

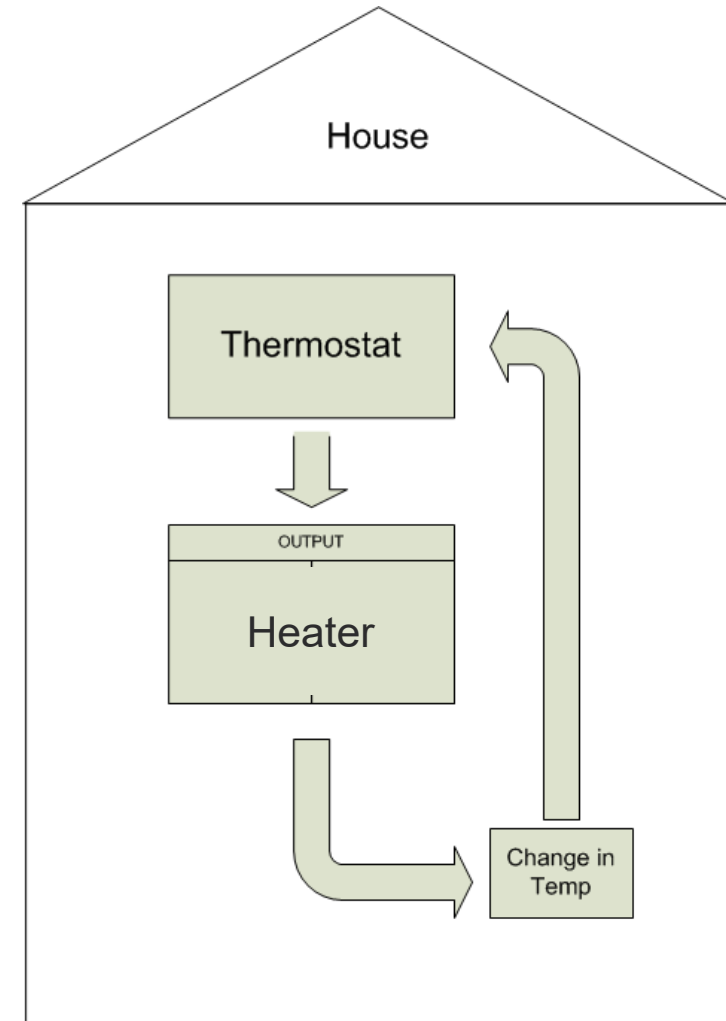
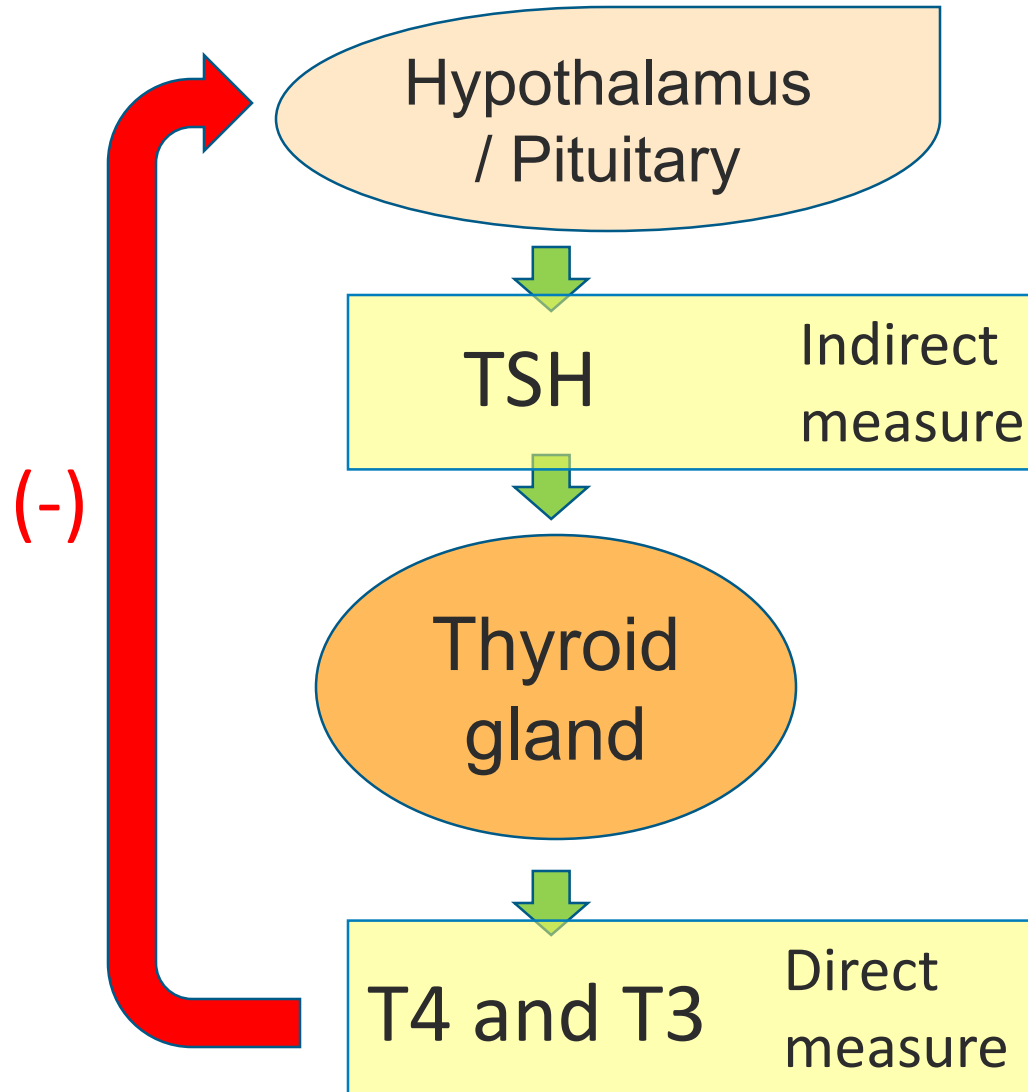
Hot Topics in Medicine: Thyroid FAQs in Primary Care

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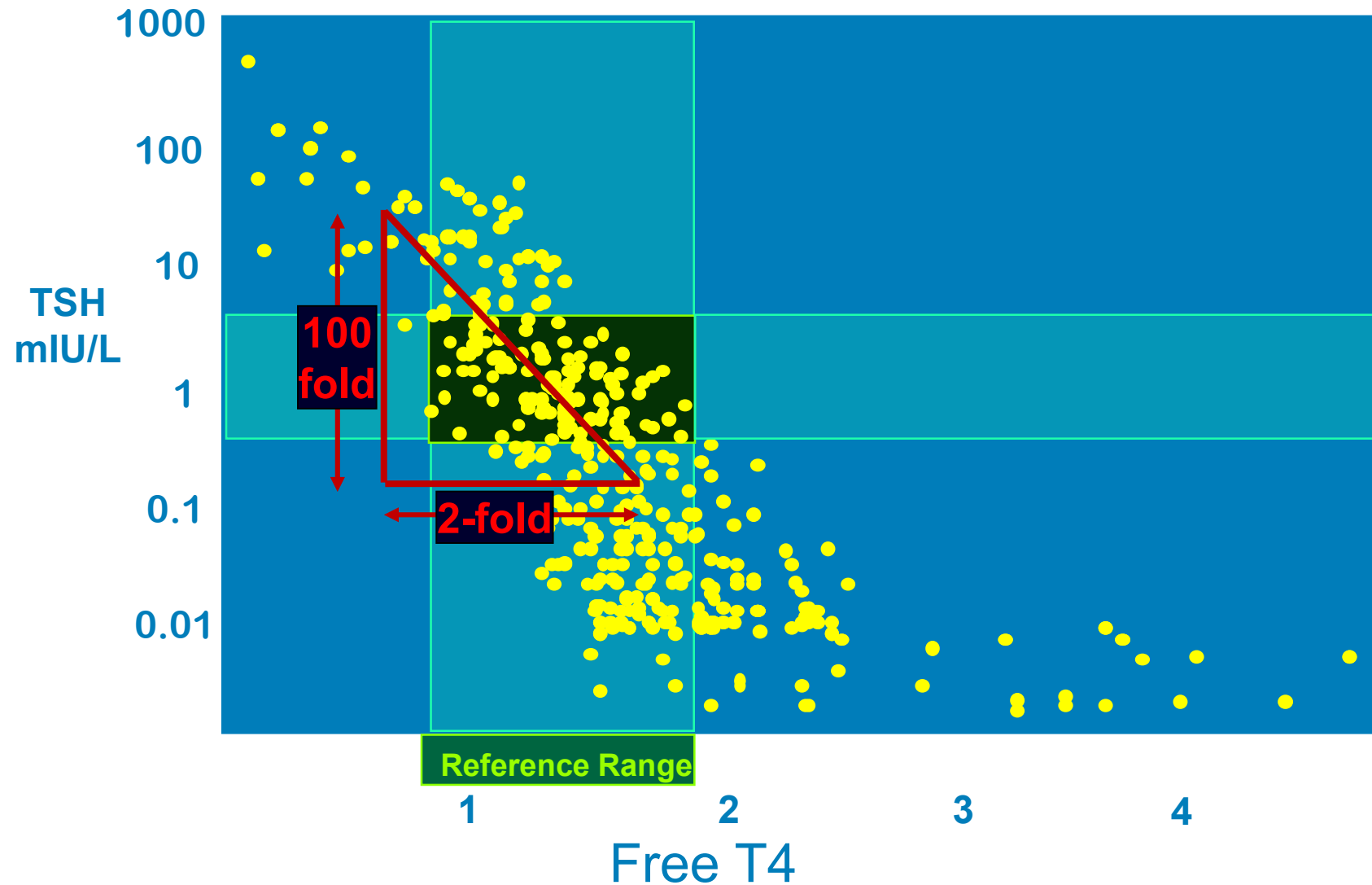
Learning Objectives

