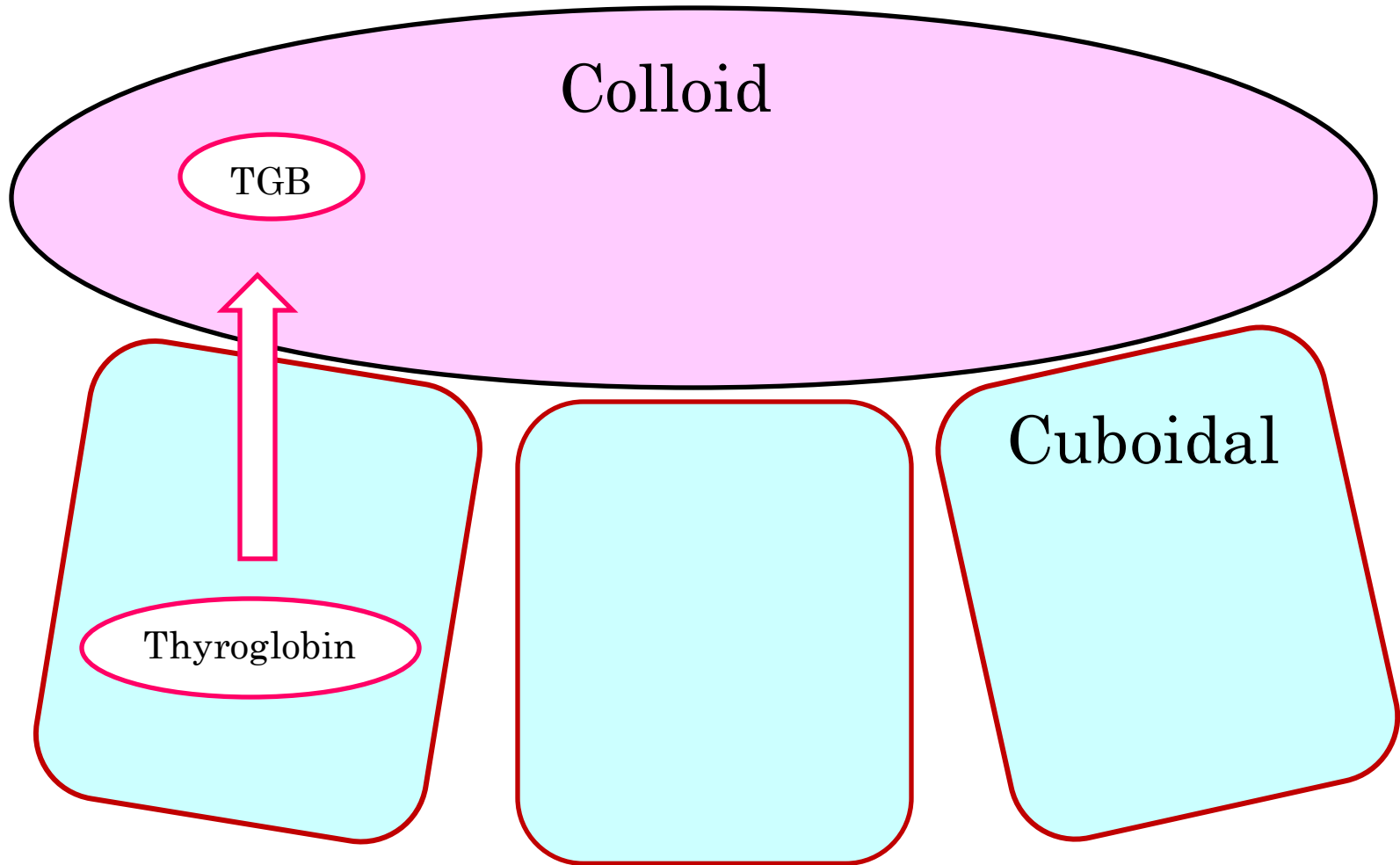
# Thyroid Hormone Synthesis, Regulation and Diagnostics



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[www.12daysinmarch.com](http://www.12daysinmarch.com)

Thyroid follicular lumen filled with colloid



Tyrosine-rich protein

**Initial Step:** Thyroglobulin (TGB) synthesized in ER of follicular cell

Thyroid follicular lumen filled with colloid

TGB

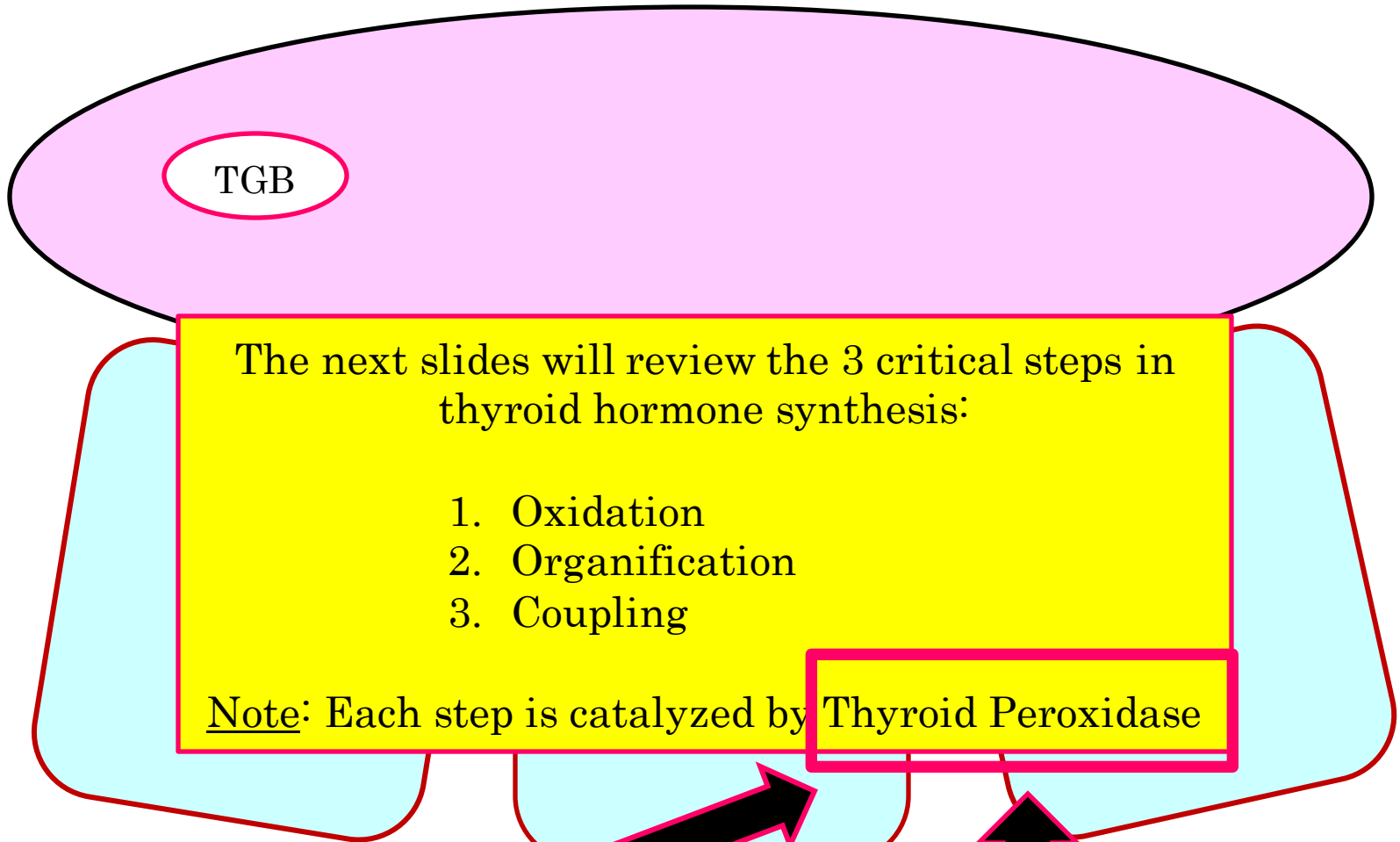
The next slides will review the 3 critical steps in thyroid hormone synthesis:

