

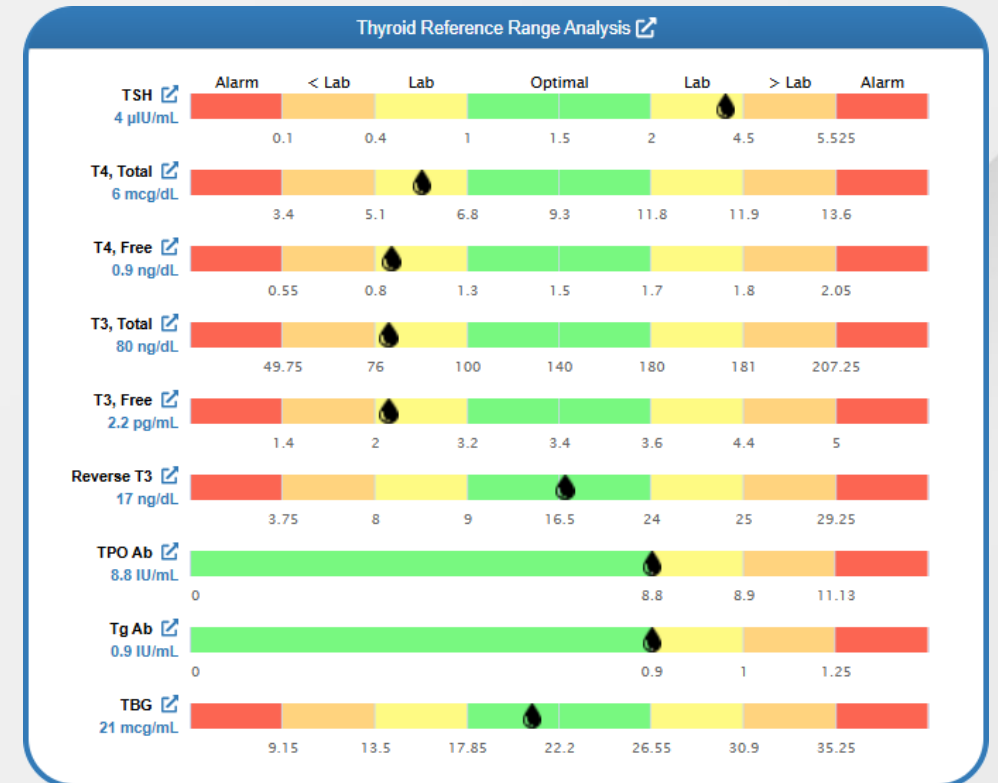
The Thyroid Physiology Framework

A Systems-Based Approach to Interpreting Thyroid Labs Across Five Areas of Physiology

Presented by:

MaryAnn Marks

Founder and CEO





MaryAnn Marks

Founder and CEO



- 🔴 **Founder of LabSmarts**, a bio-individual blood work interpretation software
- 🔴 **Educator dedicated to helping practitioners** move toward physiology-based interpretation
- 🔴 **Leveraging my background in tech** to simplify complex lab data into actionable insights





Learning Objectives

By the end of this session, you will be able to:

- 🔥 Recognize why **basic functional thyroid panels still miss important physiology**
- 🔥 Describe the **five key areas of thyroid physiology**
- 🔥 Identify the **essential blood markers** required and how each maps to a specific area of thyroid physiology
- 🔥 Apply a **physiology-based framework** to pinpoint the location of dysfunction



How to Approach Thyroid Interpretation

Step 1: Ask the question

- 🔥 Start with the right **clinical question** (conventional vs. functional)

Step 2: The Evaluation Process

- 🔥 Evaluate the **five areas** of thyroid physiology
 - **Map** markers to each physiological area
 - Pinpoint the **location** of dysfunction

Step 3: The Result

- 🔥 Identify the **root cause of dysfunction** in your client's physiology

Step 4: The Goal

- 🔥 **Improve client outcomes**



Two Key Thyroid Clinical Questions

Are there enough free thyroid hormones to adequately run metabolism?
If not, where in thyroid physiology is the dysfunction occurring?

To answer, we must measure and understand thyroid physiology:

- 1 Signaling → 
- 2 Production → 
- 3 Transport →  Thyroid Hormones
- 4 Conversion → 
- 5 Utilization → 



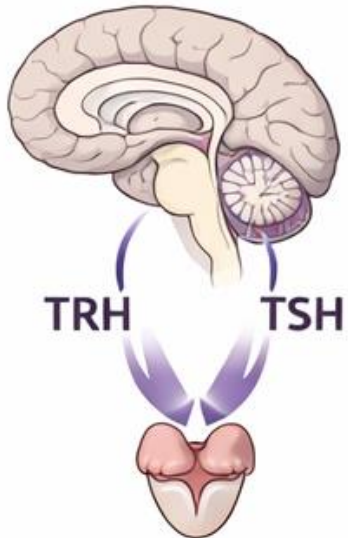
5 Areas of Thyroid Physiology

1



Signaling

HPT axis
regulation





5 Areas of Thyroid Physiology

1



Signaling

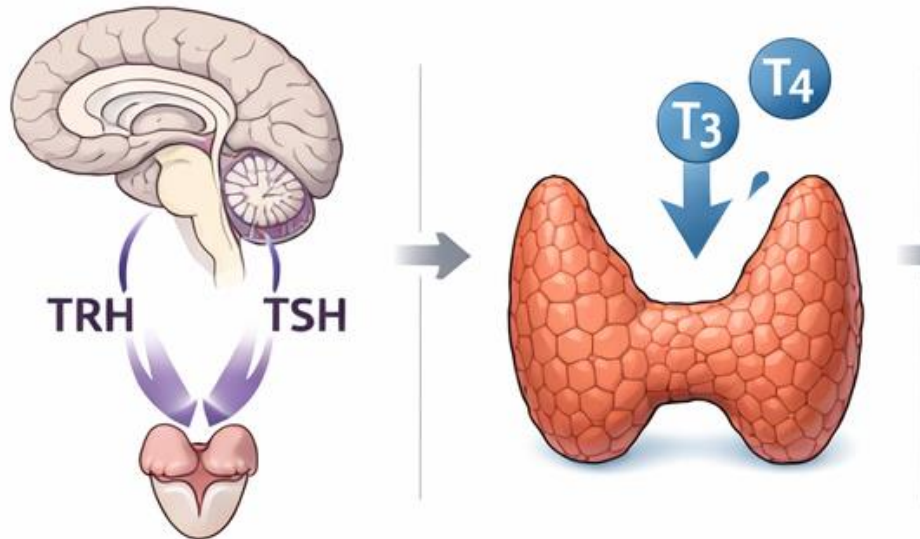
HPT axis
regulation

2



Production

Hormone synthesis
(requires nutrients)





5 Areas of Thyroid Physiology

1



Signaling

HPT axis regulation

2



Production

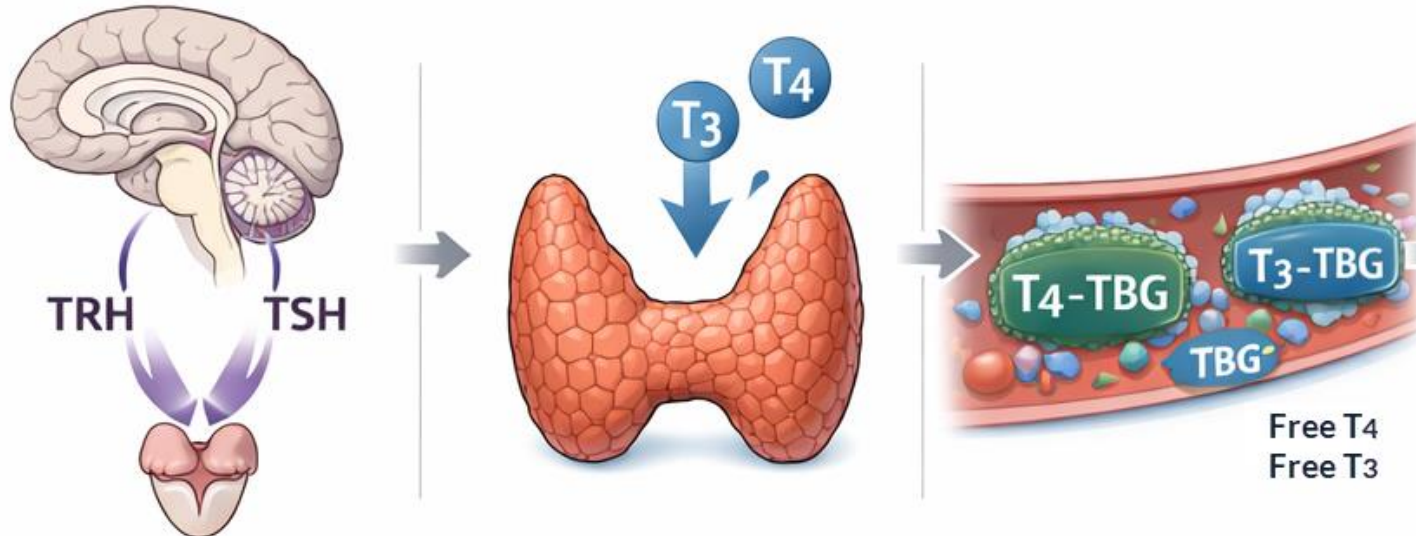
Hormone synthesis (requires nutrients)

3



Transport

Binding proteins regulate free levels





5 Areas of Thyroid Physiology

1



Signaling

HPT axis regulation

2



Production

Hormone synthesis (requires nutrients)

3



Transport

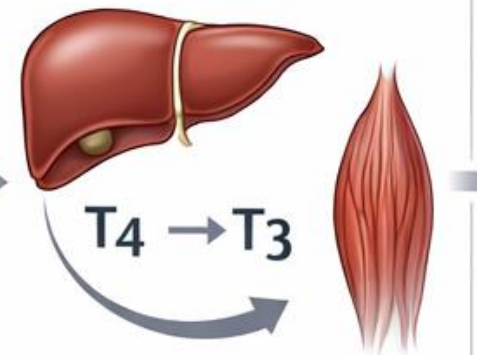
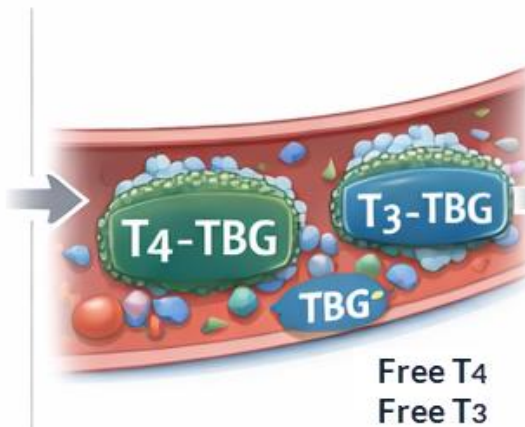
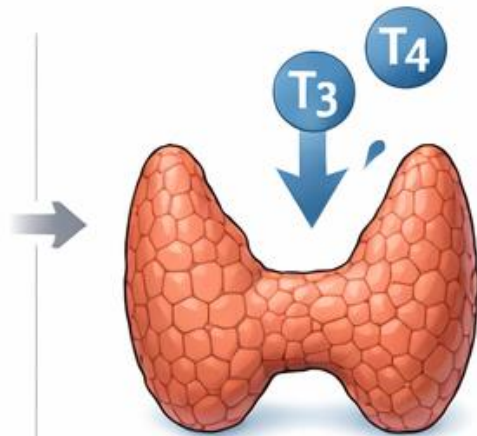
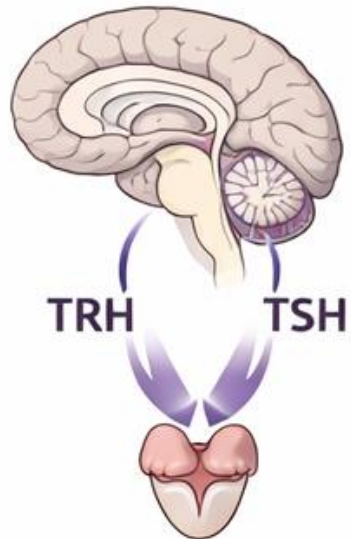
Binding proteins regulate free levels