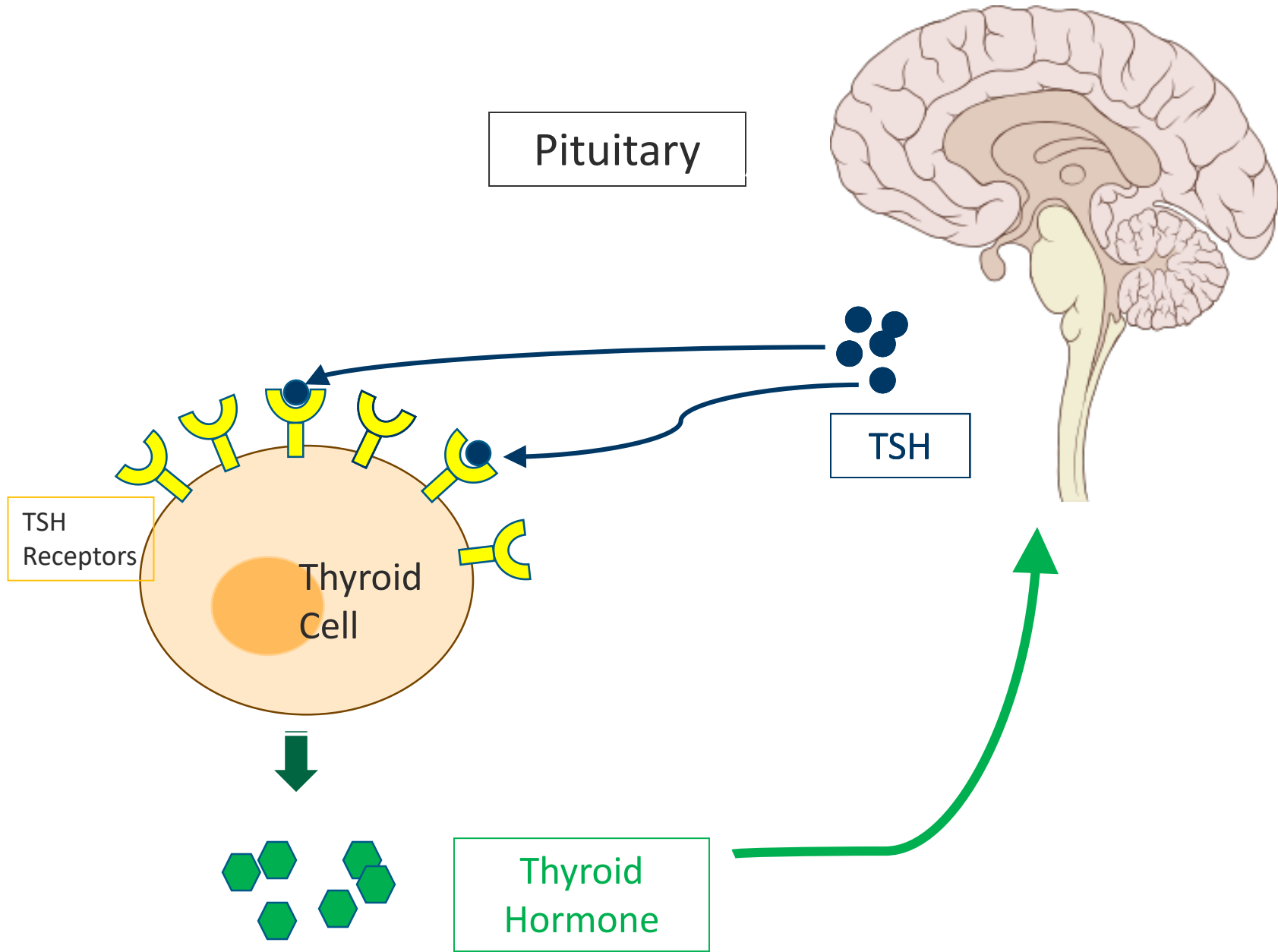
- Discuss the regulation of thyroid hormone
- Determine why and when to order the various tests
- Provide a toolkit of responses to address common patient questions
- Describe when and how to use desiccated thyroid hormone or T3/T4 combination
- Describe which thyroid nodules are most concerning and warrant referral/work up