1. Oxidation
2. Organification
3. Coupling

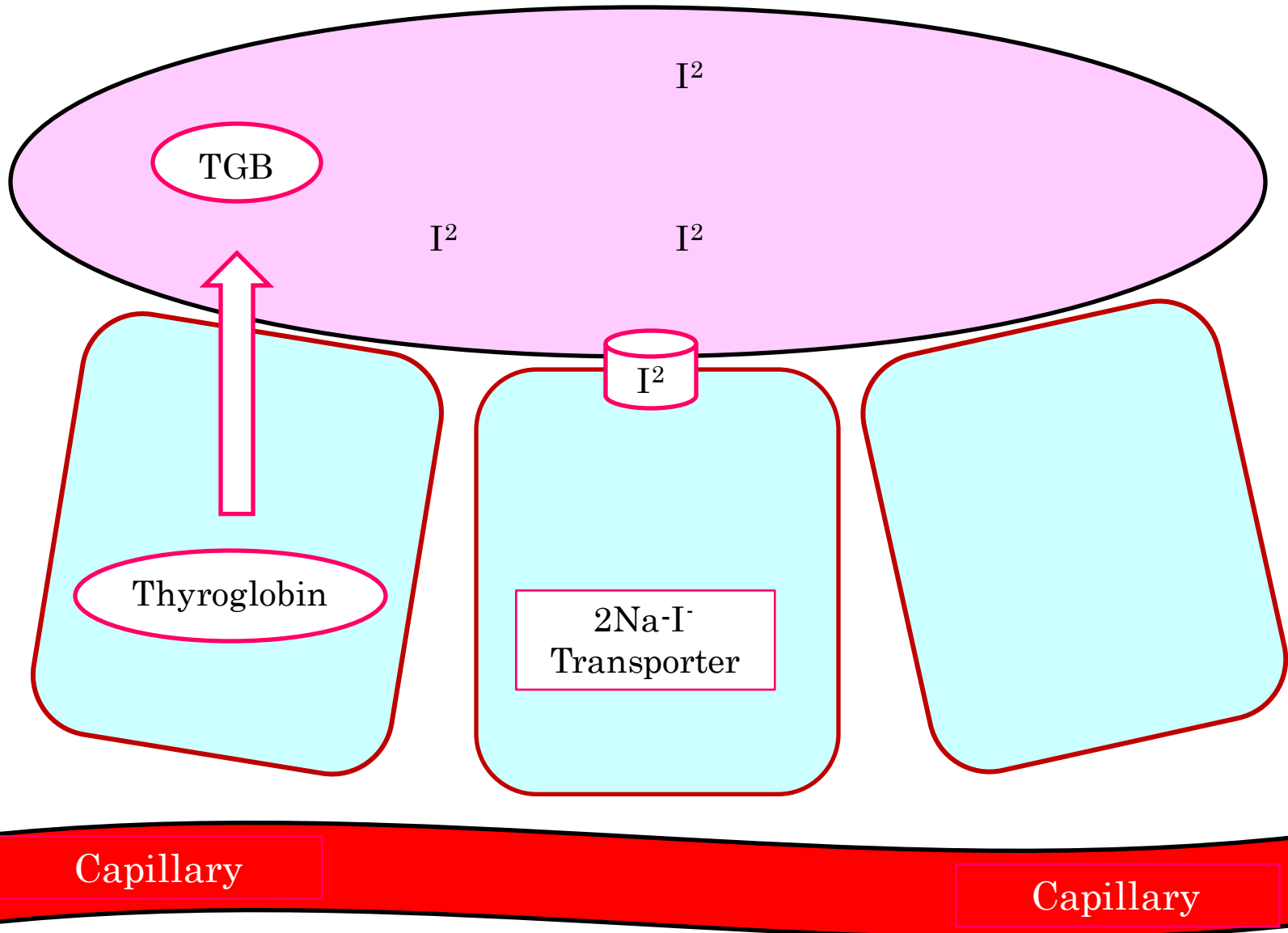
Note: Each step is catalyzed by Thyroid Peroxidase

Autoantibodies:  
Anti-TPO

Meds: PTU, MTZ

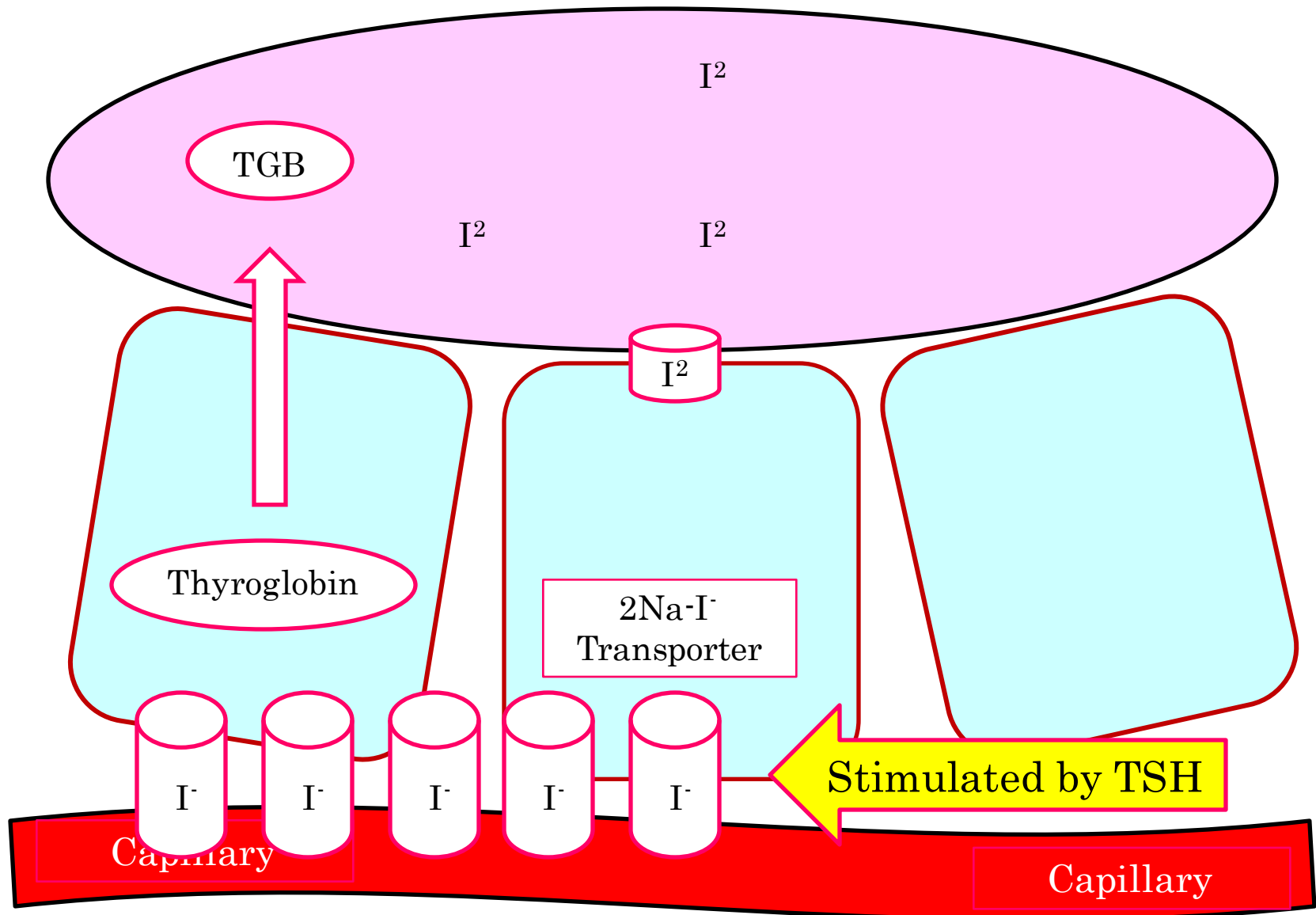


Oxidation ( $I^- \rightarrow I^2$ )