4



Conversion

Peripheral conversion (liver/kidneys/gut)





5 Areas of Thyroid Physiology

1



Signaling

HPT axis regulation

2



Production

Hormone synthesis (requires nutrients)

3



Transport

Binding proteins regulate free levels

4



Conversion

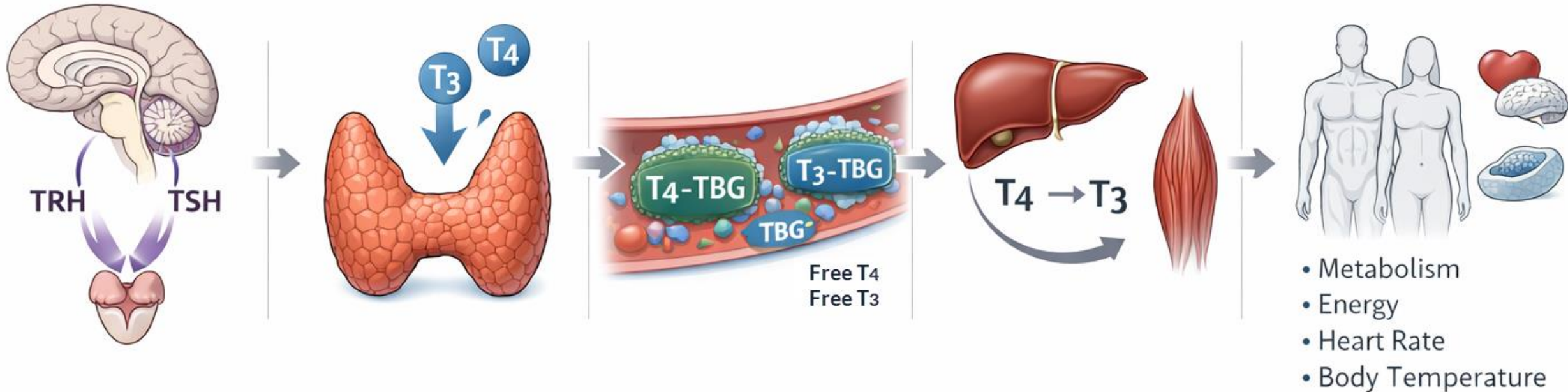
Peripheral conversion (liver/kidneys/gut)

5



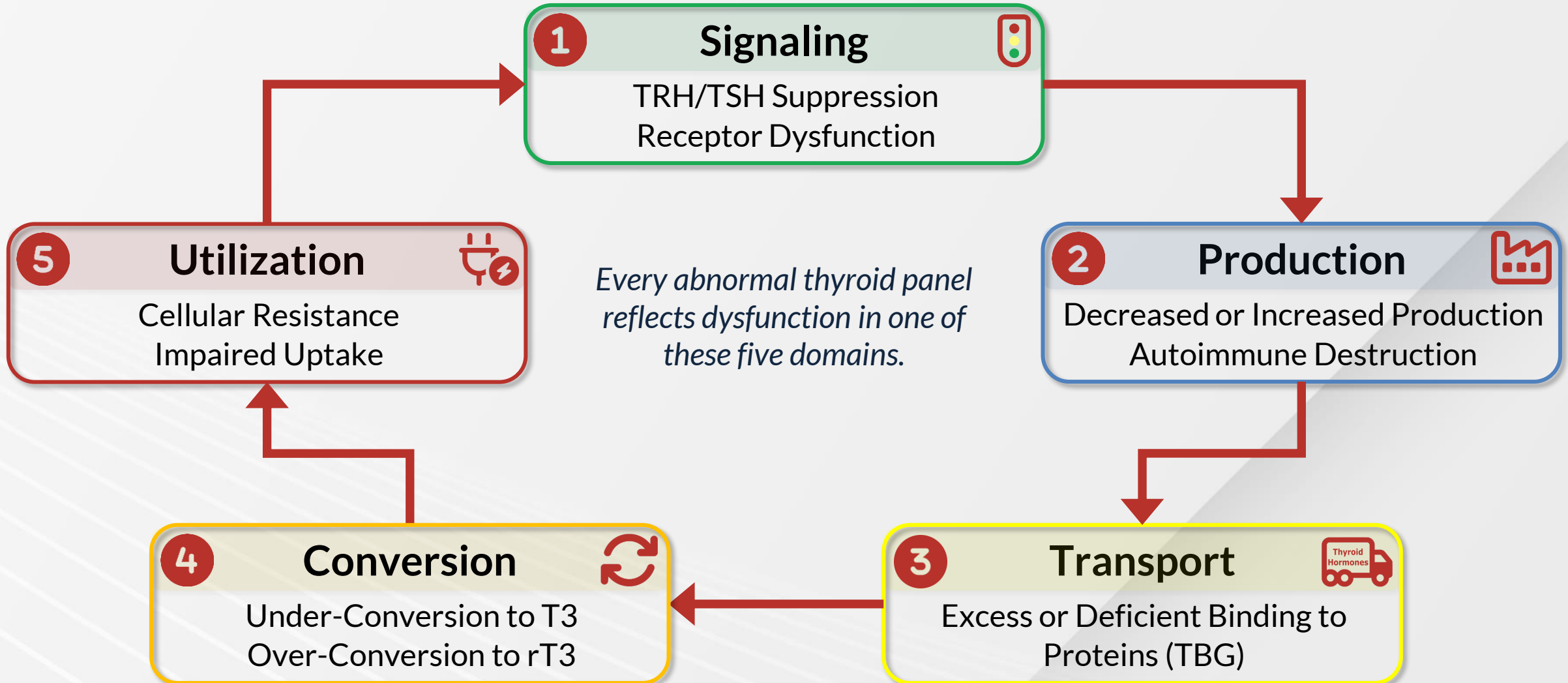
Utilization

Cellular uptake (receptor binding)





Key Dysfunctions in Each Area





Conventional Medicine Question

Conventional medicine approaches thyroid testing with a basic clinical question:

Is the thyroid producing too little or too much hormone?

They do not ask if there's enough T3 to run metabolism.

Conventional medicine asks a production question.
Physiology asks a systems question.

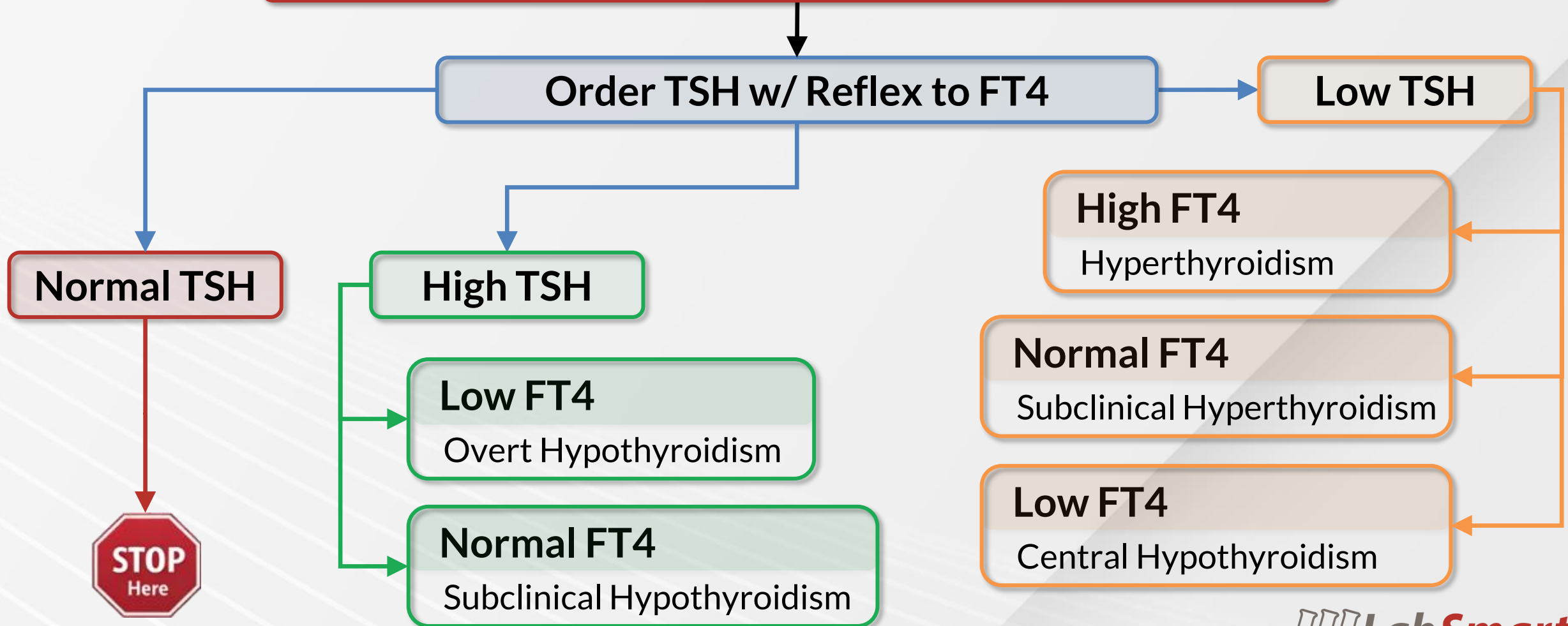
Wilson SA, Stem LA, Bruehlman RD. Hypothyroidism: Diagnosis and Treatment. *Am Fam Physician*. 2021;103(10):605-613. PMID: [33983002](#)

Henze M, Brown SJ, Hadlow NC, Walsh JP. Rationalizing Thyroid Function Testing: Which TSH Cutoffs Are Optimal for Testing Free T4? *J Clin Endocrinol Metab*. 2017;102(11):4235-4241. PMID: [28938415](#)



Conventional Medicine Algorithm

Is the thyroid producing too little or too much hormone?





Functional Reasoning Goes Further

Functional health recognized that the conventional question did not go far enough.