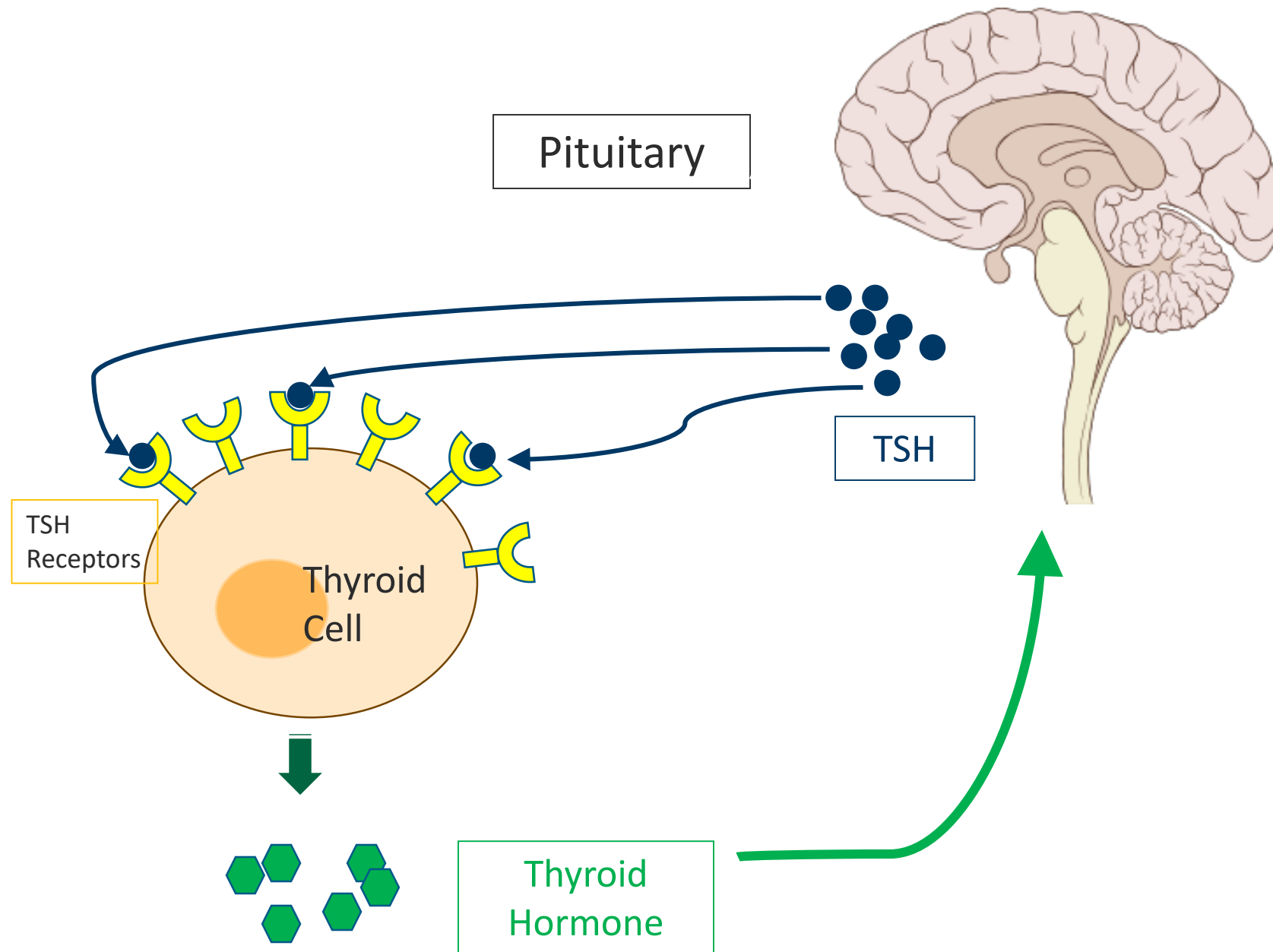
Regulation of Thyroid levels

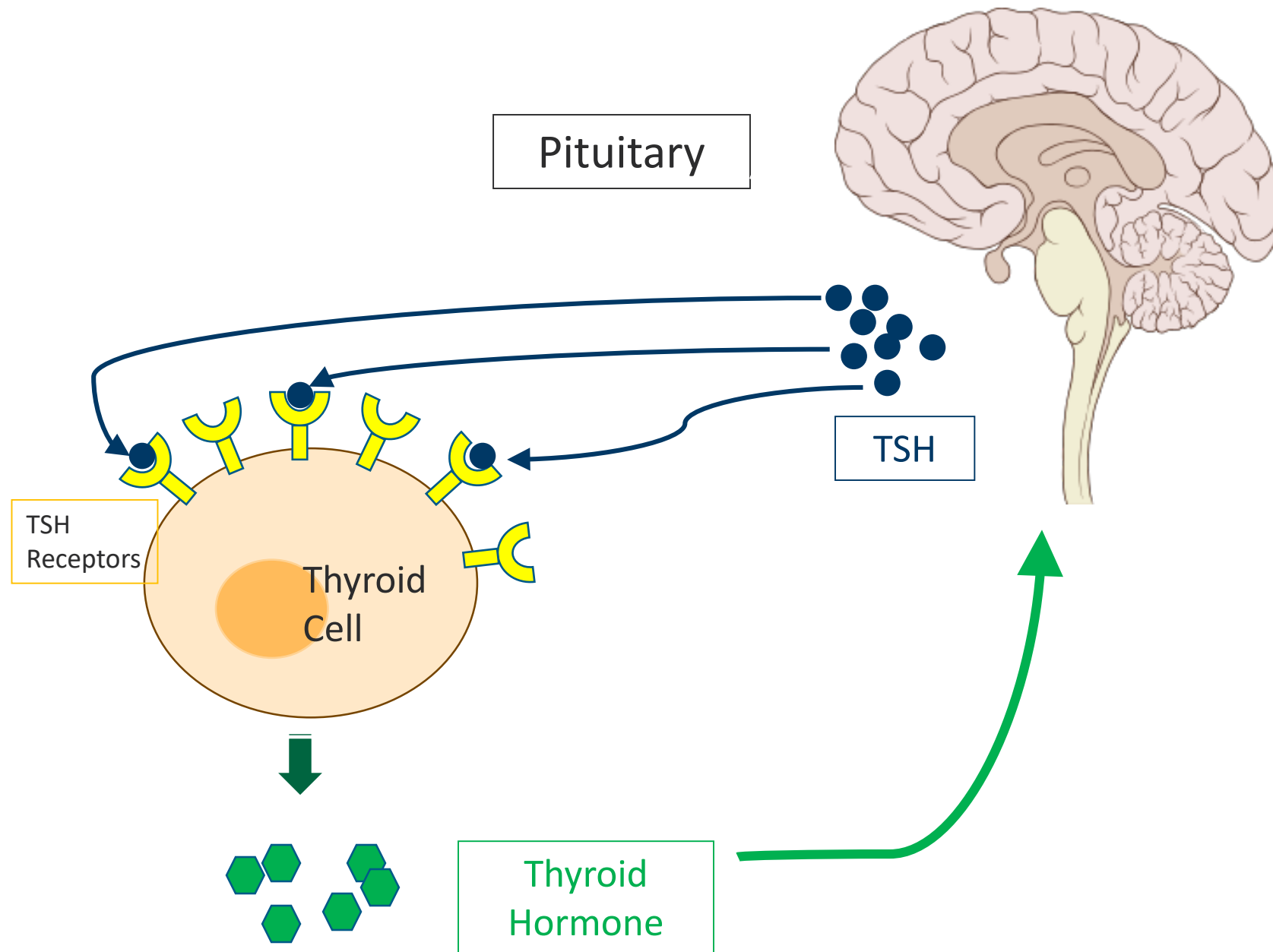


TSH is more clinically sensitive than free T4: Log/linear TSH/free T4 relationship