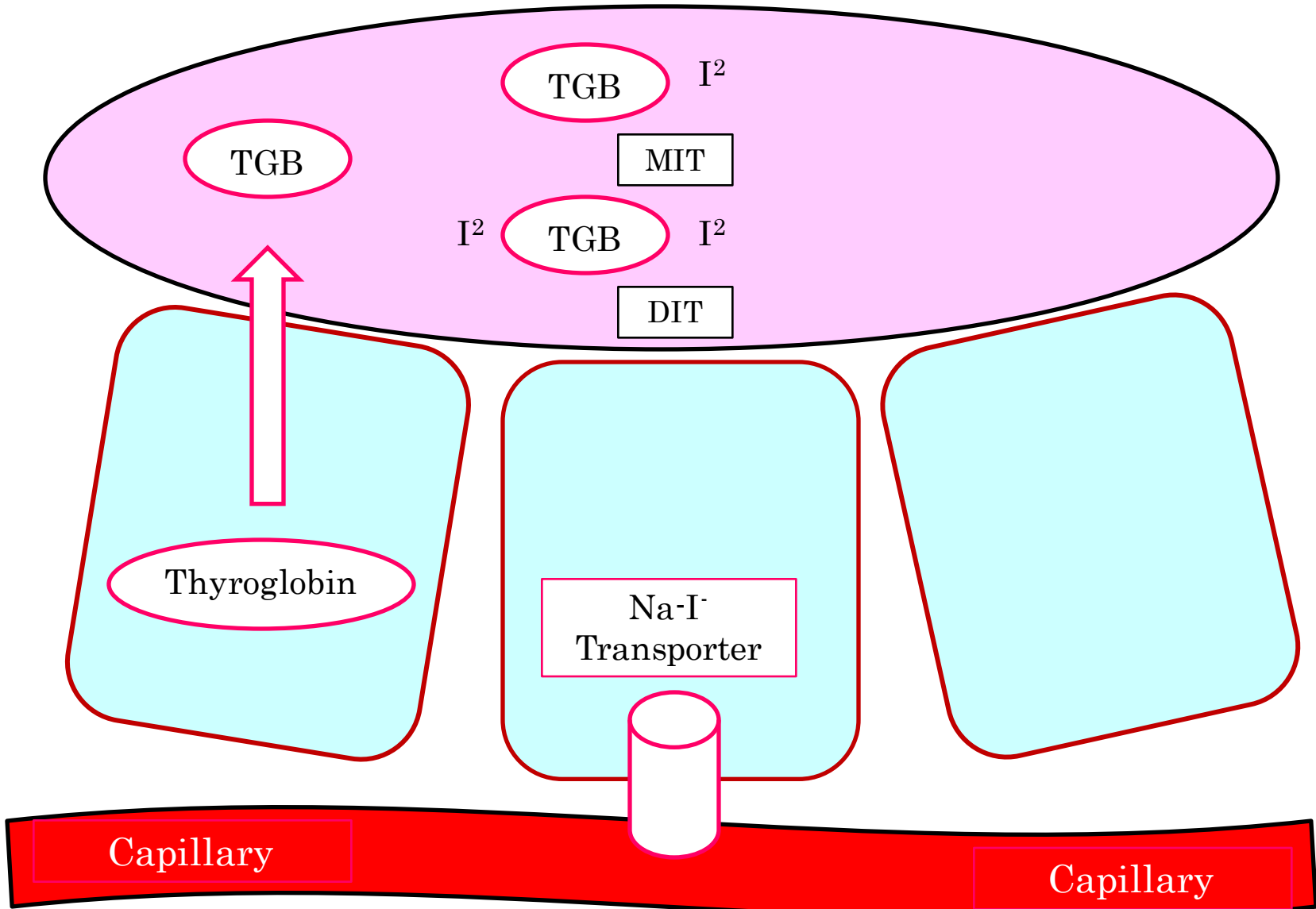
**Step One:** Iodide ( $I^-$ ) is absorbed in inverse proportion to serum concentration.  
Oxidized to Iodine ( $I^2$ )

Oxidation ( $I^- \rightarrow I^2$ )



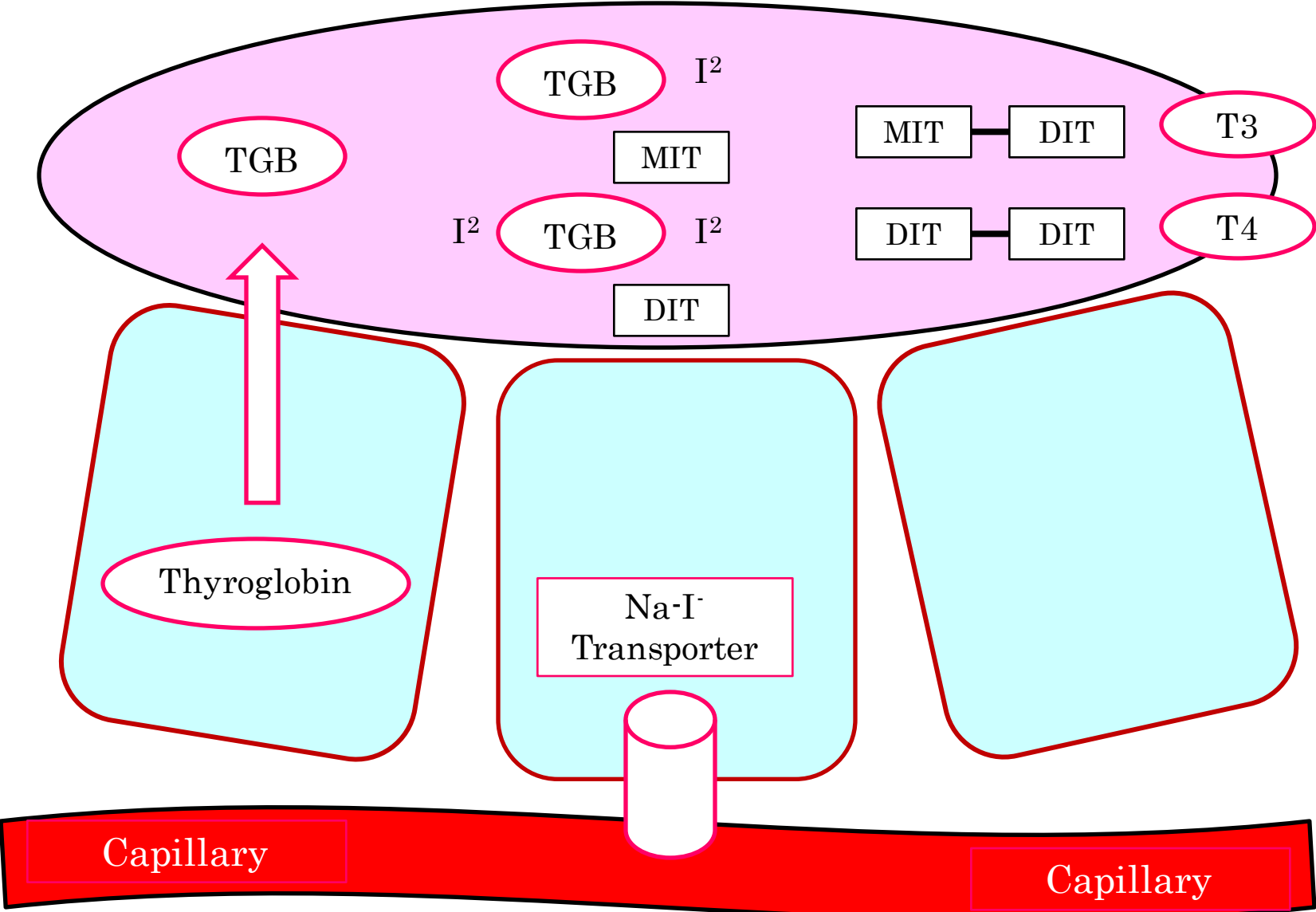
**Step One:** Iodide ( $I^-$ ) is absorbed in inverse proportion to serum concentration.  
Oxidized to Iodine ( $I^2$ )