So, the question expanded to:

**Are there enough free thyroid hormones to run metabolism,
and is autoimmunity the cause?**

And the lab panel expanded to:

Basic Functional Thyroid Panel

TSH, FT4, FT3, TPOAb, TgAb



Basic Functional Thyroid Panel



Signaling

TSH

Thyroid Stimulating Hormone
Pituitary signal to thyroid



Utilization

FT3

Free Triiodothyronine
Biologically active hormone



Production

FT4

Free Thyroxine
Available to tissues for conversion



Production (Destruction)

TPOAb

Thyroid Peroxidase Antibodies
Antibodies to TPO enzyme

FTI

Free Thyroxine Index
FT4 estimate (TT4 x T3U/100)

TgAb

Thyroglobulin Antibodies
Antibodies to Tg protein

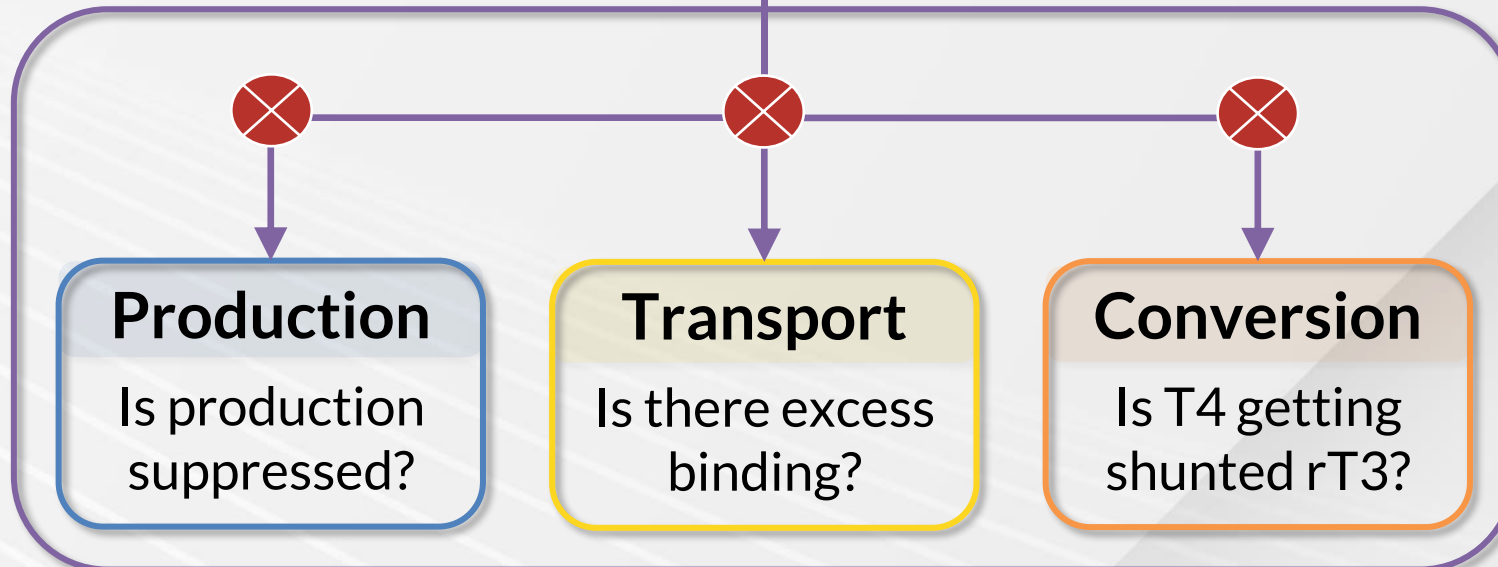


Blind Spots in the Basic Panel

What Happens if...

1. FT4 + FT3 are low
2. TSH is high
3. TPOAb + TgAb are negative

Blind Spots in Physiology



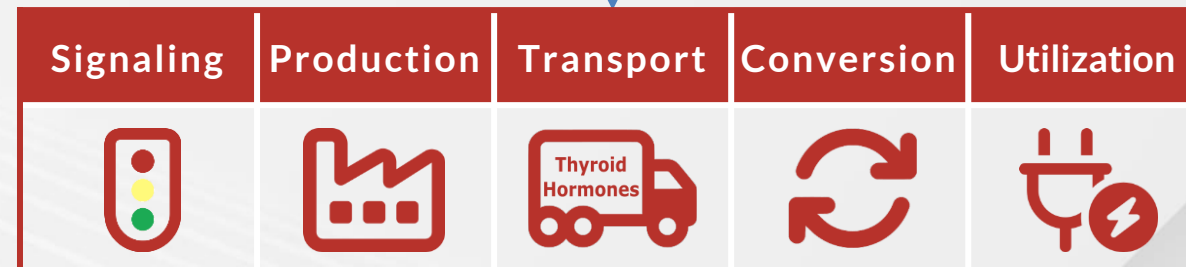


Comprehensive Thyroid Panel

Where is thyroid physiology failing?

Comprehensive Thyroid Physiology Panel

TSH, FT4, FT3, TPOAb, TgAb, TT4, TT3, rT3, TBG



Pinpoint Root Causes



Key Additional Markers



Production

TT4

Total Thyroxine
Bound & unbound to proteins

TT3

Total Triiodothyronine
Bound & unbound to proteins



Thyroid
Hormones

Transport

TBG

Thyroxine Binding Globulin
Major protein bound to T4 & T3

T3U

T3 Uptake
TBG binding capacity, TBG inverse



Conversion

rT3

Reverse Triiodothyronine
Inactive T3, competes w/ FT3



TSH Receptor Antibodies



Signaling

TSI

Thyroid-Stimulating Immunoglobulin

Binds to TSH receptor, increasing hormone production

TRAb

TSH Receptor Antibodies

TRAb = TSI + TBI (thyroid-blocking immunoglobulin)

TSI and TRAb are follow-up tests, not baseline markers.



Thyroid Dysfunction Is a Physiology Problem

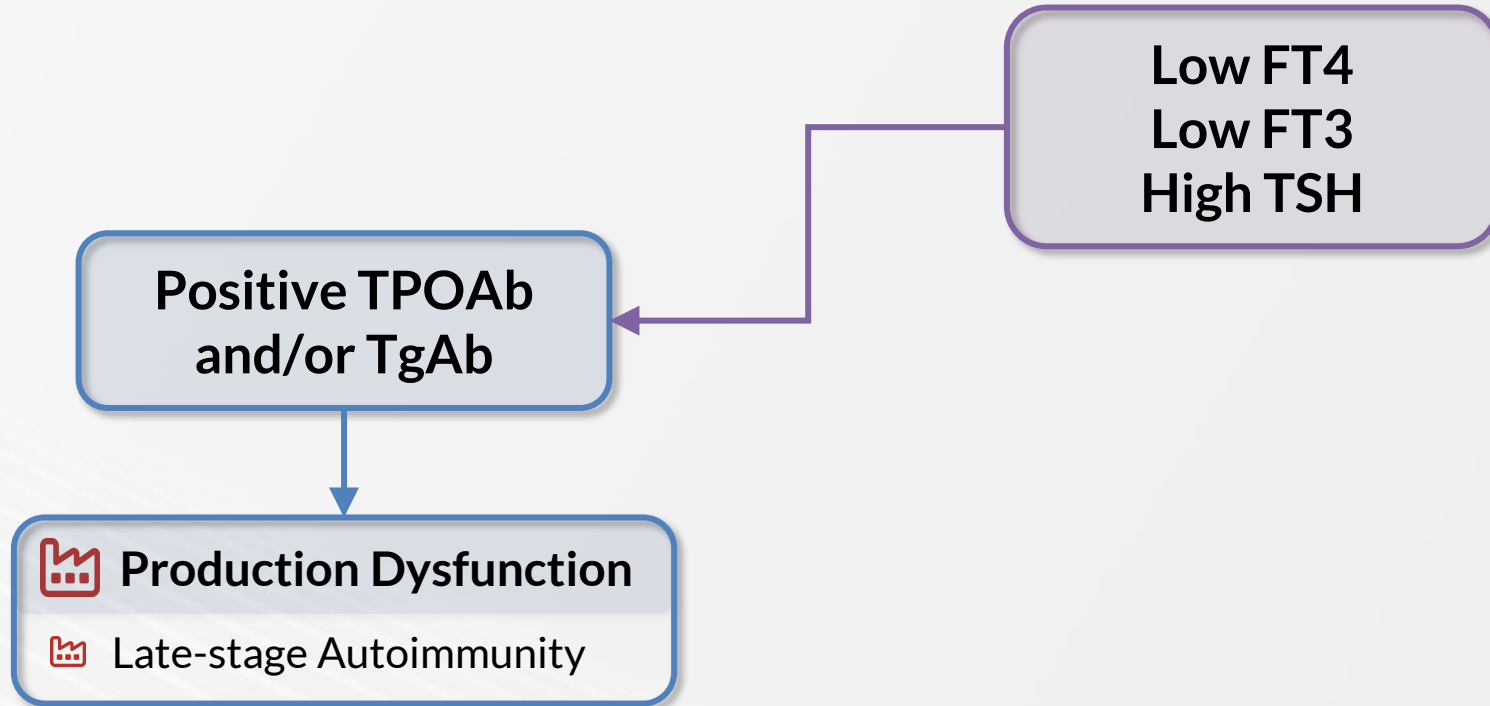
Every abnormal thyroid panel is a physiology puzzle.

Accurate interpretation requires identifying **where physiology is breaking down.**

An efficient way to do that is by using decision trees.



Positive Antibodies = Autoimmunity





No Autoimmunity? Where's Dysfunction?

Low FT4
Low FT3
High TSH

Negative TPOAb
Negative TgAb

Where is thyroid physiology failing?