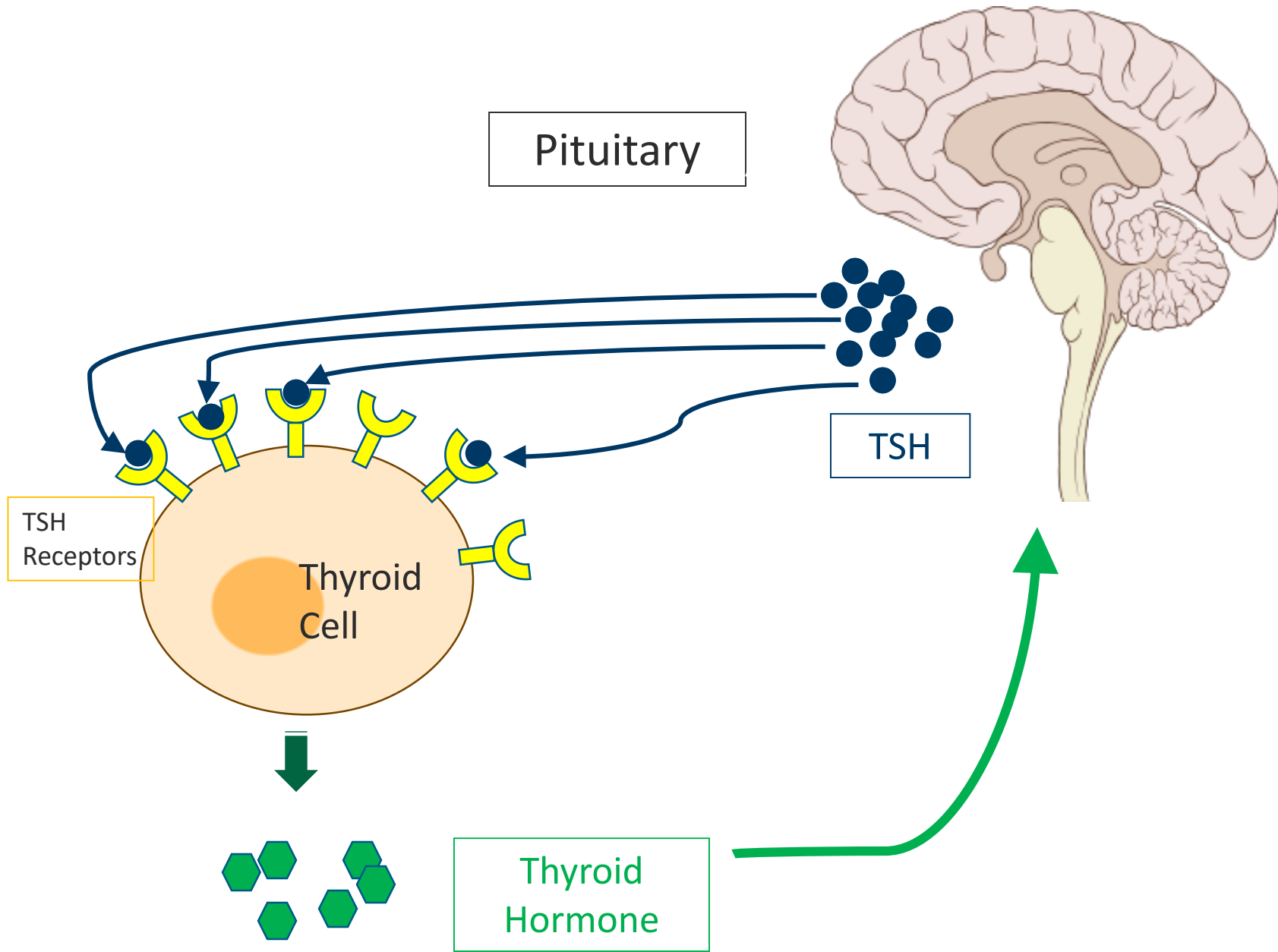


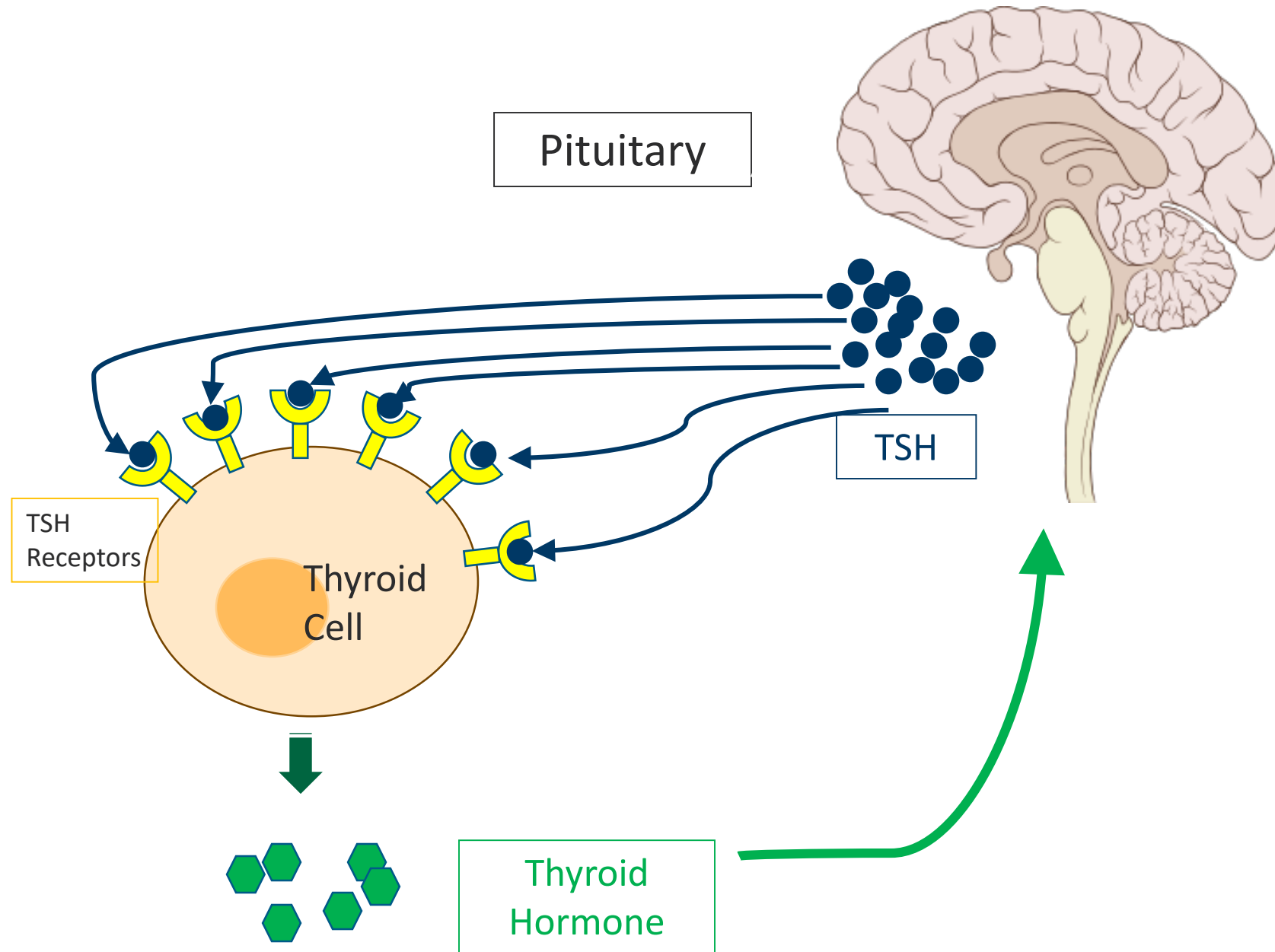


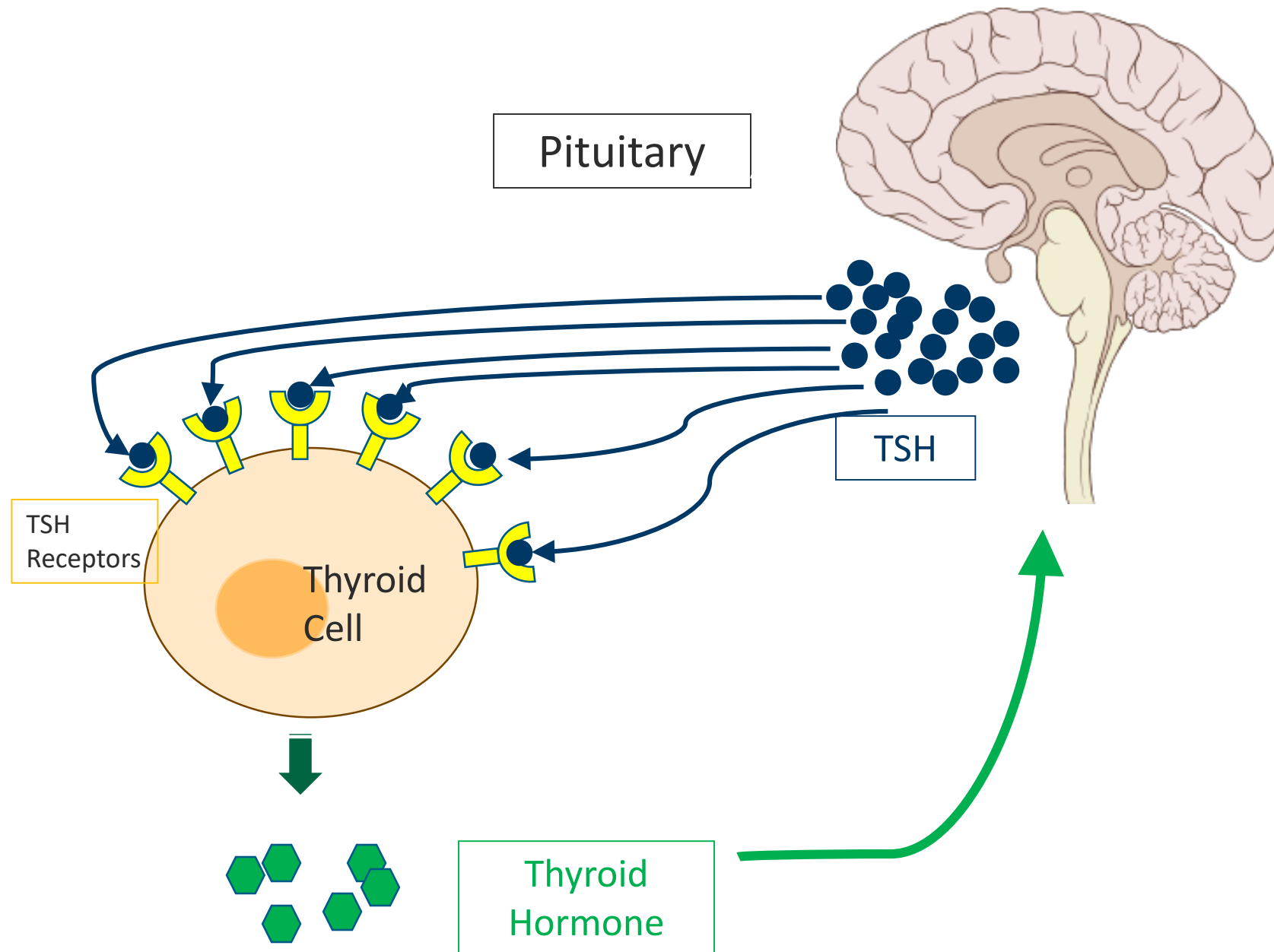












Take home points about tests

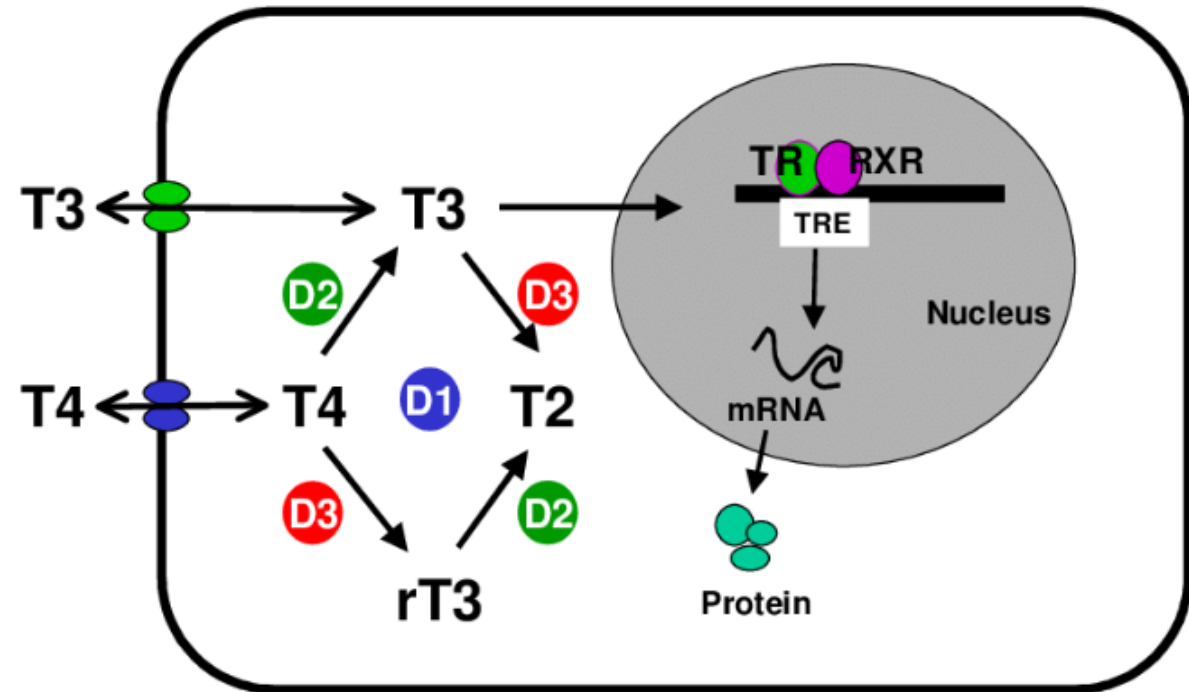
- TSH is the best assessment of thyroid status (in most cases)
- TSH magnifies any abnormality
- T3/T4 norms are based on population
- TSH reflects adequacy of thyroid levels for the individual
 - TSH shows “how happy the pituitary is with the levels of thyroid hormone (regardless of type)”

When do I check T4 and T3 levels

- Reasons to check T4 and T3 levels:
 - If TSH abnormal – check T4 and T3 levels to assess the degree of the hyperthyroidism (or hypothyroidism)
 - If TSH is normal – check T4 and/or T3 if clinical picture does not fit with the TSH
 - If known pituitary dysfunction where TSH is not likely to be reliable
 - Establish concordance between TSH and T4/T3 levels
- After I establish concordance, I rarely check T4 or T3
- If there is discordance between TSH and T4/T3, I investigate. Usually TSH is still the most reliable test.

Why aren't you giving me T3?

- T4:T3 secretion ~15:1
- T4 is a pro-hormone