Oxidation ( $I^- \rightarrow I^2$ ), Organification



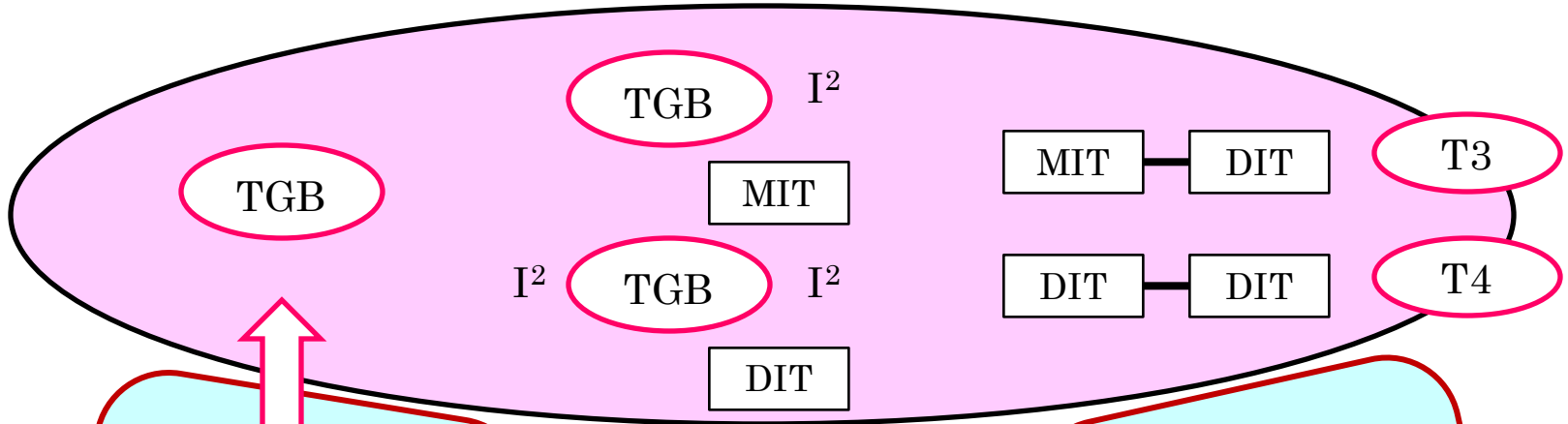
**Step Two: Organification.** Iodine binds tyrosine residues on thyroglobulin (TGB) to form mono- and di-iodotyrosine