Low Free + Low Totals


Low FT4
Low FT3
High TSH

Negative TPOAb
Negative TgAb

Low TT4 + Low TT3

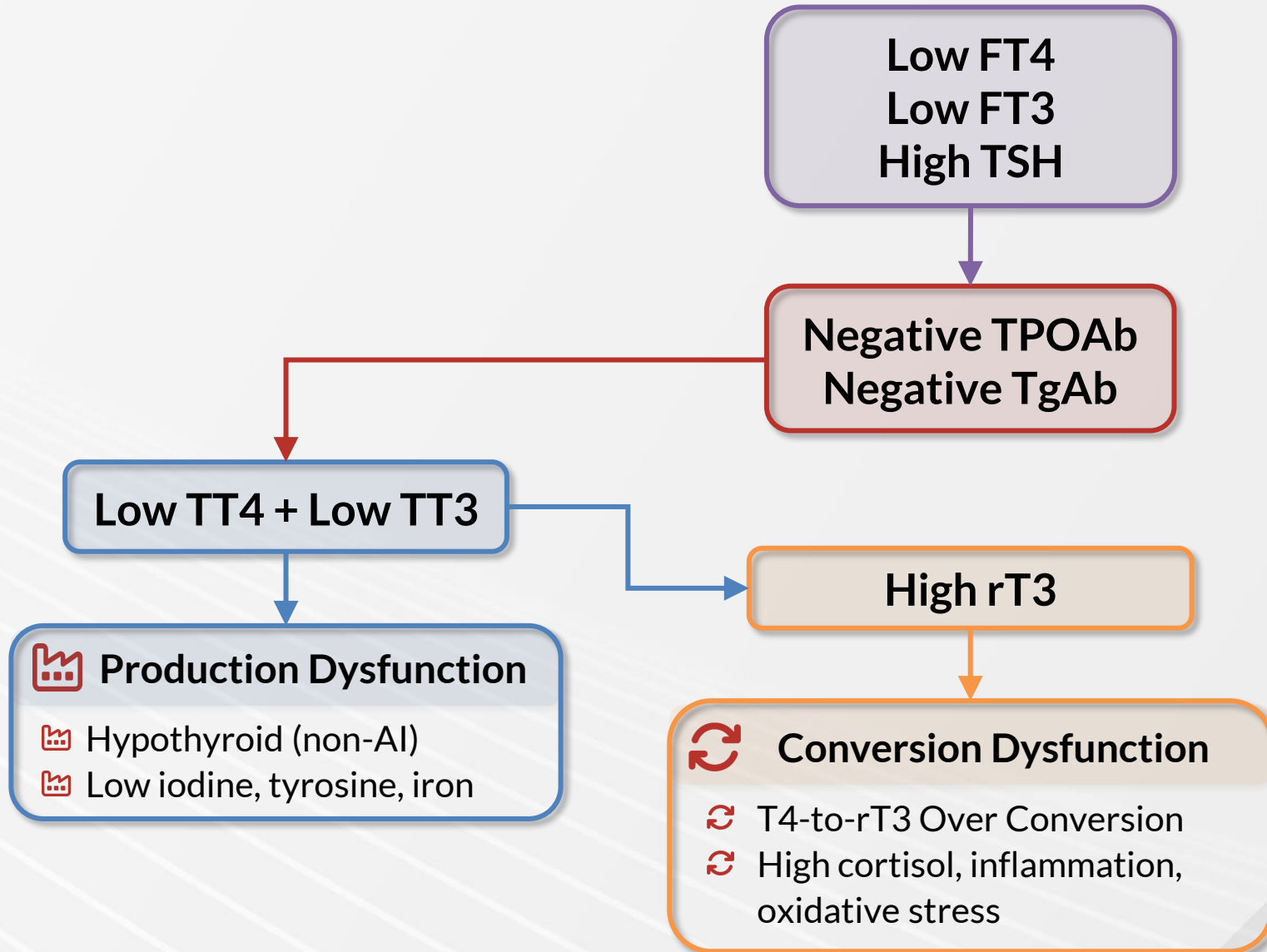
 **Production Dysfunction**

 Hypothyroid (non-AI)

 Low iodine, tyrosine, iron

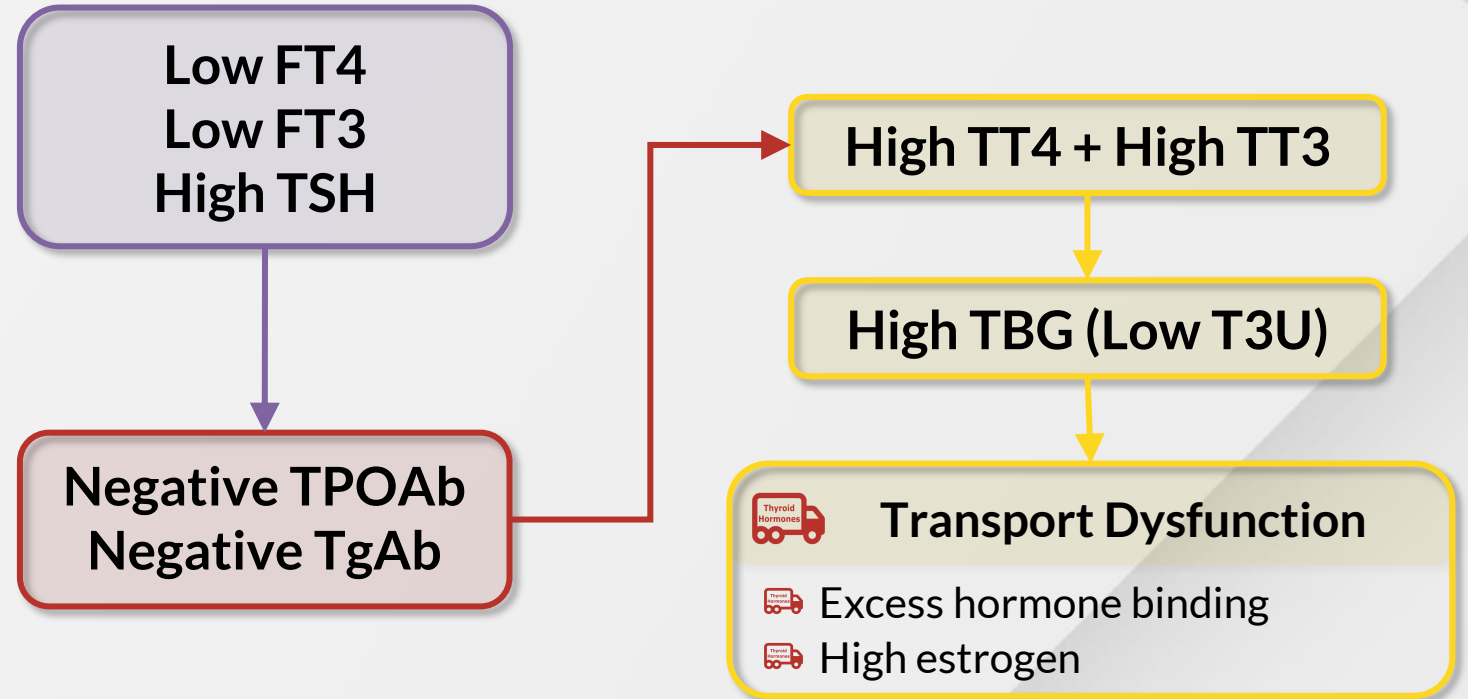


Low Free + Low Totals + High rT3



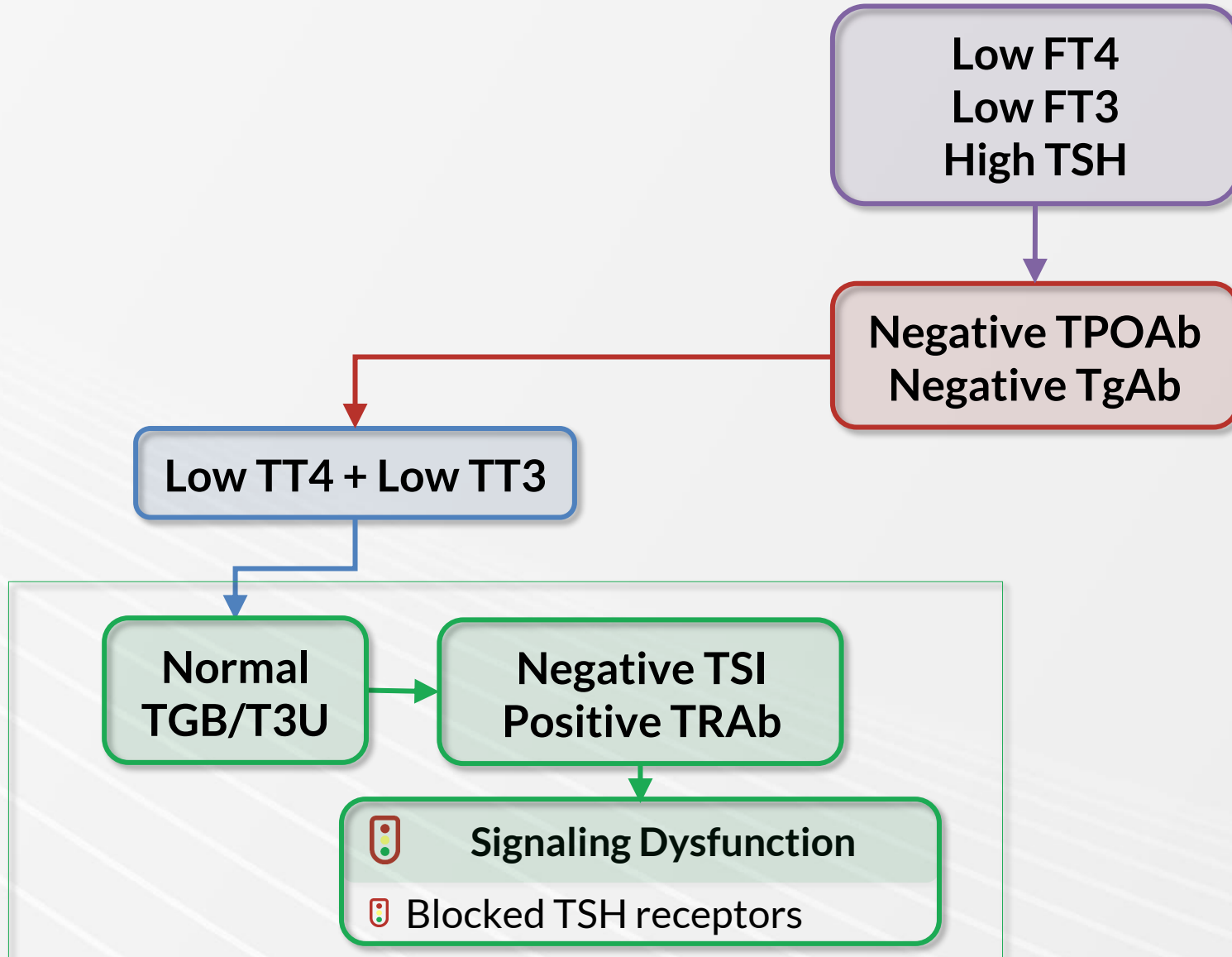


Low Free + High Totals + High TBG





TSH Receptor Antibody Testing



TSI and TRAb are **follow-up tests, not baseline markers.**

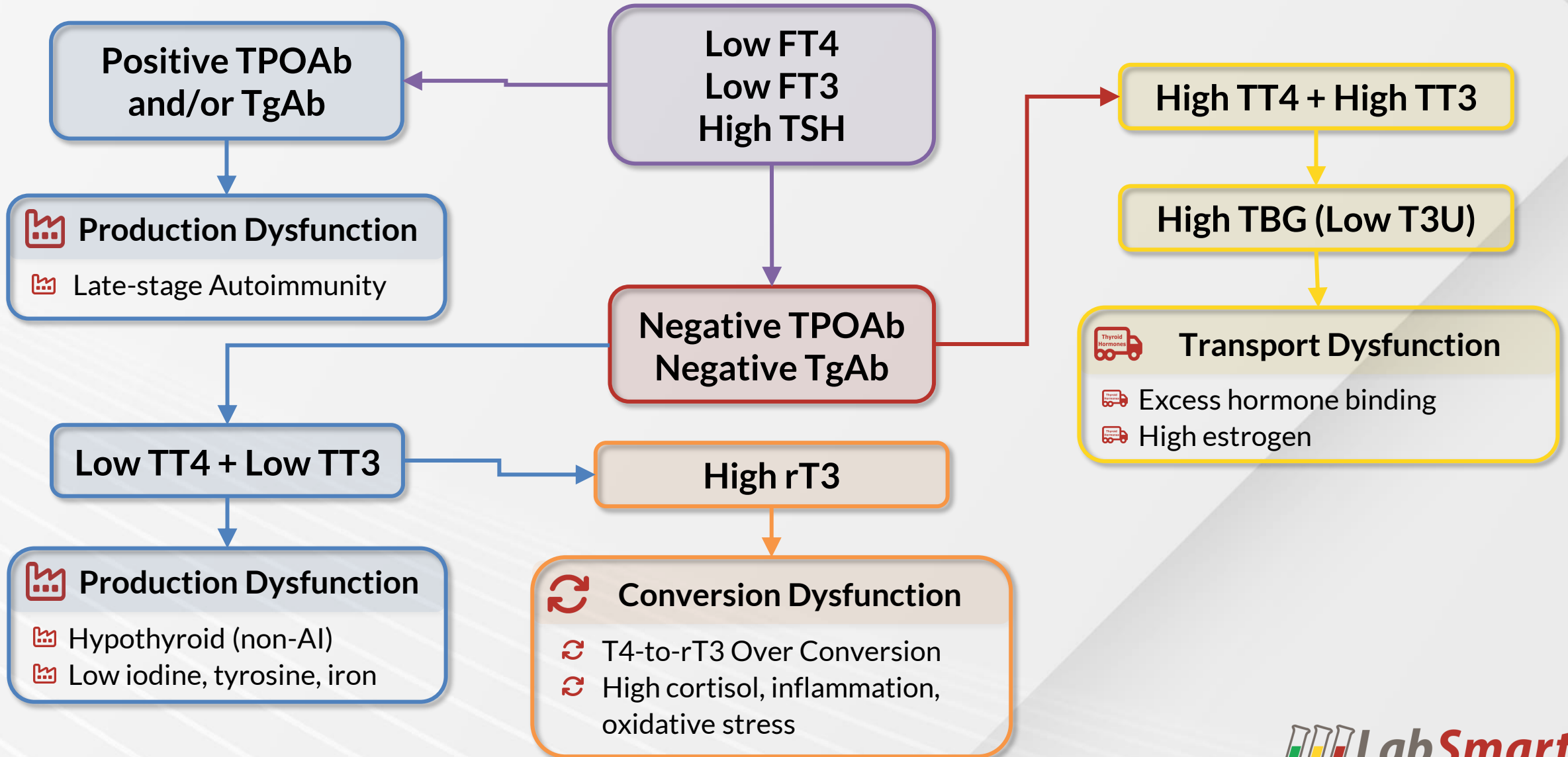
Evaluate first:

- Iodine, tyrosine, and iron status
- TBG and thyroid hormone transport
- Inflammatory drivers

If symptoms persist and the pattern remains unexplained, consider testing TSI and TRAb.



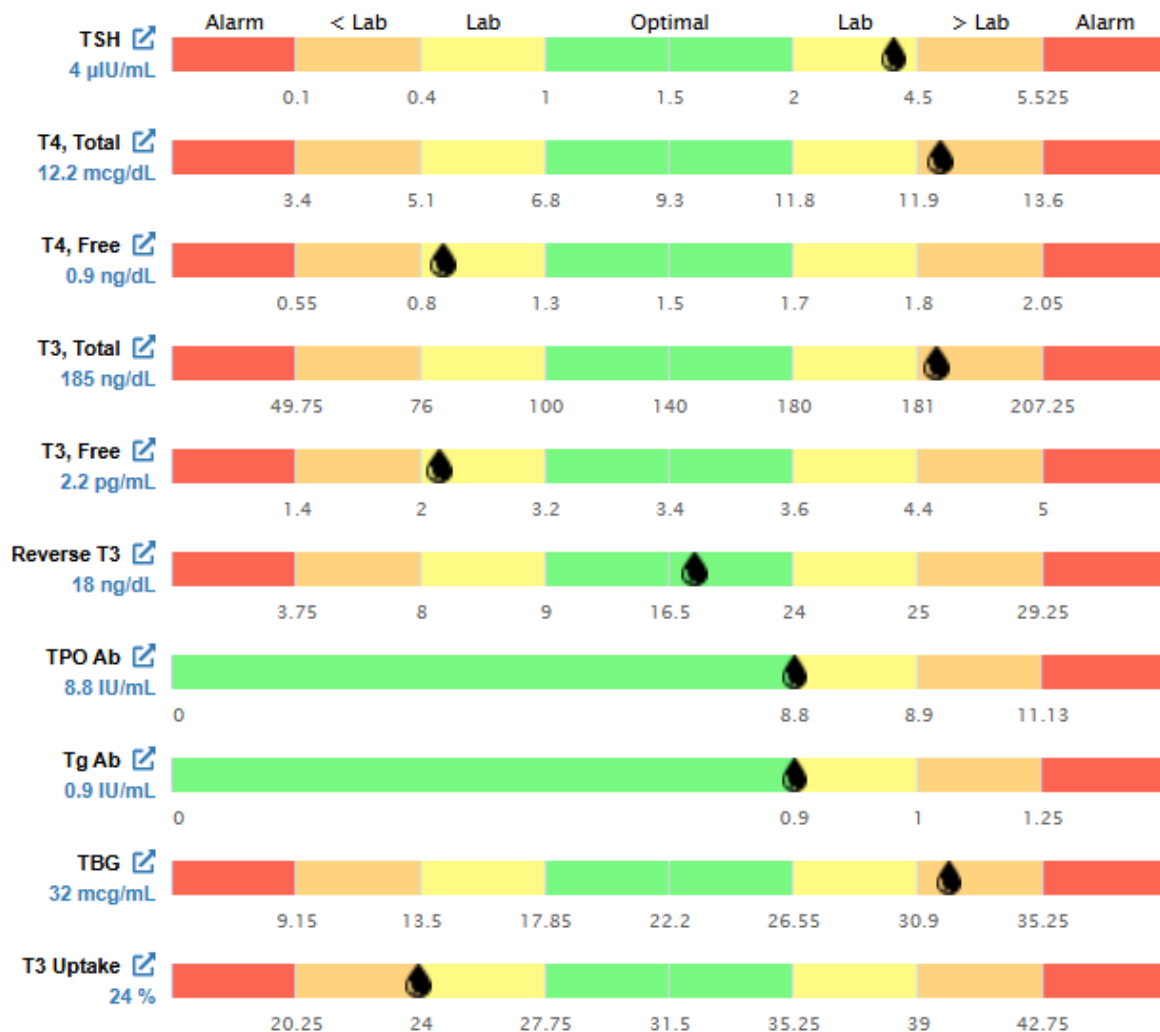
Low Free + High TSH Decision Tree





Case Study – Transport Dysfunction

Thyroid Reference Range Analysis



Pattern:

- Low FT4 + Low FT3 + High TSH
- High TT4 + High TT3
- High TBG (Low T3U)
- Autoimmune markers negative

Transport Dysfunction:

- Excess Thyroid Hormone Binding
- Excess estrogen increases TBG production, which binds more thyroid hormone and lowers the free fraction.

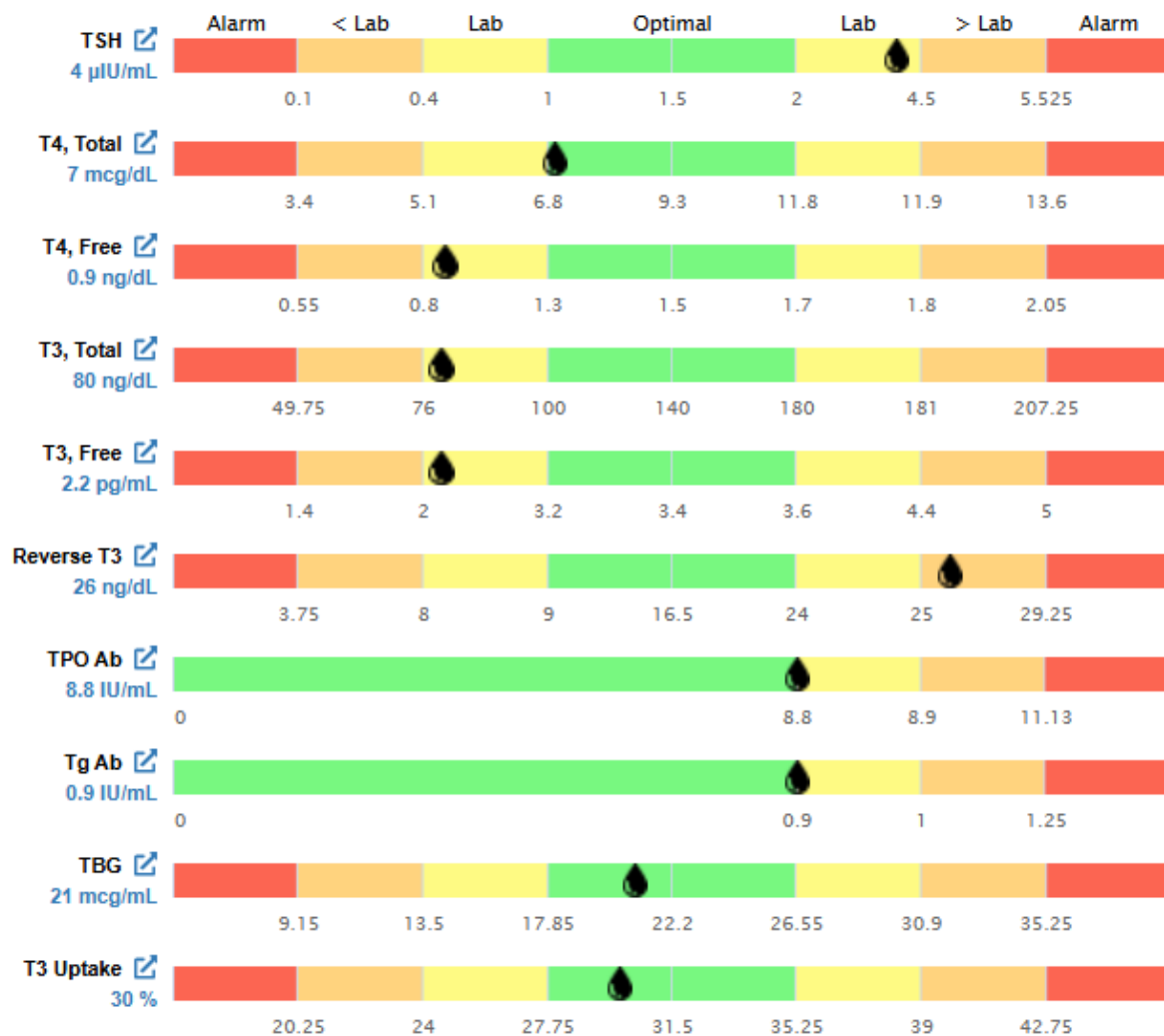
Hormones Reference Range Analysis





Case Study – Conversion Dysfunction

Thyroid Reference Range Analysis



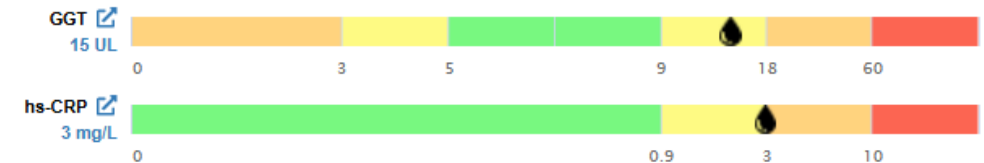
Pattern:

- Low FT4 + Low FT3 + High TSH
- Low-Opt TT4 + Low TT3
- High rT3
- Autoimmune markers negative

Conversion Dysfunction:

- T4-to-rT3 Over Conversion
- Inflammation and oxidative stress promote T4 conversion to rT3, reducing T4 conversion to T3.

