Interhospital Endocrine Conference

DEFINITIVE DIAGNOSIS

1. Resistance to thyroid hormone beta

2. Nonfunctioning pituitary microadenoma

Somatostatin suppression test

Octreotide 100 mcg sc q 8 hrs *3 dose

	0 Hr	2 Hr	24 Hr	Reference range	Unit
FT3	4.76	4.97	4.37	1.58-3.91	pg/ml
FT4	1.78	1.63	1.72	0.7-1.48	ng/dl
TSH	1.058	0.619	0.953	0.35-4.94	mIU/L

From Somatostatin suppresion test

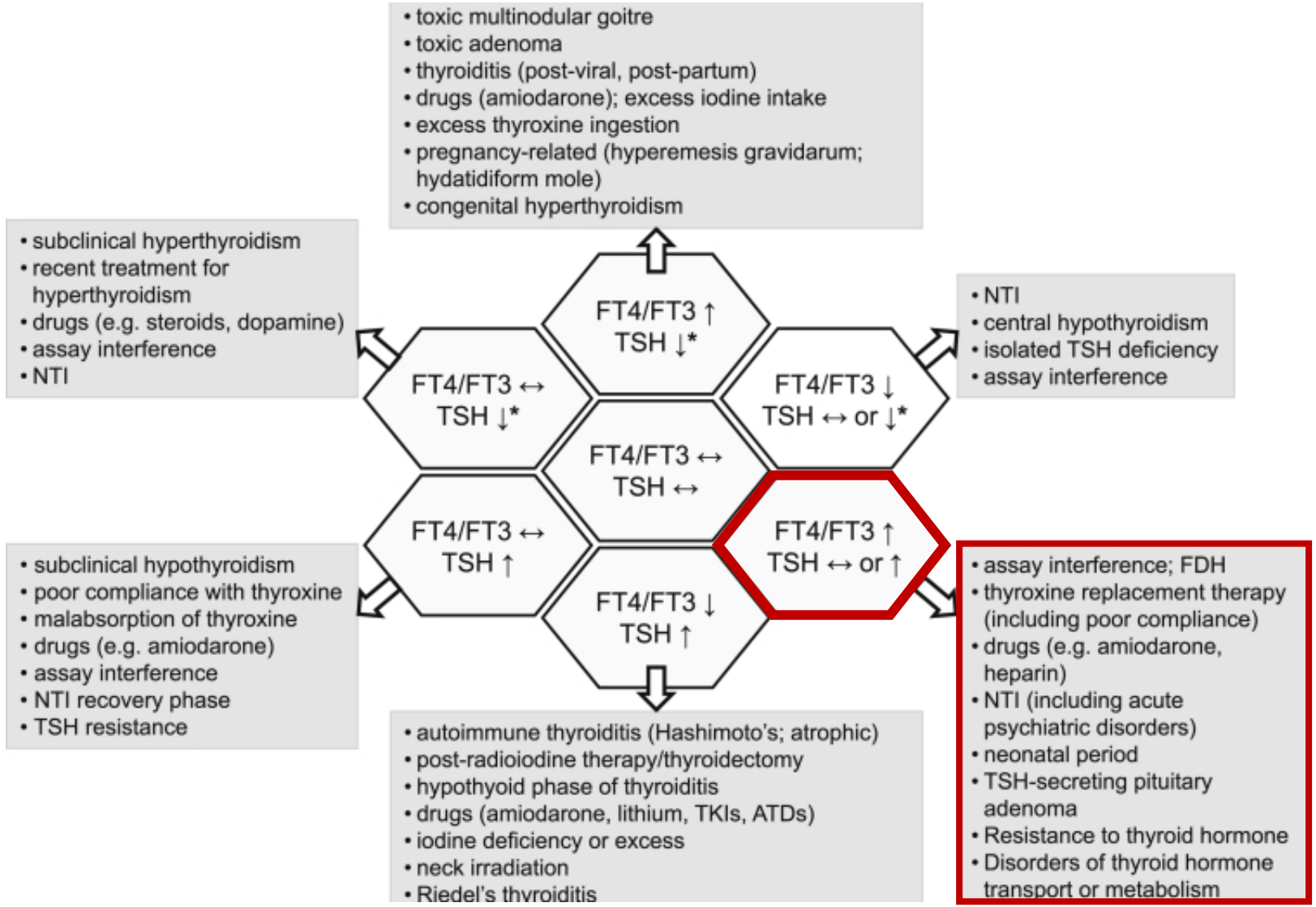
- **Inhibition 2 vs 24: TSH < 44%**

MANAGEMENT

Symptomatic Tx: Beta-blocker + Genetic counselling

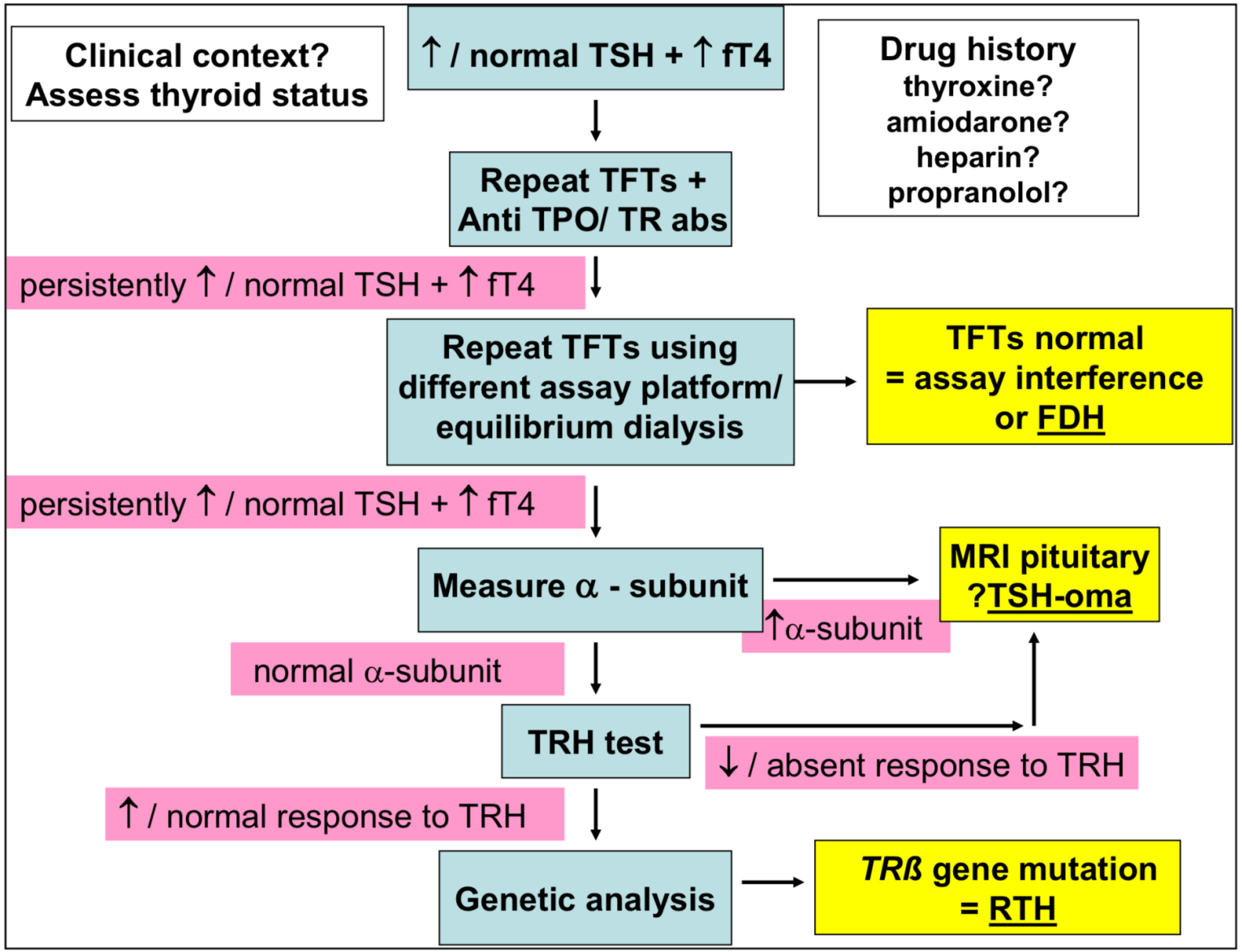
Resistance to Thyroid Hormone Beta

Different patterns of thyroid function tests and their causes



Best Pract Res Clin Endocrinol Metab. 2013 Dec;27(6):745-62.