Oxidation ( $I^- \rightarrow I^2$ ), Organification and Coupling

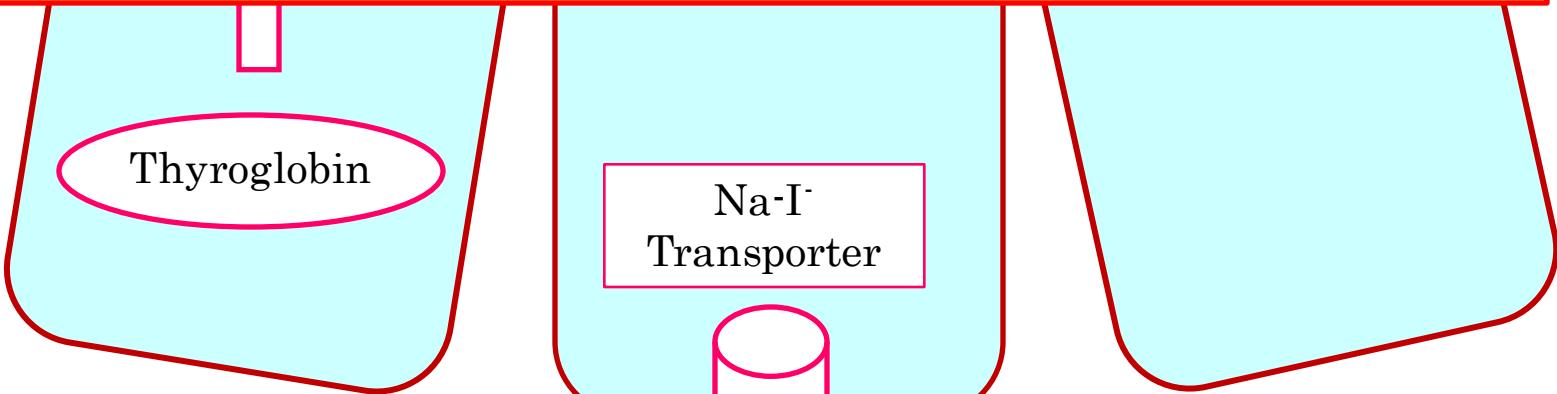


**Step Three: Coupling.** Just as it sounds! MIT and DIT couple to form T4 >>> T3

Oxidation ( $I^- \rightarrow I^2$ ), Organification and Coupling



All Three Steps Catalyzed by ~ Thyroid Peroxidase ~

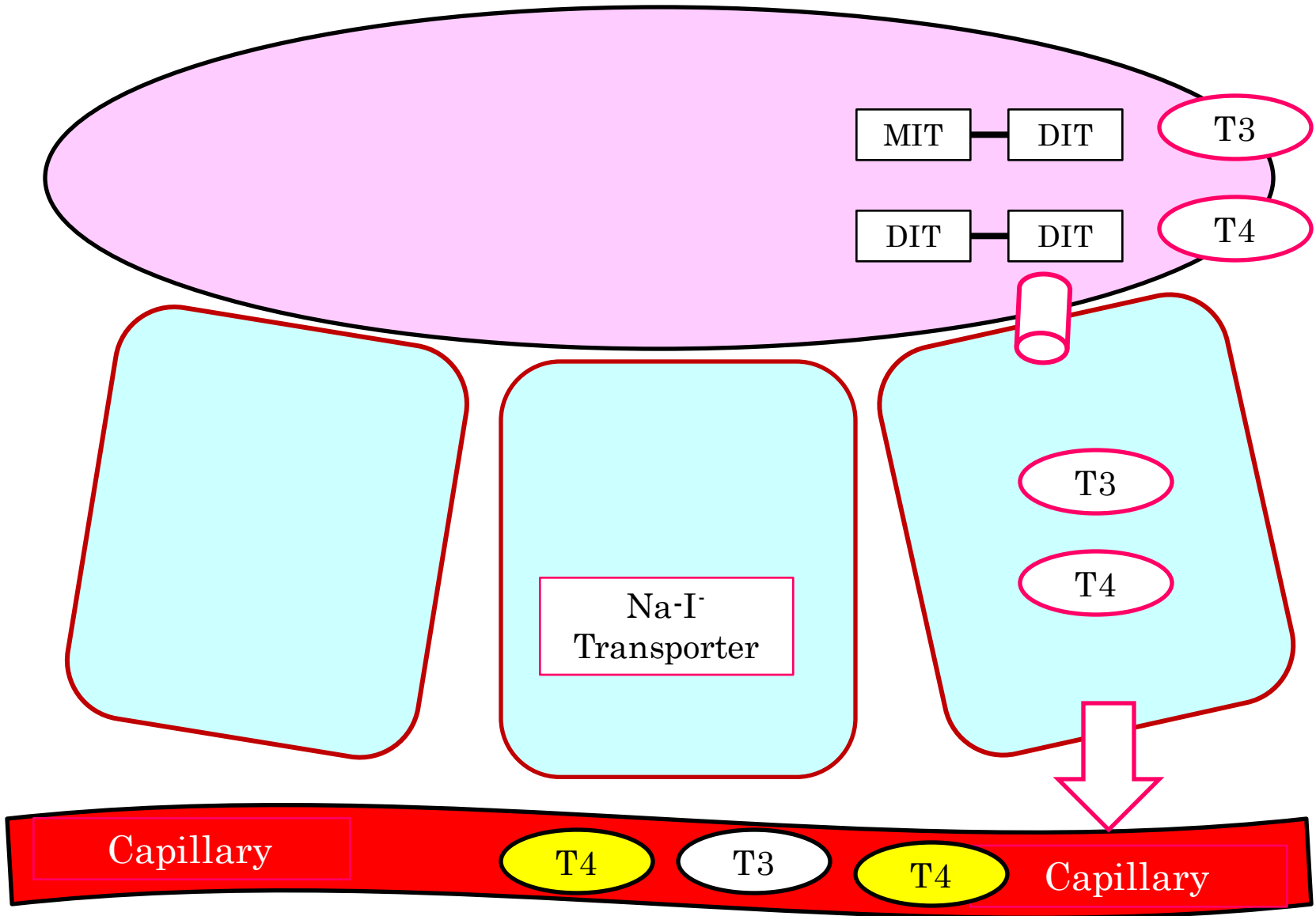


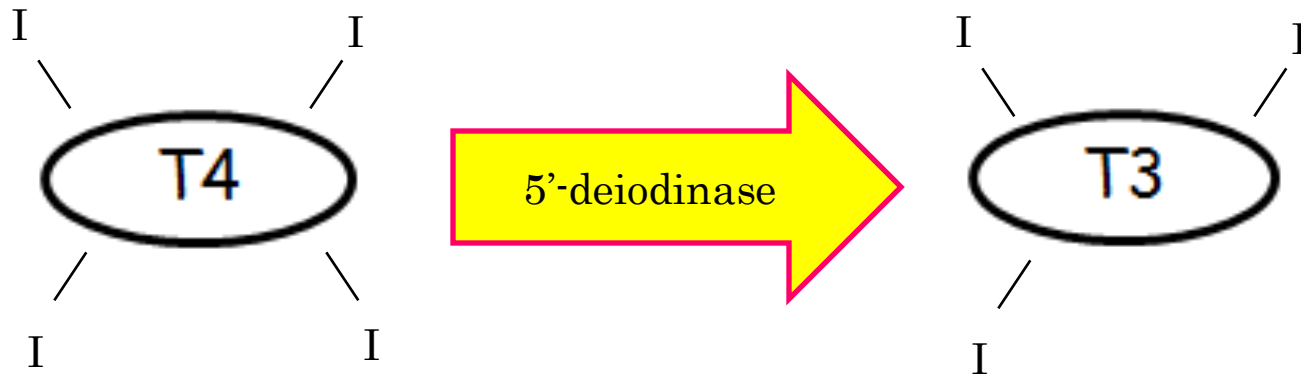
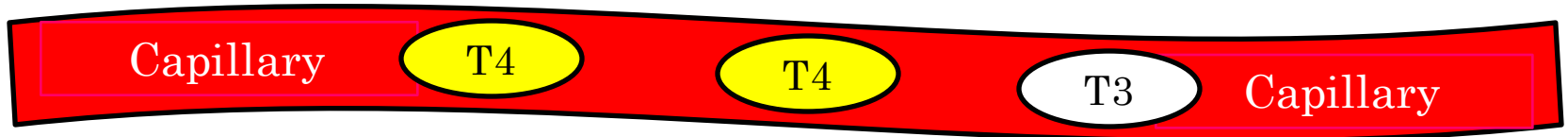
Capillary

Capillary



# Thyroid hormone release





1. T4 is released in higher concentration than T3.
2. T4 is less active than T3 (i.e. behaves as a 'prohormone').
3. T4 is converted in the periphery by 5'-deiodinase to T3, the biologically active form of thyroid hormone.

Thyroid Hormone Infomercial

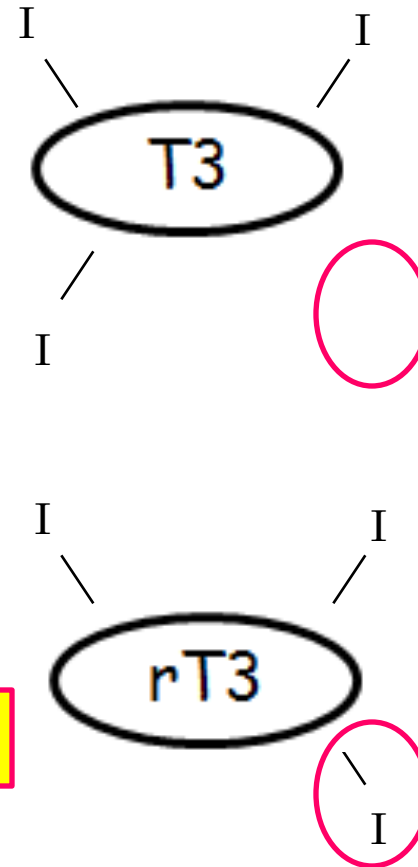
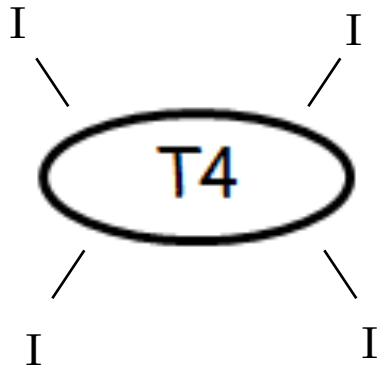
Capillary

T4

T4

T3

Capillary



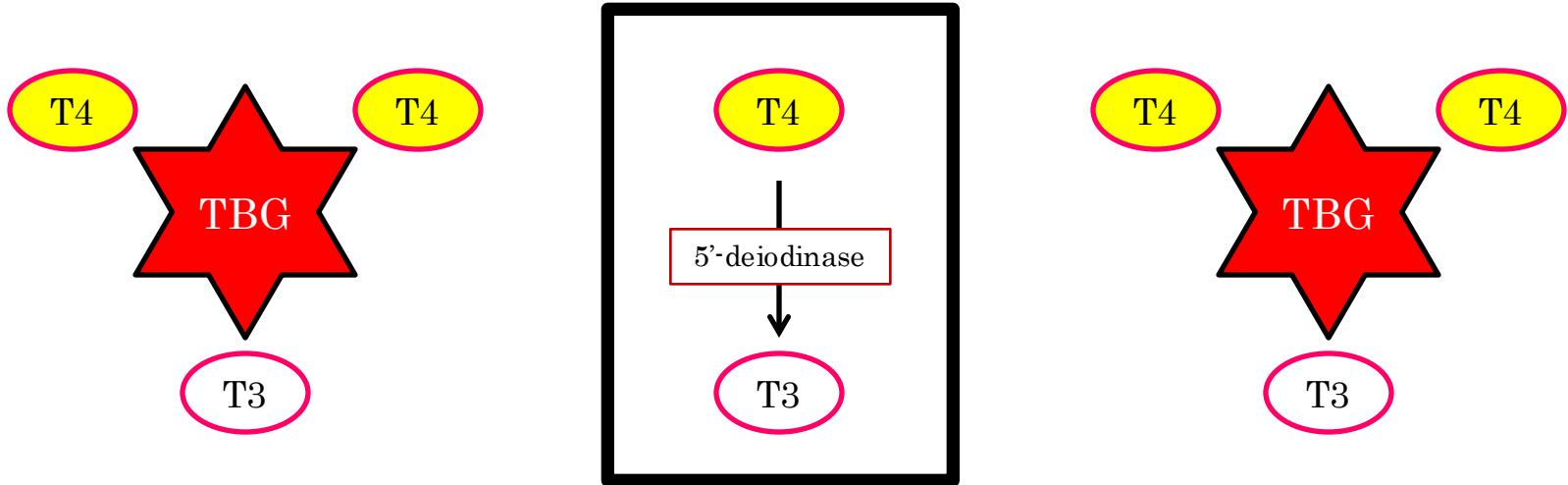
5'-deiodinase

rT3 is elevated in 'sick euthyroid syndrome'

1. During times of 'abundance', T4 may also be converted to reverse T3 (rT3).
2. rT3 has a different iodine molecule removed.
3. It is biologically **inactive**.