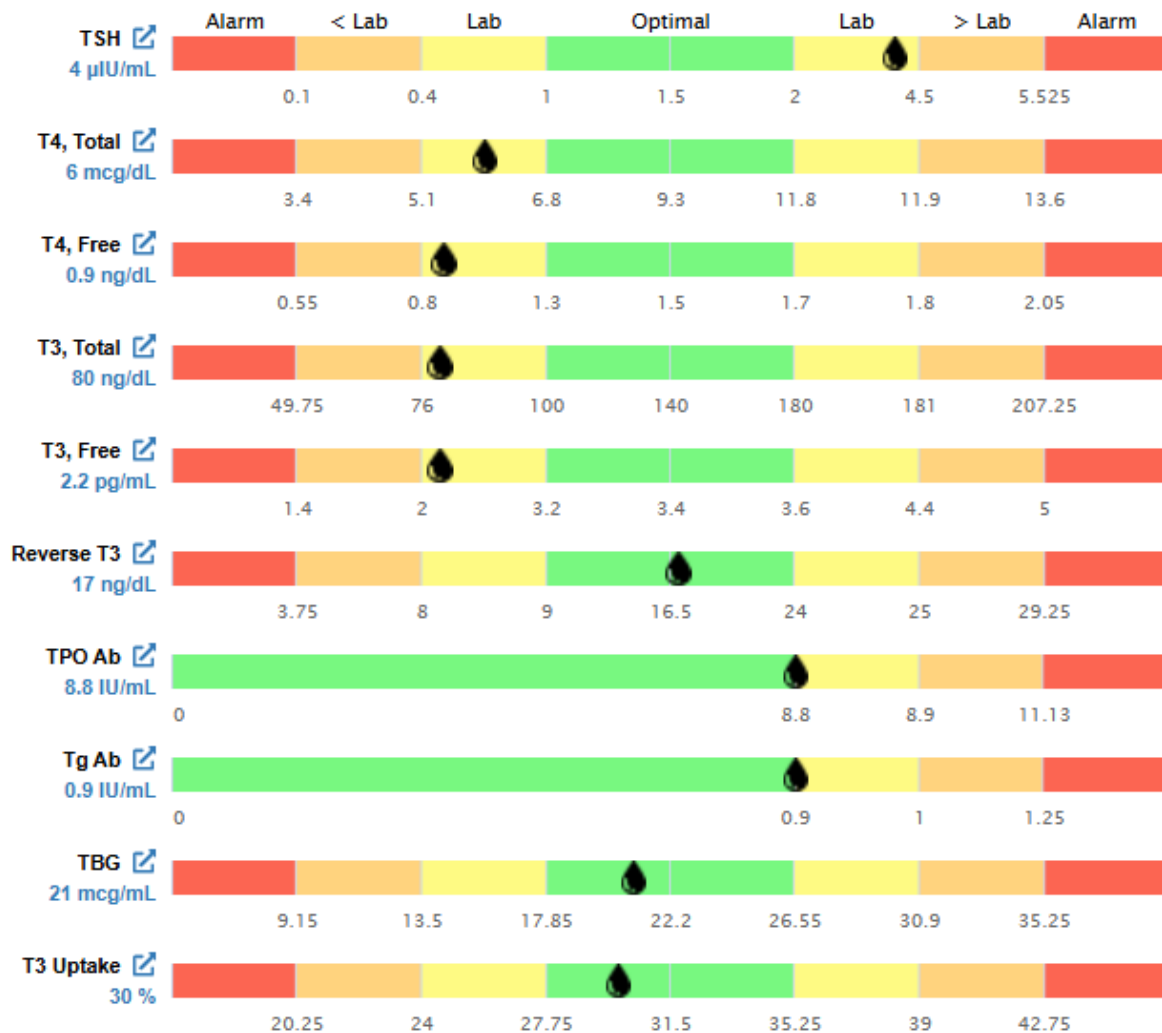
Inflammation / Oxidative Stress Reference Range Analysis





Case Study – Production Dysfunction

Thyroid Reference Range Analysis



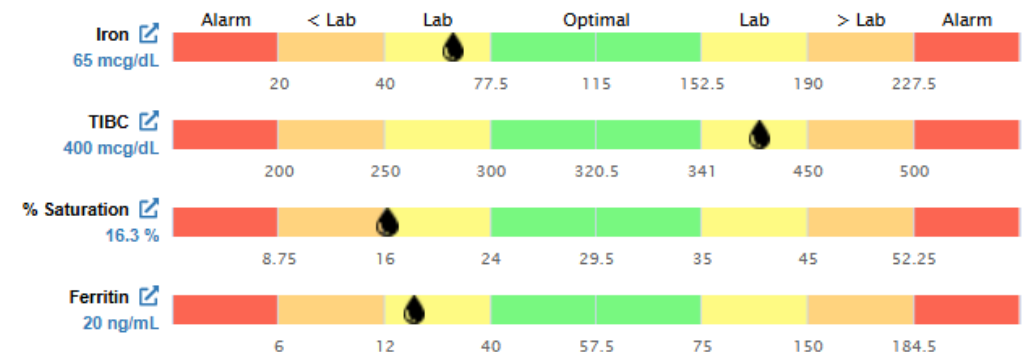
Pattern:

- Low FT4 + Low FT3 + High TSH
- Low TT4 + TT3
- Optimal rT3 + TBG
- Autoimmune markers negative

Production Dysfunction:

- Hypothyroid (non-AI)
- Iron is required for thyroid peroxidase (TPO).
- Low iron impairs TPO activity and reduces thyroid hormone production.

Iron Reference Range Analysis





Low FT4 + Low FT3 + Low TSH

Low FT4
Low FT3
Low TSH

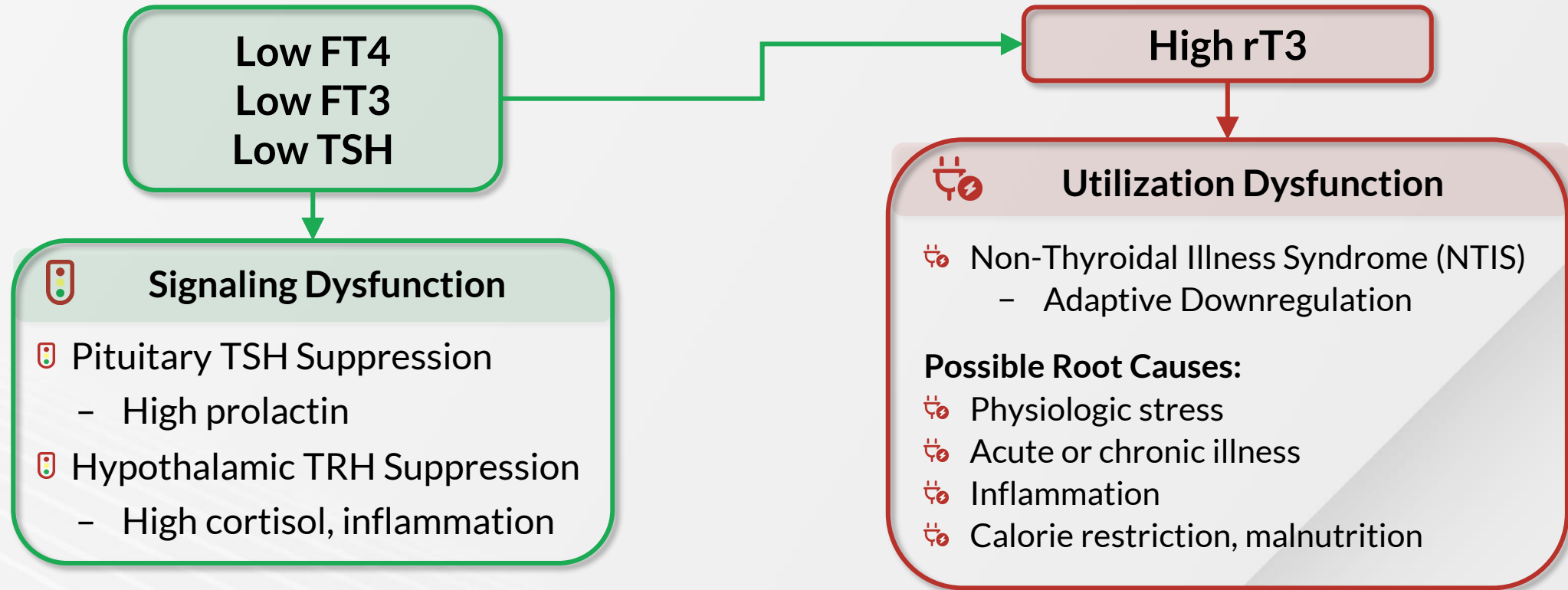


Signaling Dysfunction

- ⚠ Pituitary TSH Suppression
 - High prolactin
- ⚠ Hypothalamic TRH Suppression
 - High cortisol, inflammation



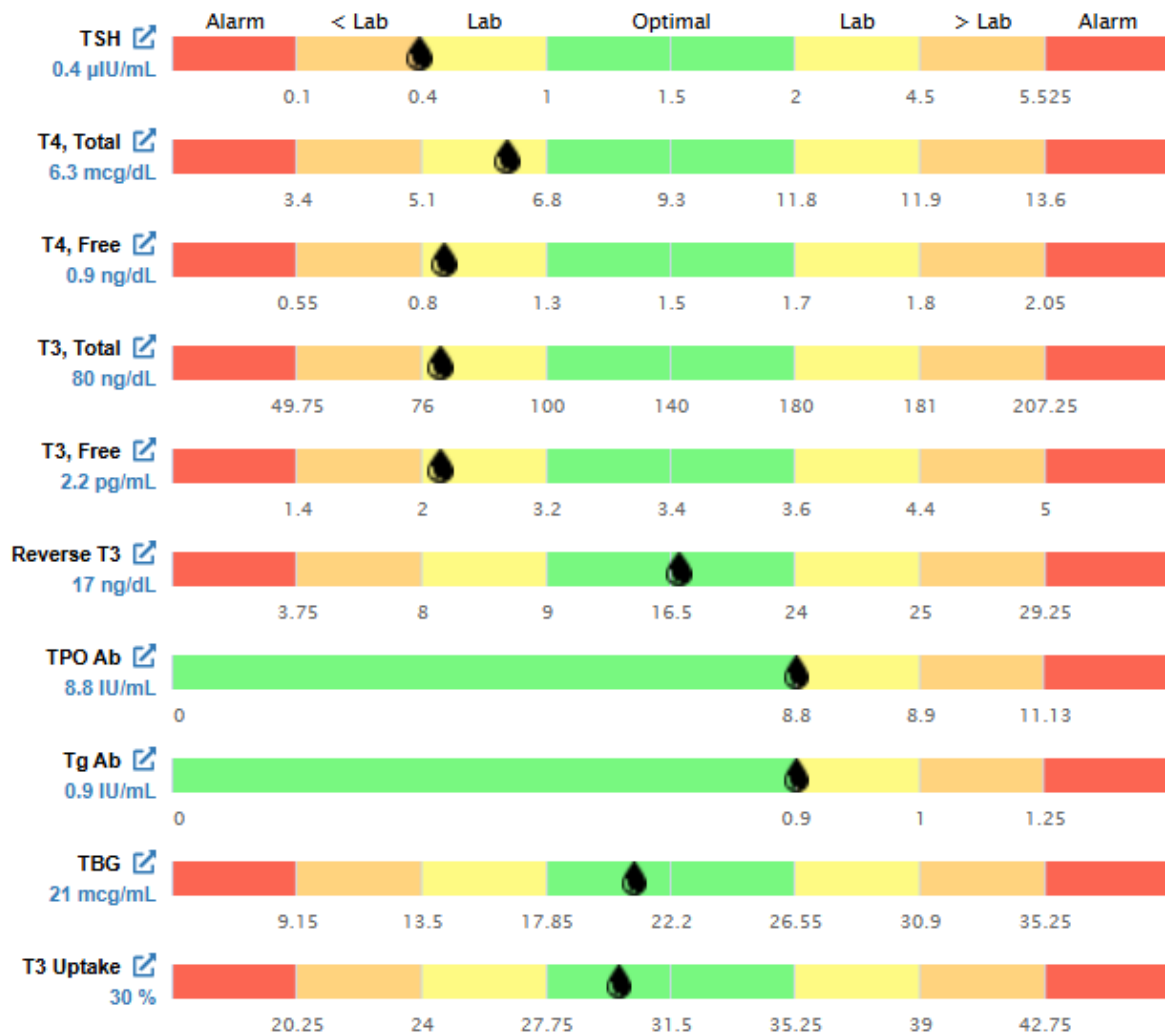
Low Free + Low TSH + High rT3





Case Study – Signaling Dysfunction

Thyroid Reference Range Analysis



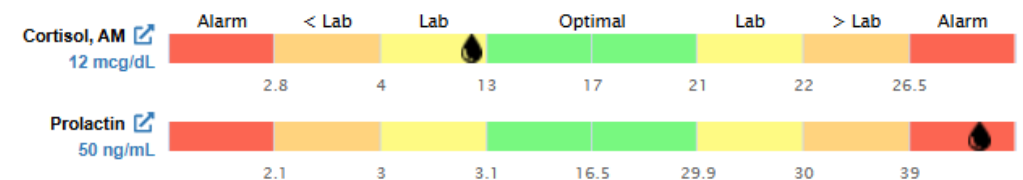
Pattern:

