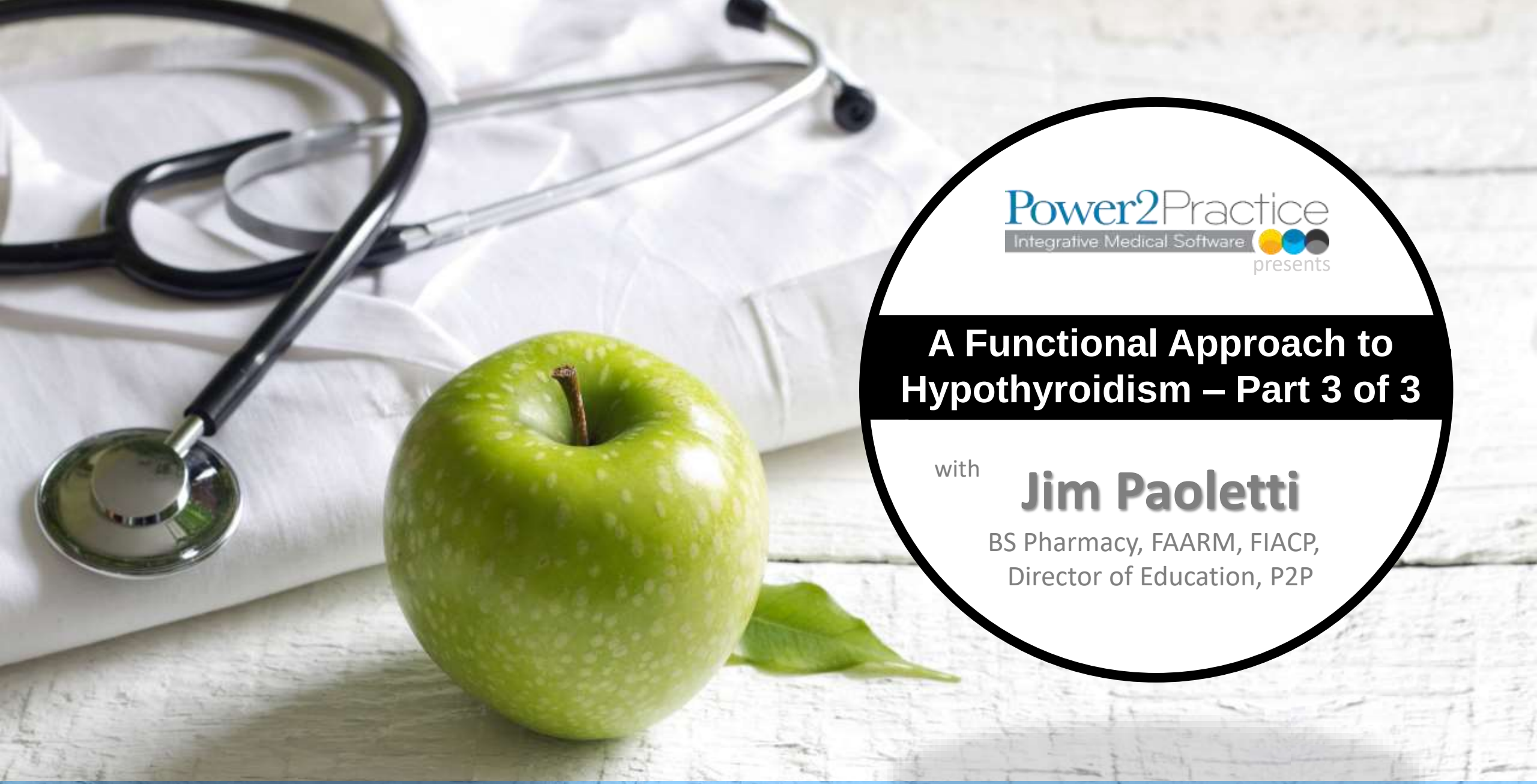


Power2Practice
Integrative Medical Software
presents

A Functional Approach to Hypothyroidism – Part 3 of 3

with

Jim Paoletti

BS Pharmacy, FAARM, FIACP,
Director of Education, P2P

- Clinical Consultant the Director of Education of Education at Power2Practice.
- 30 years of experience creating and using bio-identical hormone therapies in both retail pharmacy and clinical practice.
- Nationally recognized expert in pharmacy, BHRT and custom compounding.
- Previously served as Director of Provider Education for ZRT Laboratory and Education Director for the Professional Compounding Centers of America.