# TBG = Thyroid **B**inding Globulin

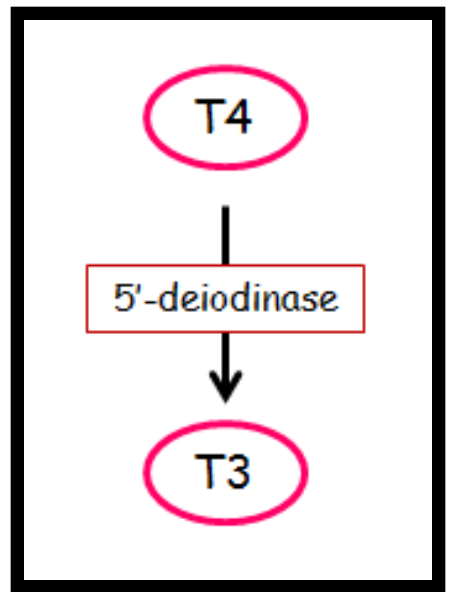
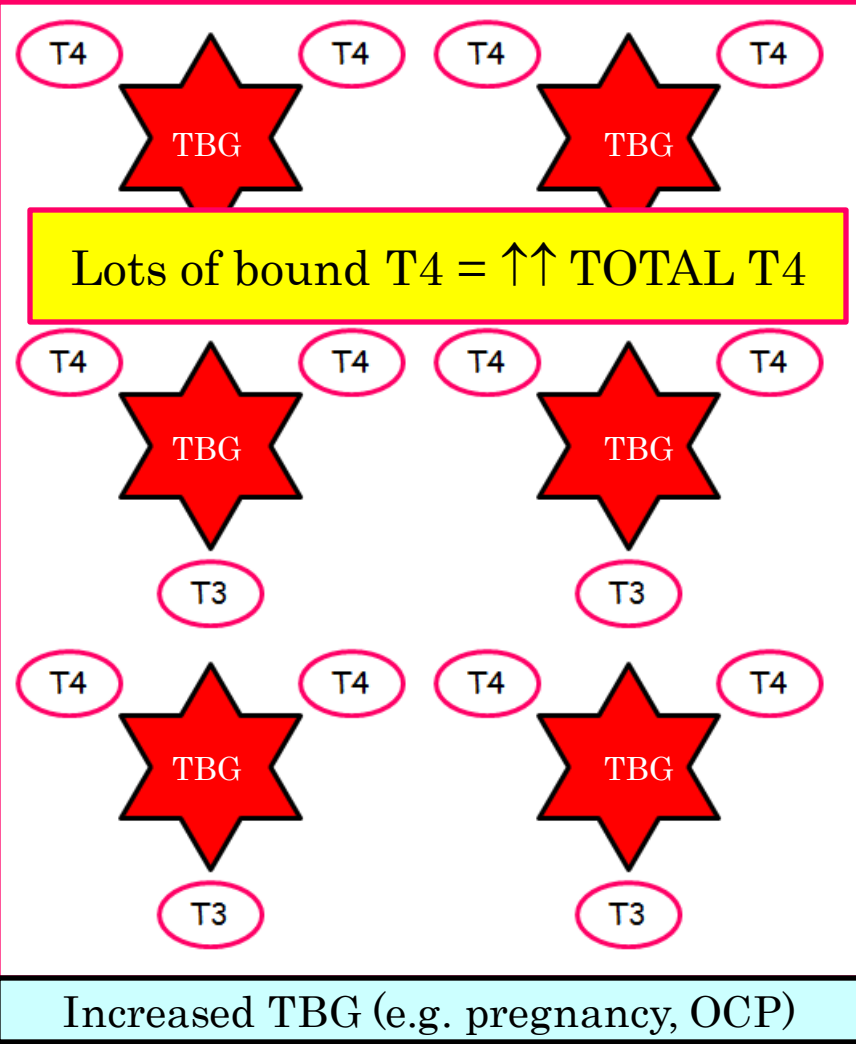
(do not confuse with thyroglobulin!)



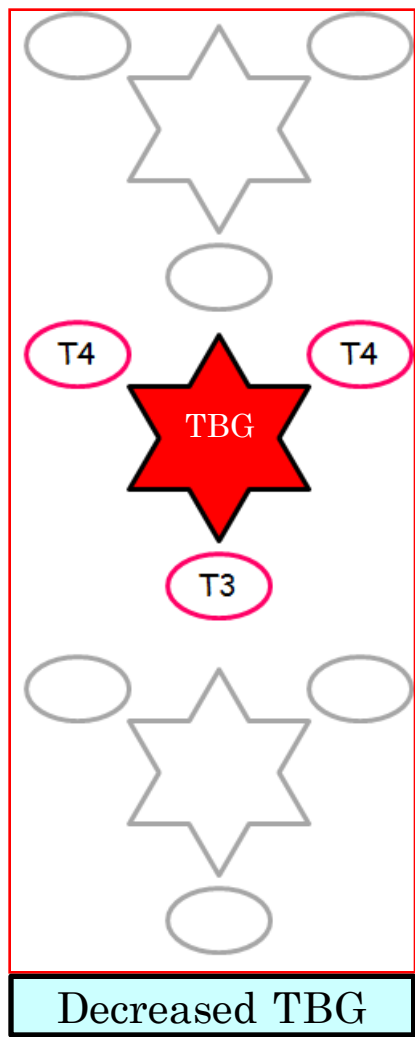
## TBG Trivia (synthesized in liver):

- Once released into the circulation, thyroid hormone circulates bound to TBG
- This serves as a 'reservoir' for hormone.
- High affinity for T4

Only free circulating hormone (~1%) is biologically active!