- Only T3 is active and binds to the TR in the nucleus
- Activity of D2 and D3 are tissue/condition specific
- The specific genes transcribed are tissue specific



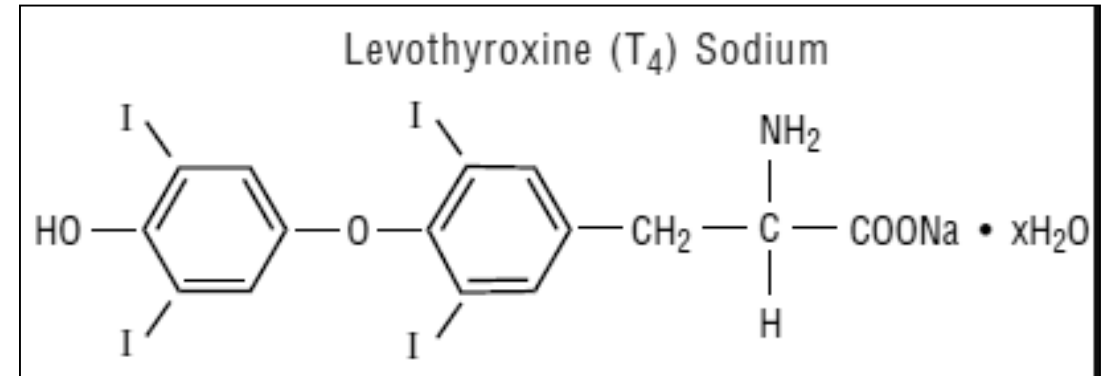
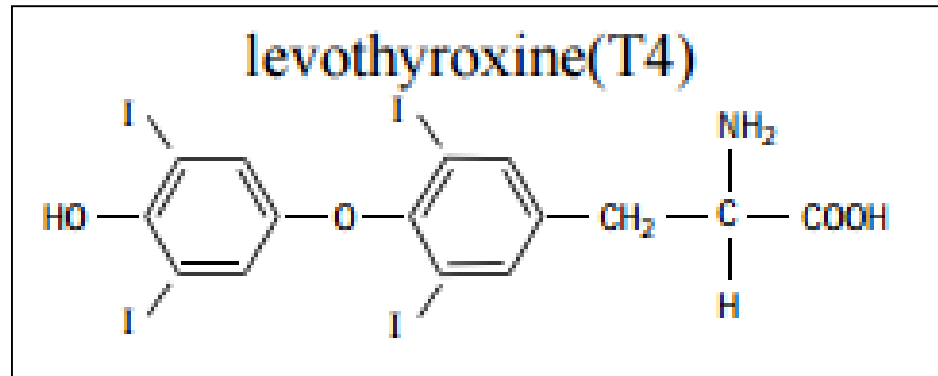
Study	N	TSH (T4)	TSH (T4/T3)	QoL	Mood	Physical	Cognition
Bunevicius 1999	33	0.8	0.5	ND	11 of 17	3 of 7	2 of 8
Bunevicius 2002	10	0.45	0.47	ND	0	0	0
Nygaard 2009	59	0.99	0.756	2 of 4	5 of 7	ND	ND
Escobar 2005	26	1.95	2.56 (5 mcg) 1.09 (7.5 mcg)	0	0	0	2 of 9
Walsh 2003	101	1.5	3.1	0	0	0	0
Rodriguez 2005	30	2.7	5.6	ND	0	0	0
Siegmund 2004	23	1.5	0.5	ND	0	ND	0
Saravanan 2005	697	0.79 (median 0.76)	1.25 (median 2.19)	0	0	0	ND
Clyde 2003	44	2.1	2	0	0	ND	0
Sawka 2003	40	1.7	1.8	0	0	ND	ND
Valizadeh 2009	60	2	2.5	ND	1 of 5	ND	ND
Appelhof 2005	140	0.64	0.35 (10:1) 0.07 (5:1)	0	0	0	0

Is T3/T4 combination replacement better?

- T4 → T3
- Lack of data showing T3/T4 Combo superiority
- Not generally recommended
 - Heart disease
 - Pregnancy

Is Thyroid Extract or Desiccated Thyroid Hormone better?

- “More natural” “not synthetic”



Is T3/T4 combination (or Desiccated Thyroid) replacement better?