Jim Paoletti

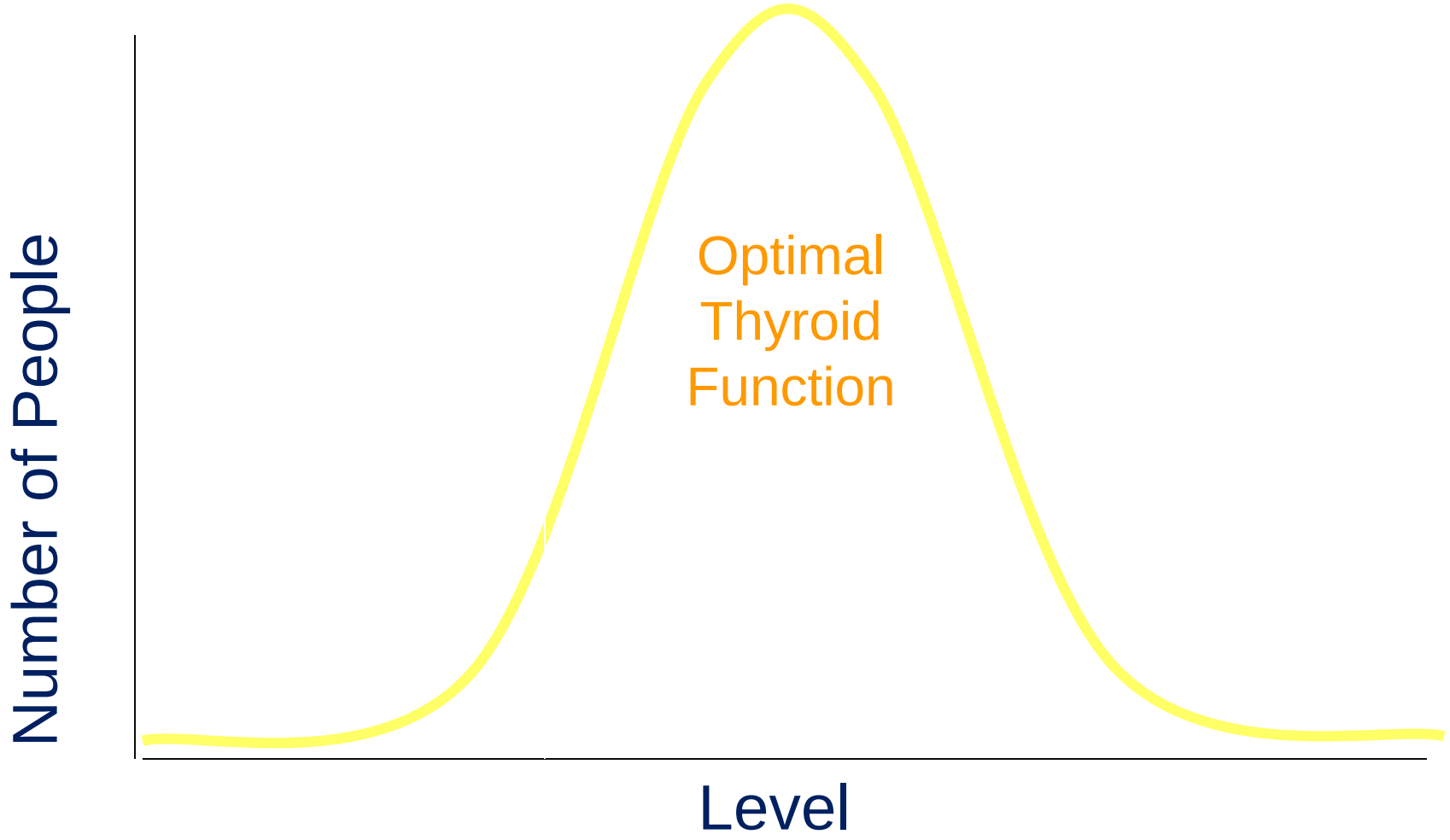
BS Pharmacy, FAARM, FIACP – Director of Education P2P