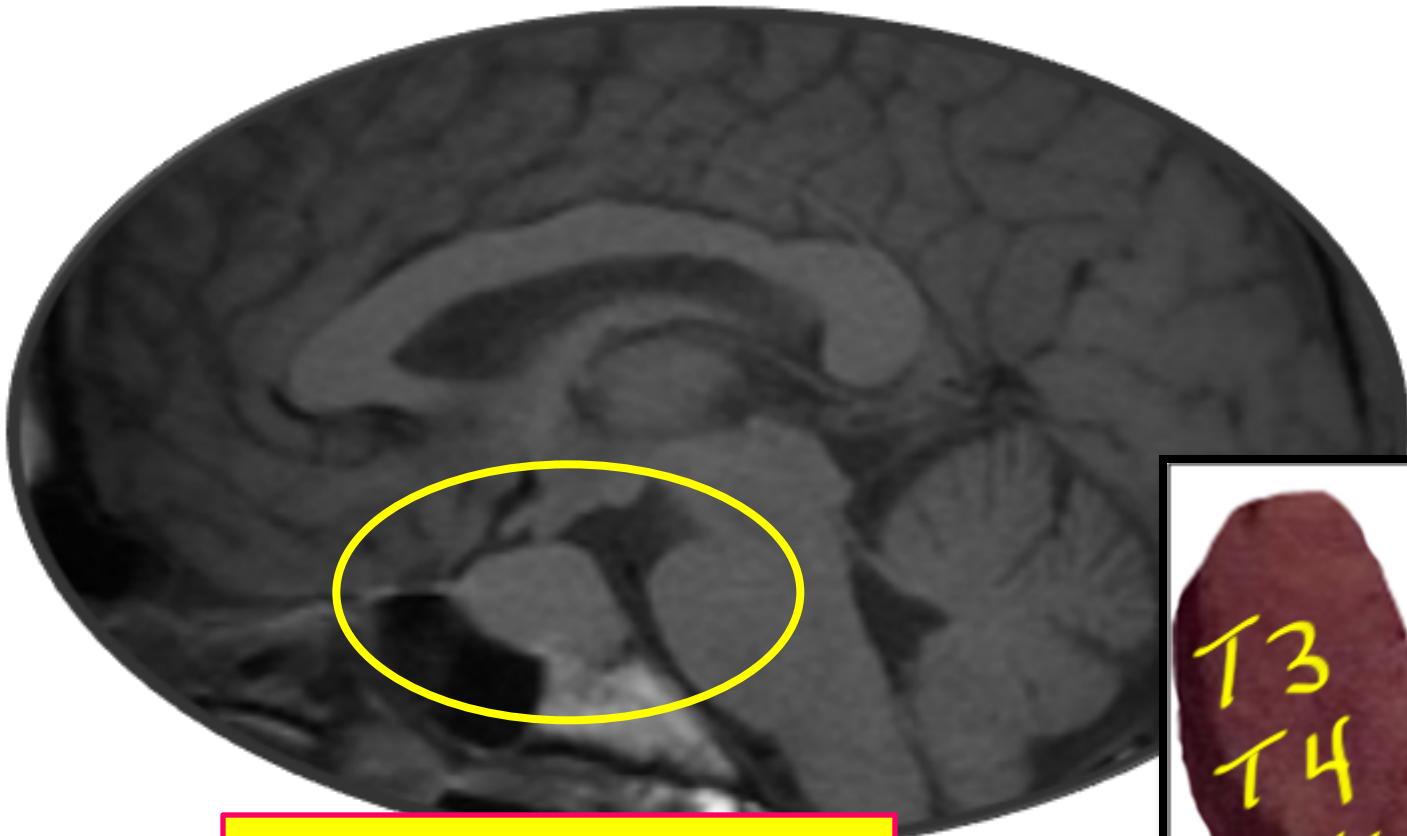
- Free T4
- Bioavailable Form



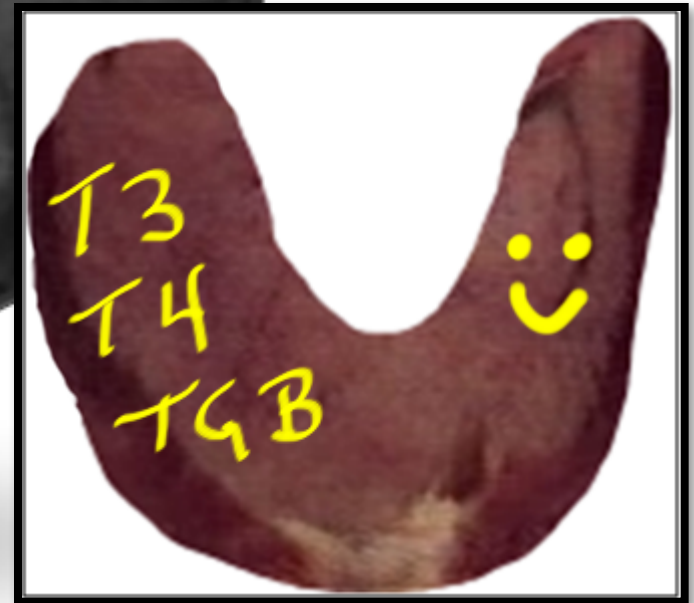
**Key Point:**

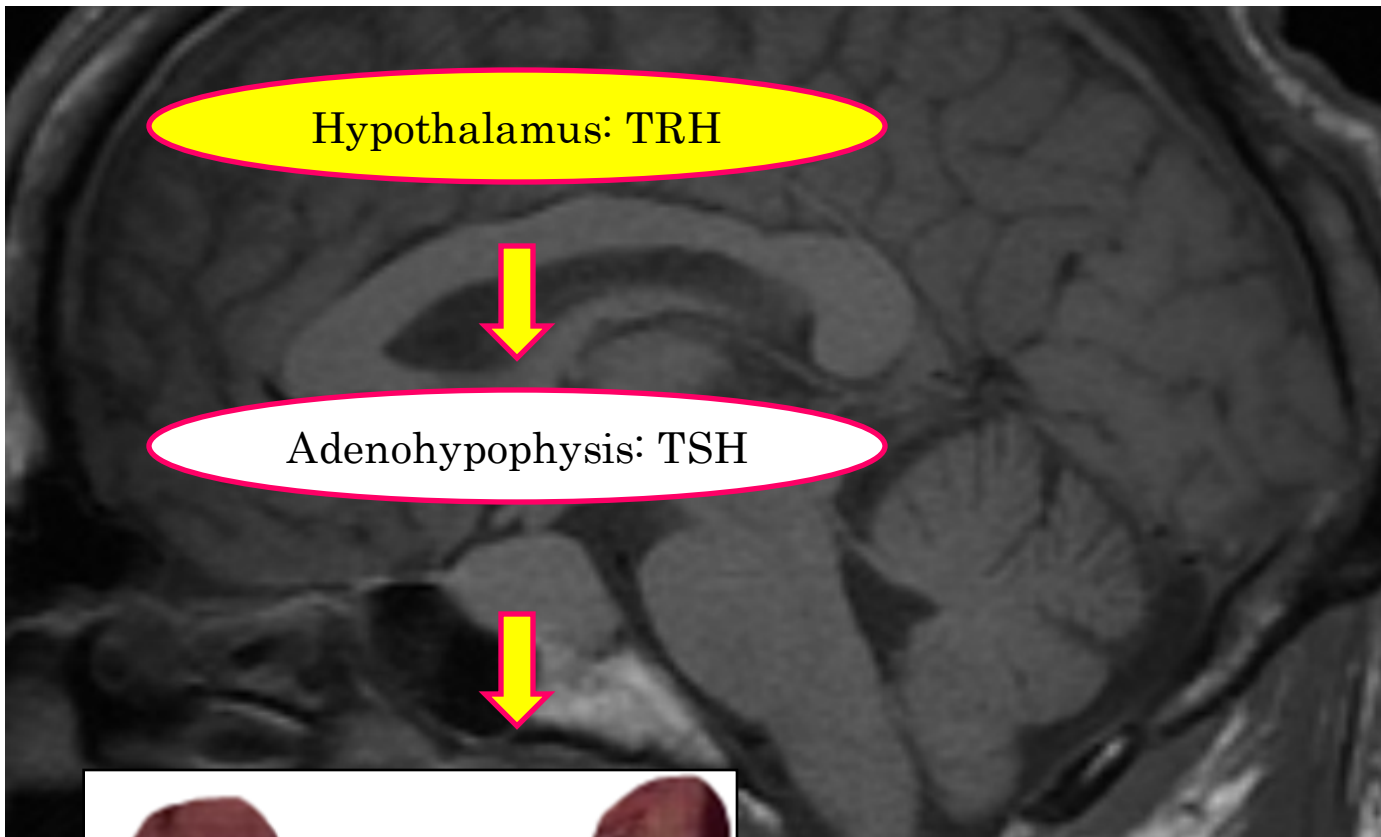
- TBG levels can increase (e.g. pregnancy) or decrease (e.g. cirrhosis).
- The total amount of hormone (**tT4**) will increase or decrease with TBG levels BUT the amount of free (bioavailable) hormone will NOT change.

# Thyroid Hormone Regulation



Pituitary and TSH  
are key players





Hypothalamus: TRH



Adenohypophysis: TSH



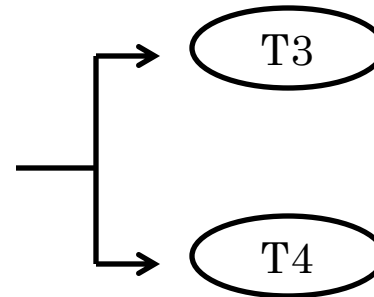
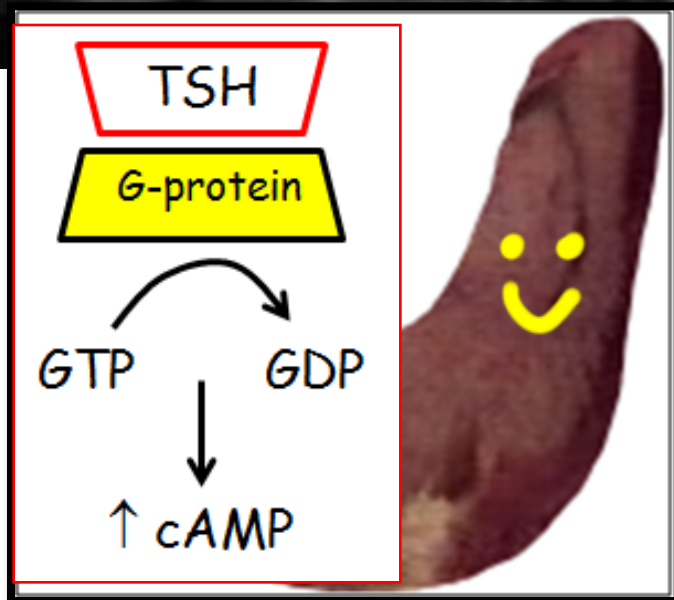
Hypothalamic-Pituitary-Thyroid,

TSH (Thyroid Stimulating Hormone)  
A trophic hormone that can cause hypertrophy and hyperplasia