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- Not more “natural”
- Desiccated thyroid hormone gives more T3 per T4
 - Human thyroid gland secretes T4:T3 at a ratio of ~11-15:1
 - Porcine/bovine T4:T3 is ~5:1

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- Desiccated thyroid hormone gives more T3 per T4
 - Human thyroid gland secretes T4:T3 at a ratio of ~11-15:1
 - Porcine/bovine T4:T3 is ~5:1
- Consider use in select individuals

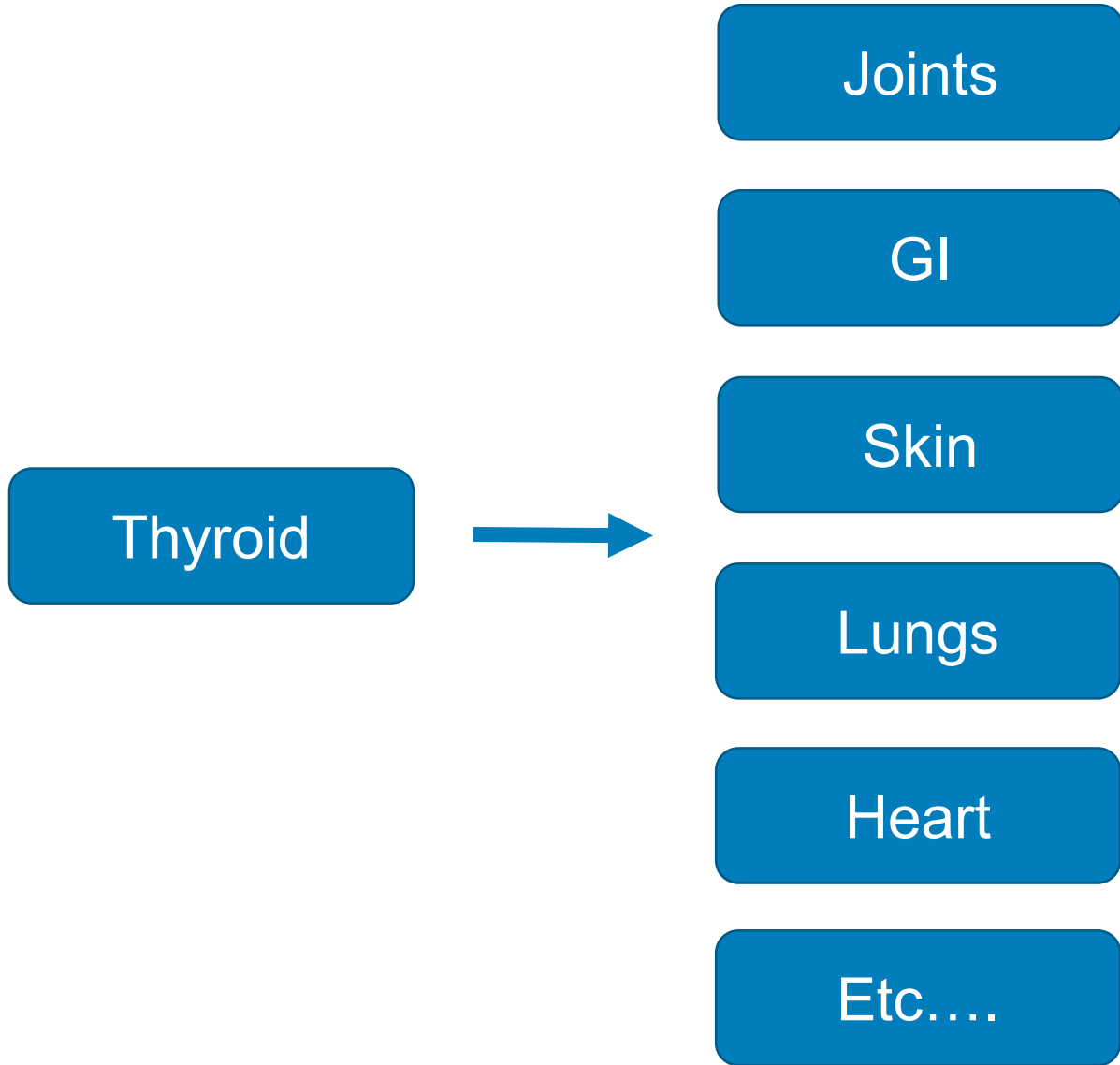
My Desiccated Thyroid “Contract”

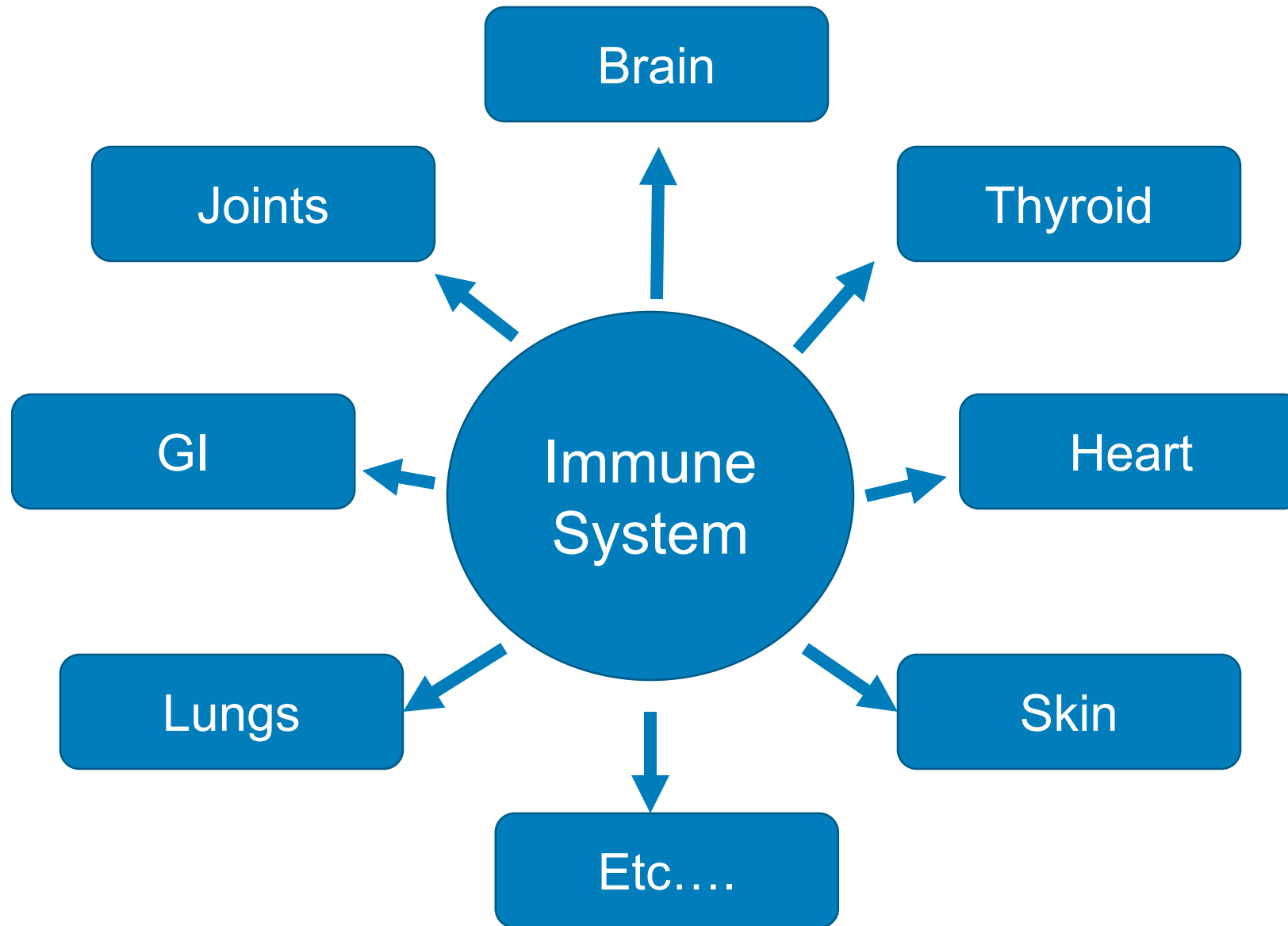
- Do I really care? Small subset do feel better.
- Use TSH, not T3 or T4, to determine dosing
- Expectation for (temporary) improve – Pbo vs T3
 - Caffeine analogy
- Open to the idea that it may not be thyroid
- If no better, go back to monotherapy
- If T4+T3, try to keep liothyronine at 5-10 mcg (15:1)

Desiccated Thyroid Hormone	Levothyroxine (T4)	Liothyronine (T3)
60 mg (65 mg)	~100 mcg	~25 mcg

What about my Hashimoto's?