- Low FT4 + Low FT3 + Low TSH
- Low TT4 + Low TT3
- Optimal rT3 + TBG
- Autoimmune markers negative

Signaling Dysfunction:

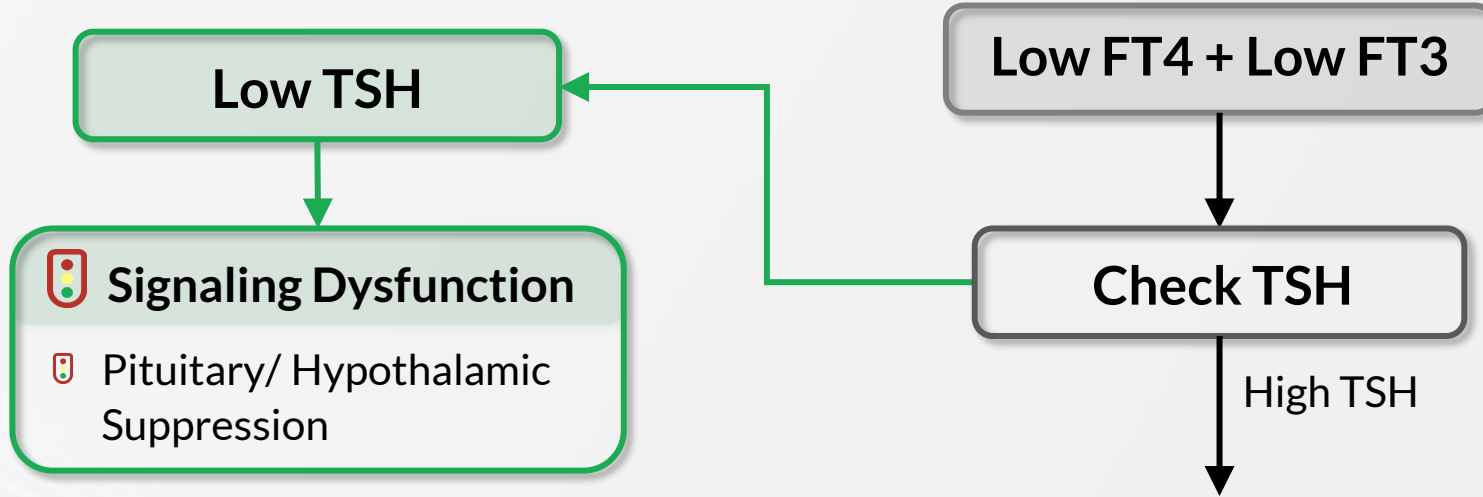
- Pituitary TSH Suppression (high prolactin)
- Hypothalamic TRH Suppression (high cortisol)