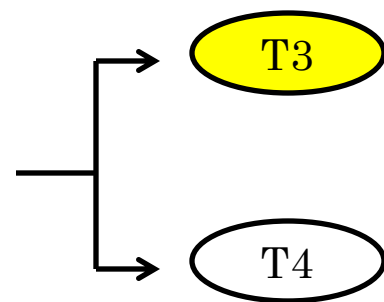
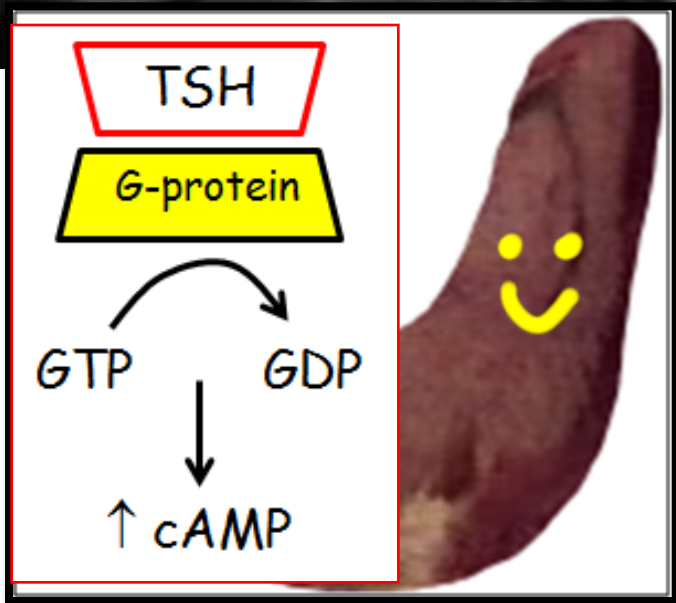
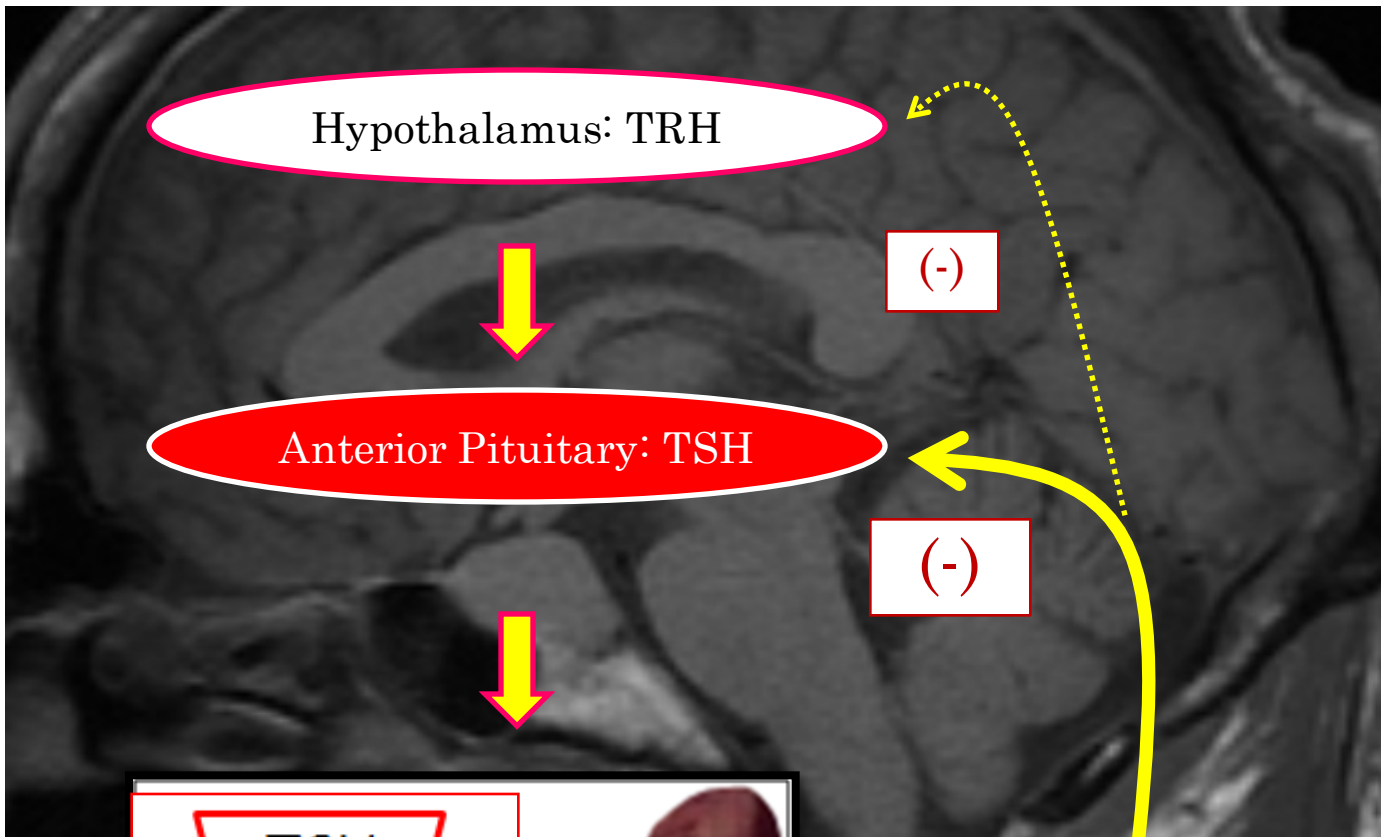
Hypothalamus: TRH



Anterior Pituitary: TSH







# Thyroid Diagnostics

Serology

TSH

Hormone

Free T4

Total T4 (tT4)

T3

rT3

Immune Markers

TSIg

Anti-TPO

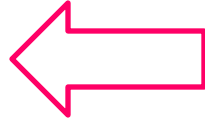
Anti-TGB

Miscellaneous:

ESR

TGB

Primary Thyroid Gland Dysfunction



# Thyroid Diagnostics

Serology

TSH

Hormone

Free T4

Total T4 (tT4)

T3

rT3

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TSIg

Anti-TPO

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Miscellaneous:

ESR

TGB

Patient is treated with T3 for hypothyroidism. How do the following respond?

TSH

T4

rT3

# Thyroid Diagnostics

Serology

TSH

Hormone

Free T4

Total T4 (tT4)

T3

rT3

Immune Markers

TSIg

Anti-TPO

Anti-TGB

Miscellaneous:

ESR

TGB

Patient is treated with T3 for hypothyroidism. How do the following respond?

↓ TSH

↓ T4

↓ rT3

Question Hierarchy:  
Data >> Physical Exam >> Language

# Thyroid Diagnostics

Serology

TSH

Hormone

Free T4

Total T4 (tT4)

T3

rT3

Immune Markers

TSIg

Anti-TPO

Anti-TGB

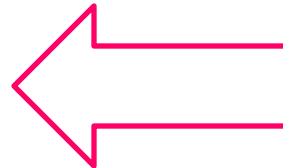
Miscellaneous:

ESR

TGB

Graves Disease

Hashimoto's  
Lymphocytic



# Thyroid Diagnostics

Serology

TSH

Hormone

Free T4

Total T4 (tT4)

T3

rT3

Immune Markers

TSIg

Anti-TPO

Anti-TGB

Miscellaneous:

ESR

TGB

Granulomatous (Viral) Thyroiditis

Serial monitoring, Neoplasm  
Hyperthyroidism, Inflammatory



# Thyroid Diagnostics

Serology

TSH

Hormone  
Total T4 (tT4)  
Free T4  
T3  
rT3

Immune Markers  
TSIg

Anti-TPO  
Anti-TGB

Miscellaneous:  
ESR  
TGB

Imaging

Ultrasound

Nuclear  
Radioactive Iodide  
Uptake (RAIU)

Technetium

Anatomic

Functional

Cystic v Solid

Increased v Decreased  
Uptake

# Thyroid Diagnostics

Serology

TSH

Hormone  
Total T4 (tT4)  
Free T4  
T3  
rT3

Immune Markers  
TSIg

Anti-TPO  
Anti-TGB

Miscellaneous:  
ESR  
TGB

Imaging

Ultrasound

Nuclear  
Radioactive Iodide  
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Technetium

Anatomic

Functional

Pathology

FNA: Cytopathology

(Excisional) Biopsy



Tumors, 4  
Hashimoto  
Graves  
Granulomatous  
Riedel's



# Thyroid Diagnostics

Serology

Imaging

Pathology

TSH

**FNA most useful for  
Papillary Carcinoma**

FNA: Cytopathology

Hormones  
Total T4  
Free T4  
T3  
rT3

(Excisional) Biopsy

Nuclear  
Radioactive Iodide  
Uptake (RAIU)



Technetium

**Tumors, 4  
Hashimoto  
Graves  
Granulomatous  
Riedel's**

Immune Markers  
TSIg

Anti-TPO  
Anti-TGB

Anatomic

Miscellaneous:  
ESR  
TGB

Functional

# Thyroid Hormone Synthesis, Regulation and Diagnostics



Key Derivatives