DON’T RELY SOLELY ON LAB TESTS

“Are not the feelings of the patients often as clinically valuable as the other findings? In no case can we wholly discount them. A good laboratory report is cold comfort to a patient whose symptoms remain unchanged, and the doctor can repeat such reports until he is blue in the face, but they will not help his patient much if unaccompanied by controlled symptoms and changed feelings. The successful physician is the one who knows best how to make his patients feel better.”

Henry Harrower, M.D. *Endocrine Fundamentals* 1931

OPTIMAL THYROID LEVELS?



TSH

Test was designed as a screening tool only -- not for diagnostic or therapeutic measurements.

- Not VALIDATED in to use to judge effectiveness or TRT.
- Not VALIDATED to use to adjust dosage.

Measuring TSH alone does *not:*

- Convey pituitary function.
- Indicate proper conversion of T4 in the body.
- Reflect thyroid receptor functionality.
- Reflect an autoimmune disorder.

TSH

TSH can often be misleading and unreliable.

- Assumes that hypothalamic-pituitary function is intact and normal.
- Assumes that the patients thyroid status is stable, i.e. the patient has had no recent therapy for hypo-or hyperthyroidism.

Thyrotropin test is unreliable with significant stress, illness, inflammation, aging, chronic physiological stress, and calorie reduction.

- Significantly diminished thyroid levels in peripheral tissues no longer correlate with TSH levels.
- TSH cannot be relied in for accurate measure of tissue thyroid effect.

TSH

Despite the clinical sensitivity of TSH, a TSH-centered strategy has inherently two primary limitations:

- First, it assumes that hypothalamic-pituitary function is intact and normal.
- Second, it assumes that the patients thyroid status is stable, i.e. the patient has had no recent therapy for hypo- or hyperthyroidism [Section-2 A1 and Figure 2] (19). If either of these criteria is not met, serum TSH results can be diagnostically misleading

http://www.nacb.org/lmpg/thyroid/3c_thyroid.pdf

NACB: Laboratory Support for the Diagnosis and Monitoring of Thyroid Disease Laurence M. Demers, Ph.D., F.A.C.B.and Carole A. Spencer Ph.D., F.A.C.B.

http://www.nacb.org/lmpg/thyroid/3c_thyroid.pdf

T4 Serum Levels

- With stress, illness, inflammation and aging, tissue-specific alterations:
  - Suppressed T4 levels due to suppressed TSH
  - Reduced tissue T3 levels
    - Reduced T4 uptake into tissue cells and
    - Decreased T4 to T3 conversion
  - The correlation between serum T4 and TSH and peripheral thyroid activity no longer follows
- T4 levels of little use in most cases

THS and T4 Serum Levels

- With stress, illness, inflammation and aging,

TSH and T4 levels cannot be relied on to detect decreased cellular T3 levels

REVERSE T3

- With stress, illness, inflammation and aging, T4 is preferentially converted to reverse T3

  Serum reverseT3 levels can be useful because of inverse correlation to diminished cellular uptake of T4, decreased conversion to T3, and decreased cellular T3 levels.

ADEQUATE TESTING

In patients having symptoms consistent with hypothyroidism but normal TSH and T4 levels, obtaining fT3, rT3 and fT3/rT3 ratios may help obtain a more accurate evaluation of tissue thyroid status and may be useful to predict those who respond favorably to T3 supplementation.