Hyperthyroxinemia with a non-suppressed TSH



Hormones (2020) 19:311–315

Clinical manifestations and diagnostic features of TSHoma and resistance to thyroid hormone beta

Feature	TSHoma	Resistance to Thyroid Hormone Beta
Goiter	Mostly yes(70%)	Mostly yes(80%)
Incidence	1-2/million	1/40,000
α-GSU:TSH ratio	Increased	Normal
SHBG	High	Normal
TRH response	Flat or decreased response to TRH	Elevated baseline TSH
T3 suppression	TSH unsuppressed	Decreased TSH
Somatostatin suppression	Decreased TSH	TSH unsuppressed
DNA mutation analysis	Negative	Mutation *THRB* gene
MRI pituitary	Macro-(80%)/micro-adenoma	No adenoma

Clin Endocrinol (Oxf). 2005 Feb;62(2):176-81.
European Journal of Endocrinology, Volume 148, Issue 4, Apr 2003, Pages 433–442
CMAJ. 2006 Aug 15;175(4):351.
European Journal of Endocrinology (2021) 185, R65–R74

Static tests for differential diagnosis of TSHoma

- **α-GSU/TSH molar ratio** = [α – GSU (mcg/l)/TSH (mU/l)] x 10
  - A high molar ratio (> 1.0) is present in about 80% of TSHomas.
  - molar ratios ranging from 0.3 in normal men to 29.1 in postmenopausal women
  - calculation of the molar ratio cutoff must take the circulating levels of other pituitary glycoprotein hormones (LH and FSH) into account.

- **SHBG** are useful in differentiating TSHoma from RTH (lack specificity)

Eur Thyroid J. 2013 Jun;2(2):76-82.

Dynamic tests for differential diagnosis of TSHoma

- **TRH stimulation**
  - TRH 200 mcg bolus intravenously, sampling at 0, 20, 60, 90 and 120 min
    - Blunted TSH responses in TSHoma

- **T3 suppression test**
  - T3 80–100 mcg/day divided in 3 administrations for 10 days, sampling at 0, 5, and 10 days
    - A partial inhibition of TSH secretion after T3 suppression test is seen only in RTH patients

- TRH or T3 tests may not be available or suitable in elderly or cardiac patients

Front Endocrinol (Lausanne). 2021 Mar 31:12:656551.

Eur Thyroid J. 2013 Jun;2(2):76-82.

Somatostatin suppression test

TSHomas express somatostatin receptors (SSTR2, SSTR5)

	Previous Study Insight	Short-Term SSA Test Protocol
Drug and dose	SSA (e.g., long-acting octreotide) 20–30 mg i.m. every 28 days for 2–4 months	Sandostatin (short-acting octreotide) 100 mcg, administered sc every 8 hours, for a total of 3 doses
TSH Monitoring Timepoints	At 0 (baseline), and every 28 days just before the new injection	At 0 hr (baseline), 2 hr, 24 hr after the first injection
	• TSHoma: decrease of FT4 and FT3 levels in • RTH: did not respond	• **TSHoma**[1]: The 24 vs 2 hr TSH suppression ratio >44.46% • **RTHB**[2]**:** The 24 vs 0 hr TSH and FT3 suppression < 30%

Clin Endocrinol (Oxf). 2005 Feb;62(2):176-81.

1 Thyroid. 2020 Sep;30(9):1236-1244

2 Medicine (Baltimore). 2019 Mar;98(9):e14675

Resistance to Thyroid Hormone Beta

A rare endocrine disorder where target tissues have reduced sensitivity to thyroid hormone

Characterized by: High FT3, FT4, Non-suppressed or normal TSH

Epidemiology

- First described by **Refetoff in 1967**.
- Estimated prevalence: **1 in 40,000**.

Clinical Features

- Highly **variable presentation** — from **asymptomatic** to **multiple symptoms**.
- Common signs: **Goiter**, **thyrotoxicosis**, **color blindness**, **somatic defects, CNS involvement**

Front Endocrinol (Lausanne). 2021 Mar 31:12:656551.

Medicine 98(9):p e14675, March 2019.