Hormones Reference Range Analysis



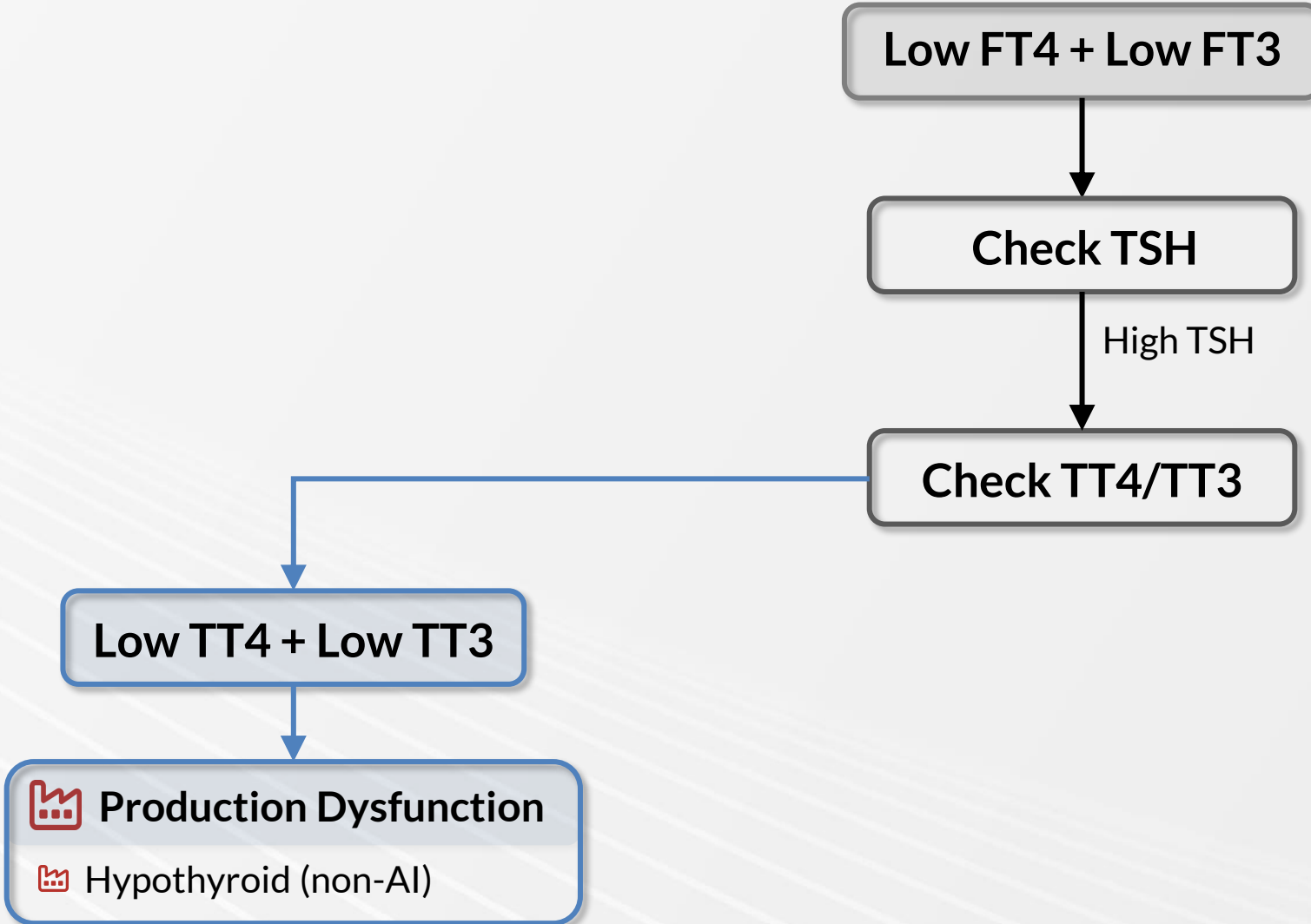


Low Free Decision Tree + No AI



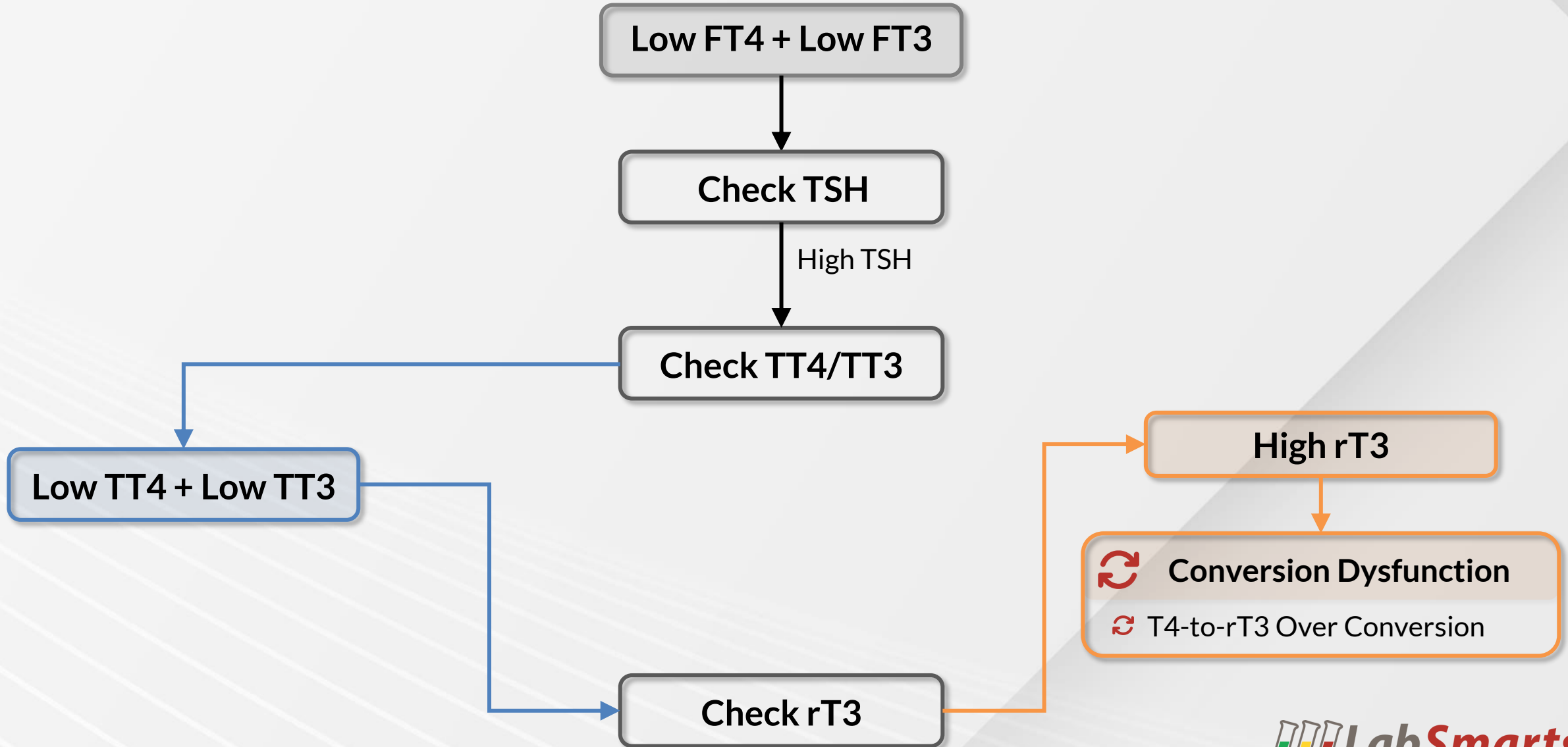


Low Free Decision Tree + No AI



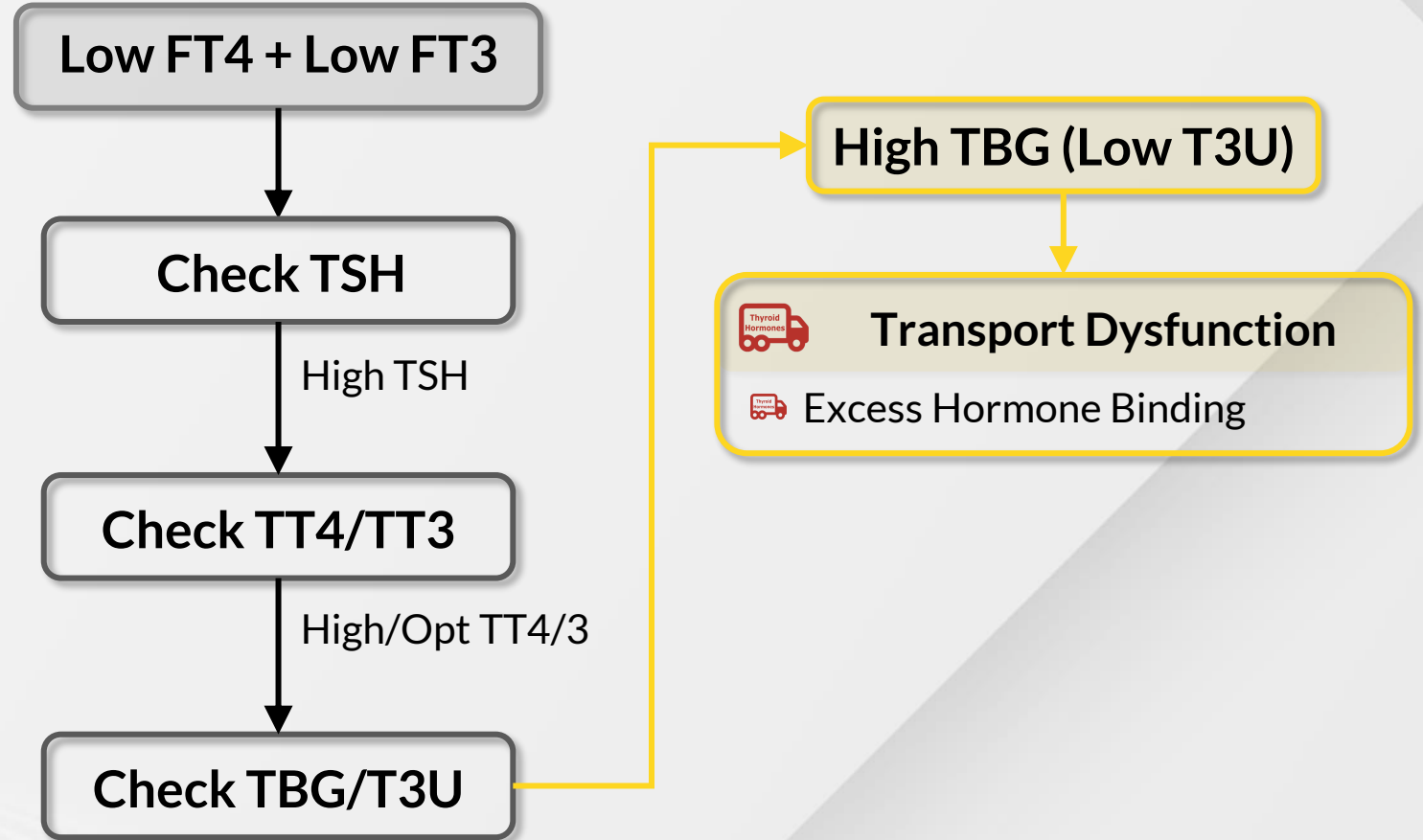


Low Free Decision Tree + No AI



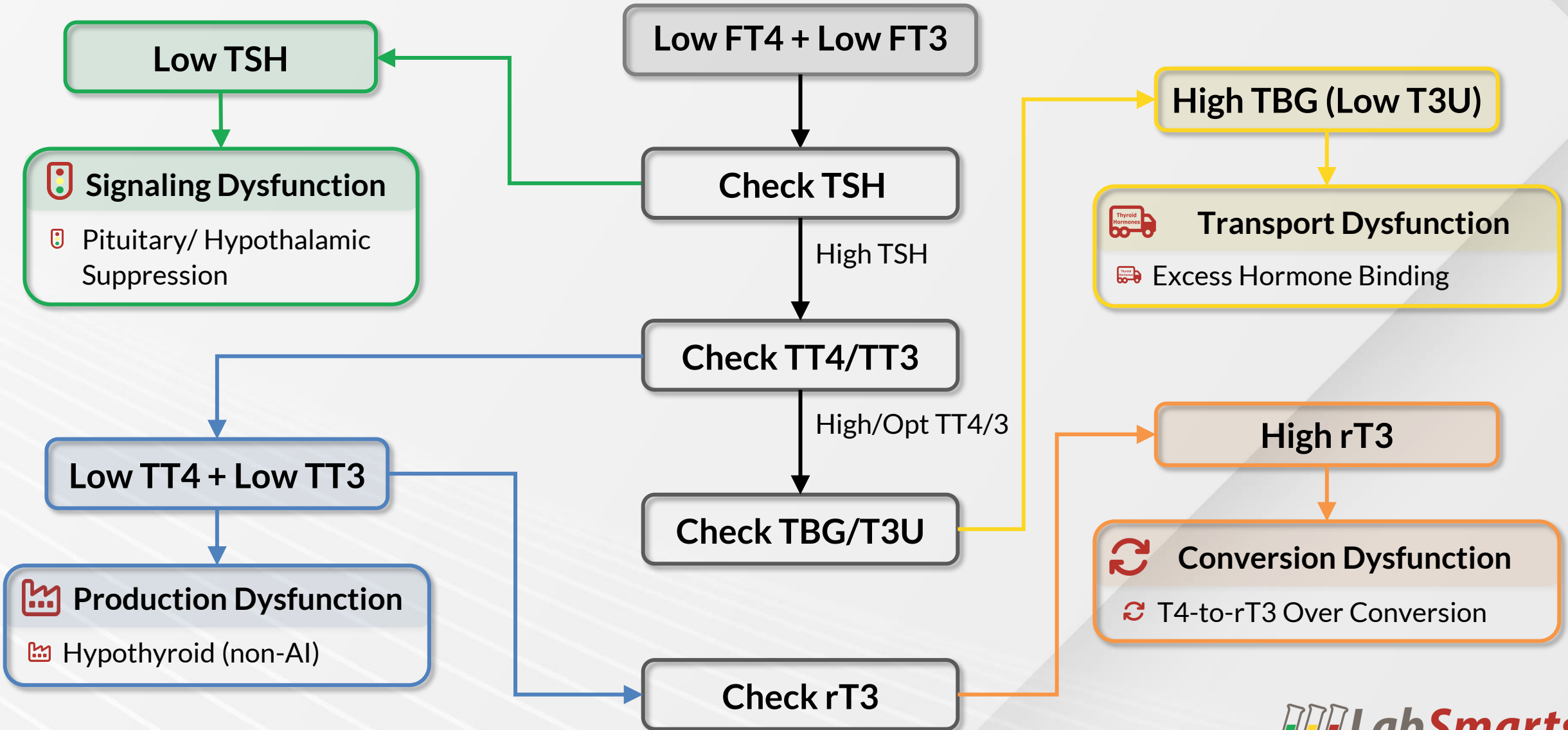


Low Free Decision Tree + No AI





Low Free Decision Tree + No AI





3 Levels of Thyroid Assessment

Conventional

Markers:

- 🔥 TSH w/ Reflex to FT4
- 🔥 Only if TSH is >5.0 or <0.3

Goal:

- 🔥 Disease screening
- 🔥 Overt Hypo/Hyperthyroidism

Question it Answers:

- 🔥 Is the thyroid producing too little or too much hormone?

Failure:

- 🔥 Misses early dysfunction
- 🔥 Can't identify location of dysfunction in physiology
- 🔥 Can't identify autoimmunity

Basic Functional

Markers:

- 🔥 TSH, FT4, FT3
- 🔥 TPOAb, TgAb

Goal:

- 🔥 Identify free hormone availability and autoimmunity

Question it Answers:

- 🔥 Are the active hormones low, and is the immune system attacking the gland?

Failure:

- 🔥 Can't identify of location of dysfunction in physiology

Comprehensive Functional

Markers:

- 🔥 Add-on: TT4, TT3, TBG, rT3
- 🔥 If needed: TSI, TRAb

Goal:

- 🔥 Map labs to the entire thyroid physiology system

Question it Answers:

















- 🔥 Where is the location of dysfunction in physiology?

Success:

- 🔥 Gets answers and improves outcomes



Blood Marker Physiology Mapping

Thyroid Blood Marker	What it Reveals in Physiology
 TSH	 The Brain's request for more hormone
 Total T4	 The Gland's actual production output
 TBG	 The efficiency of the Transport system
 Free T4	 What is available for conversion
 Reverse T3 (rT3)	 Diversion/shunting (The "Brake")
 Free T3	 Metabolic Activation (The "Gas")
 TPOAb and TgAb	 Immune system interference inside thyroid
 TSI and TRAb	 Immune system interference signaling to thyroid













A Physiology-Based Framework

Free hormones are a signal of imbalance within thyroid physiology.

Mapping a comprehensive panel to the 5-Area Framework reveals exactly where the system is breaking down.

This gives you a clear clinical roadmap for targeted client support.









Physiologic Domain	Thyroid Blood Markers
 Signaling	 TSH
 Production	 TT4, TT3, FT4, FTI, TPOAb, TgAb
 Transport	 TBG, T3U
 Conversion	 rT3
 Utilization	 FT3



Free Hormones Are Not Enough

Low FT4 and low FT3 do not tell us where dysfunction occurs.

Additional markers reveal the physiologic area.

Physiologic Domain	Thyroid Blood Marker Pattern
 Signaling	 Low TSH
 Production	 High TSH + Low TT4/TT3
 Transport	 High TSH + High TT4/TT3 + High TBG (Low T3U)
 Conversion	 High rT3

Same low free hormones → different physiology



Thyroid Dysfunction is a Physiology Problem

Thyroid labs are a map.

When you map markers to physiology,
you stop guessing.

You start pinpointing dysfunction.

And that changes clinical outcomes.



Apply This Framework in Practice

Create a FREE practitioner account in LabSmarts and start applying this framework to your clients' labs.

[LabSmarts.com/signup](https://labsmarts.com/signup)

Automated thyroid pattern analysis based on this framework is currently in development.