- Not a distinct disease from hypothyroidism
- Leading cause of hypothyroidism in U.S.
- Symptoms of Hashimoto's listed on internet from effect on the thyroid
- Elevated TPO and Tg antibodies associated with risk for developing hypothyroidism
- TPO and Tg Ab levels do not correlate with severity of thyroid disease
- TPO and Tg Ab do not directly cause symptoms





My approach to Thyroid Antibody testing

- Rarely check TPO or Thyroglobulin antibodies for hypothyroidism
- Rarely impacts my decision to treat or dose
- Pregnant or likely to get pregnant
 - Lower threshold for treatment
- If checked, I do not check serially

ULTRASOUND NECK SOFT TISSUE

FINDINGS:

Nodule 1. Location: Right mid-pole
Size: 0.7 x 0.4 x 0.4 cm.
Composition: Solid (2 pt)
Echogenicity: Hypoechoic (2 pt)
Shape Taller-than-wide: No (0 pt)
Margins: Smooth (0 pt)
Echogenic foci: Macrocalcifications (1 pt)
Comparison to prior exam: none
TR 5 (7 to 14 points)

Nodule 2. Location: Inferior left lobe.
Size: 1.4 x 1.2 x 1.3 cm.
Composition: Solid (2 pt)
Echogenicity: Hypoechoic (2 pt)
Shape Taller-than-wide: No (0 pt)
Margins: Smooth (0 pt)
Echogenic foci: None (0 pt)
Comparison to prior exam: none
TR 4 (4 to 6 points)

IMPRESSION:

*A highly suspicious right thyroid nodule meets size criteria for follow-up, but not FNA.

*A moderately suspicious left thyroid nodule meets size criteria for follow-up, but not FNA

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*A highly suspicious right thyroid nodule meets size criteria for follow-up, but not FNA.

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ACR TI-RADS 2017 RECOMMENDATIONS:

TR 1 (0 pt): *Benign.*

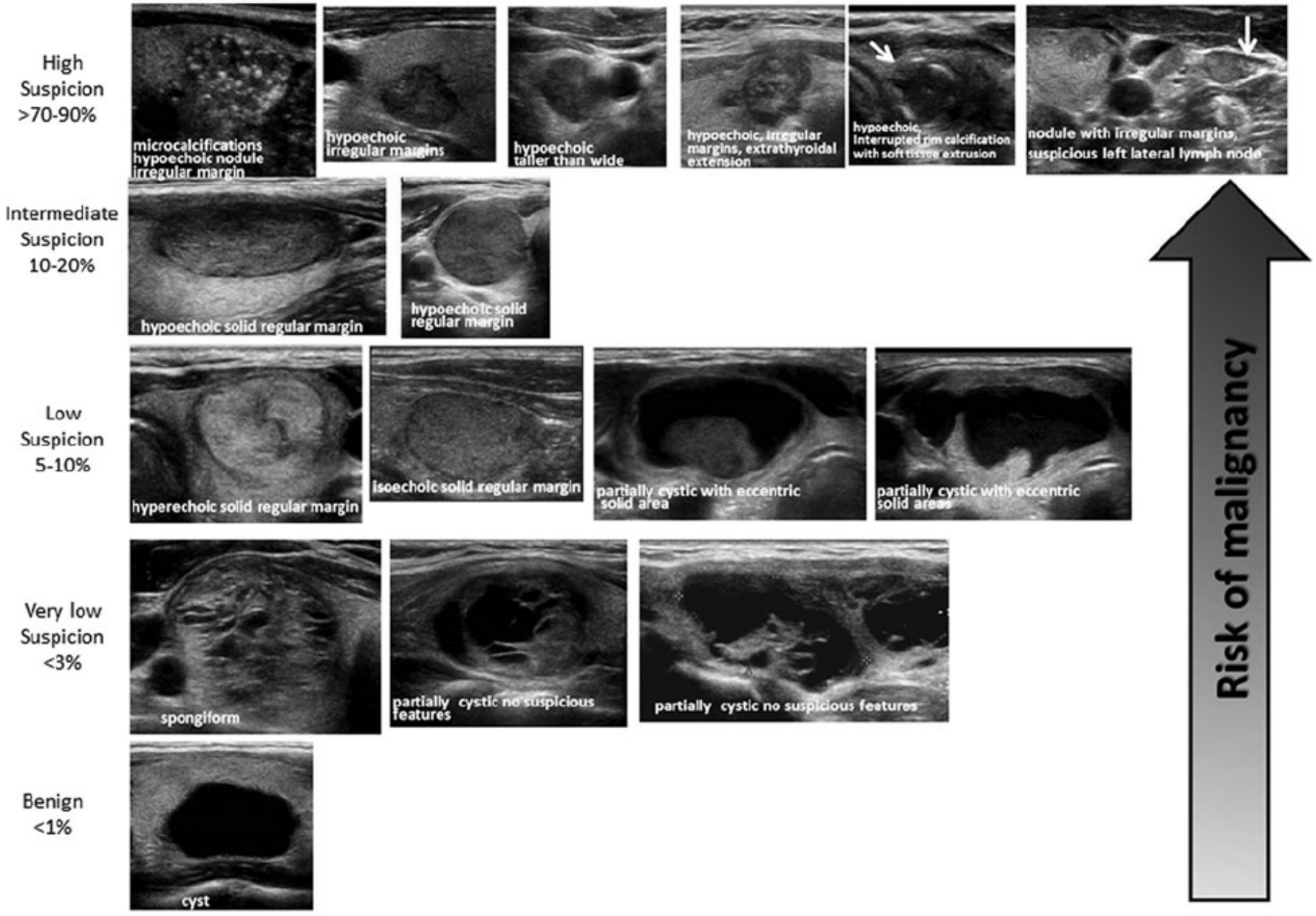
TR 2 (2 pt): *Not suspicious.*

TR 3 (3 pt): *Mildly suspicious.* ≥ 1.5 cm follow up (1, 3, 5 years), ≥ 2.5 cm FNA

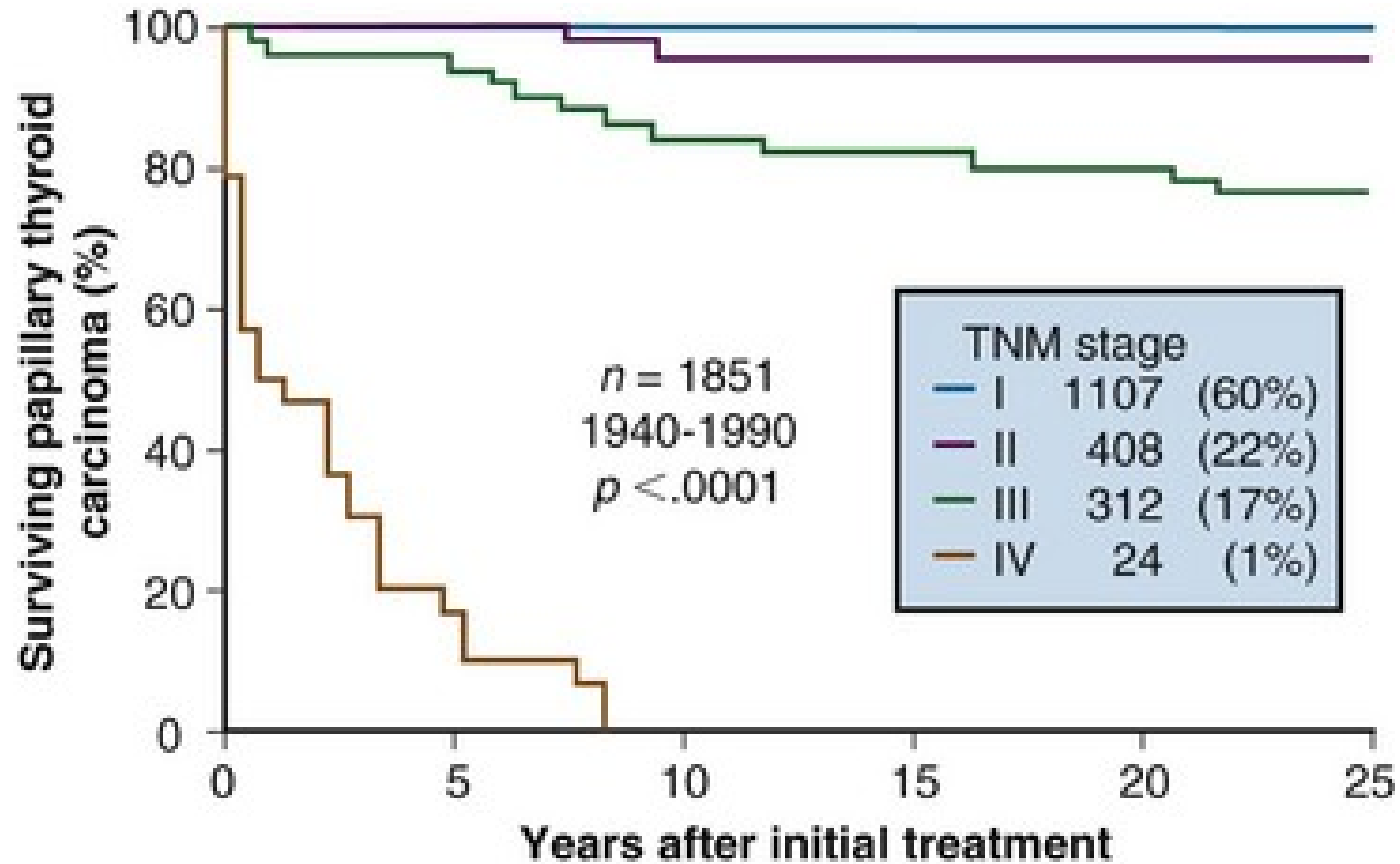
TR 4 (4-6 pt): *Moderately suspicious.* ≥ 1.0 cm follow up (1, 2, 3, 5 years), ≥ 1.5 cm FNA