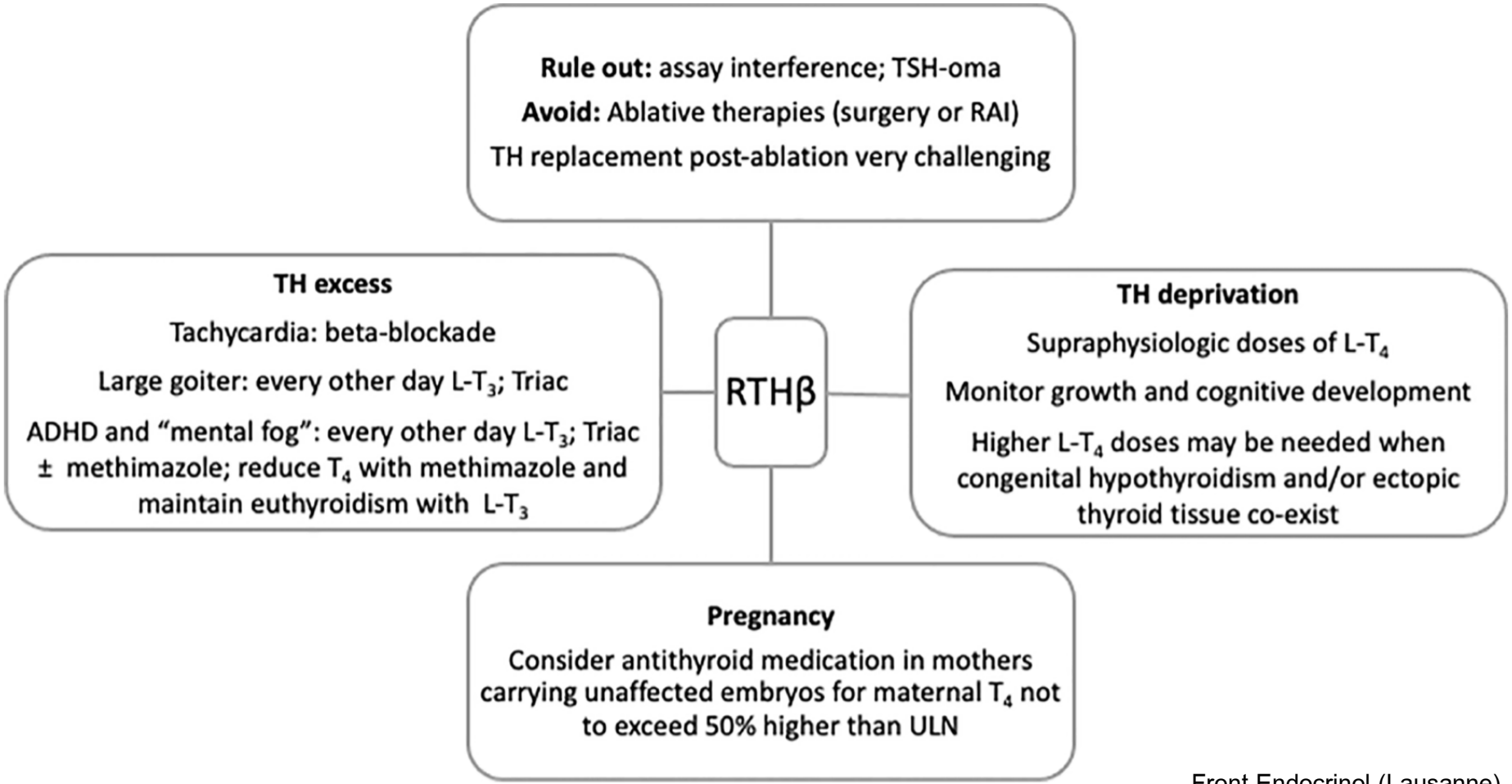
Resistance to Thyroid Hormone Beta

Genetic Cause

- Mainly caused by mutations in the **thyroid hormone receptor beta (*THRB*) gene**.
- The inheritance of RTHB is typically autosomal dominant
- In 14% of RTHB cases, *THRB* mutations are absent, possibly due to mosaicism or mutations in regulatory elements(enhancers, repressors or cofactors).

Front Endocrinol (Lausanne). 2021 Mar 31:12:656551.
Medicine 98(9):p e14675, March 2019.

Resistance to Thyroid Hormone Beta



Front Endocrinol (Lausanne). 2021 Mar 31:12:656551.

TAKE HOME MESSAGES

- **Combined clinical evaluation and gene testing** is crucial for diagnosing RTHB.
- **Do not mistake** RTHB for hyperthyroidism—recognizing RTH is crucial to avoid unnecessary antithyroid drugs or thyroid ablation.