TR 5 (≥ 7 pt). *Highly suspicious.* ≥ 0.5 cm follow up (every year for 5 years), ≥ 1.0 cm FNA

ATA Guidelines



Survival from Papillary Thyroid Cancer



From Larsen PR, Davies TF, Hay ID: The thyroid gland. In Wilson JD, Foster DW, Kronenberg HM, et al, editors: Williams Textbook of Endocrinology, 9th ed, Philadelphia, 1998, WB Saunders, pp 389-515.

AJCC TNM Staging for Thyroid Cancer (Papillary & Follicular)

Staging guide for thyroid cancer (AJCC 8e)

Age at diagnosis	T category	N category	M category	Stage	Expected 10-yr DSS
<i>Differentiated thyroid cancer</i>					
<55 years	any T	any N	M0	I	98–100%
	any T	any N	M1	II	85–95%
≥ 55 years	T1	N0/NX	M0	I	98–100%
	T1	N1	M0	II	85–95%
	T2	N0/NX	M0	I	98–100%
	T2	N1	M0	II	85–95%
	T3a/T3b	any N	M0	II	85–95%
	T4a	any N	M0	III	60–70%
	T4b	any N	M0	IVA	< 50%
	any T	any N	M1	IVB	< 50%

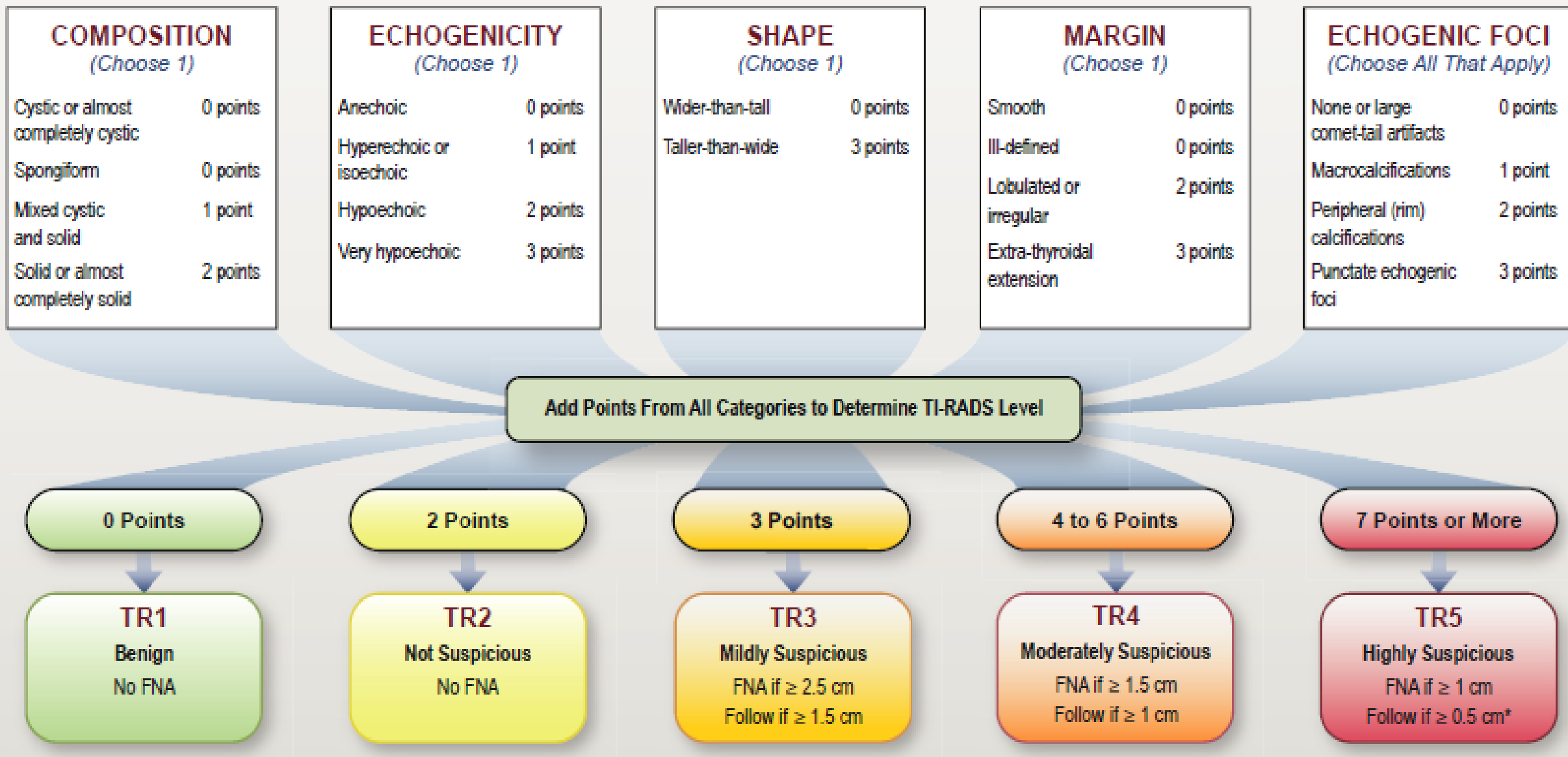
Treatment Trends

- Less extensive/aggressive surgery
- Active surveillance for some small papillary thyroid cancer (<1 or <1.5 cm)
 - New lymph node mets in 3.4% at 10 years
 - 109 of the 340 patients underwent surgical treatment
 - ***None showed cancer recurrence***

Thyroid Nodule Take Home Points

- Thyroid cancer is different than most other cancers
- More selective about which nodules to FNA
- Not just size, Appearance
 - Follow TI-RADS recs on radiology report

ACR TI-RADS



Thyroid Nodule Take Home Points

- Thyroid cancer is different than most other cancers
- More selective about which nodules to FNA
- Not just size, Appearance
 - Follow TI-RADS recs on radiology report
 - Radiology frequently labels as higher TR category
- Urgency generally months, not days or weeks

- Hypothyroidism \neq Thyroid U/S

High Urgency Thyroid Nodules

- TR 4-5 and larger size (~4 cm)
 - <1.5 cm urgency is lower
- Rapidly enlarging
- Pathologic lymph node or neck mass
- Vocal cord paralysis (marked hoarseness)

Subclinical Hypothyroidism: What is the “normal” range for TSH?

- High TSH with normal T4
 - Presence or absence of sx's not part of the definition
- Lab reference range (0.3-4.5) vs. <2.5-3.0
- TSH trends higher with age
 - Should there be age-specific reference ranges?
- TSH up to 6-8 may be normal for adults age 80-89
 - If age specific ranges used, 70% of older adults with TSH >4.5 would be reclassified as normal



Treat all subclinical hypothyroidism?

- Up to 62% of people with an elevated TSH, normalized within 5 years
- Associations between subclinical hypothyroidism and heart disease, stroke, depression, cognitive dysfunction, mortality
 - Some studies show association (espec if TSH >10 or younger age)
 - Many studies show no association (espec if TSH <10)
 - Few studies show reverse association in older people

My approach to subclinical hypothyroidism

- Repeatedly abnormal?
- Does vs does not want treatment?
- Symptoms/signs of hypothyroidism present?
- Age?
- TSH >8-10?
- Pregnant, trying to get pregnant, likely to get pregnant?

Thank you!