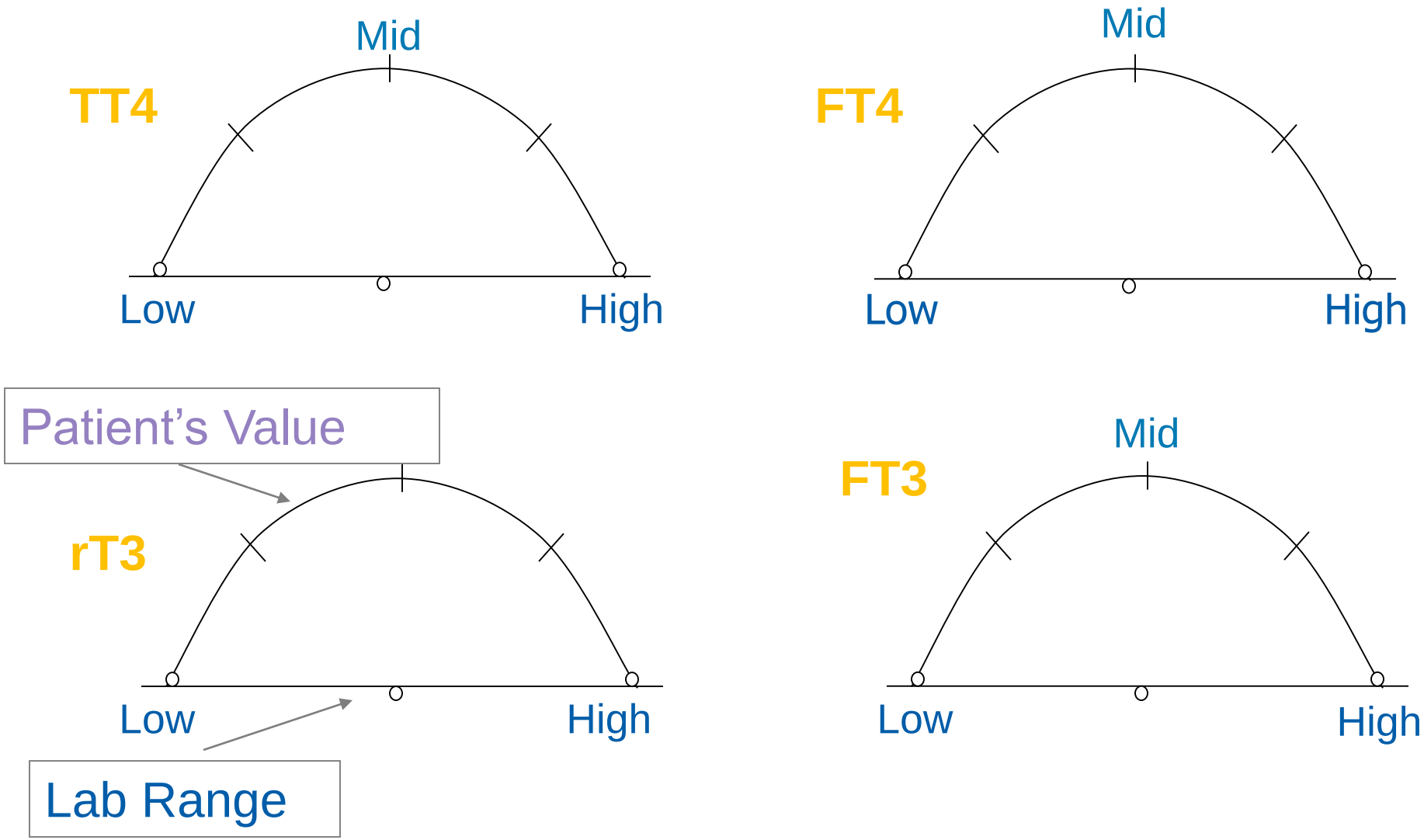
Schwartz ET, Holtorf K. Hormones in Wellness and Disease Prevention: Common Practices, Current State of the Evidence, and Questions for the Future. *Prim Care* 2008 Dec;35(4):669-705.

THYROID “PANEL”

- TSH, TT4, RT3U or T3U(T3 resin uptake), and Free Thyroxine Index (FT4I)
- Total T4
  - May be normal, but not enough converted to T3
- T3 resin Uptake
  - Does not measure Free T3 levels
  - *Estimates* the amount of unbound TBG.
    - How much binding sites are available
    - Low T3 uptake = lots of T3 - few empty binding sites and

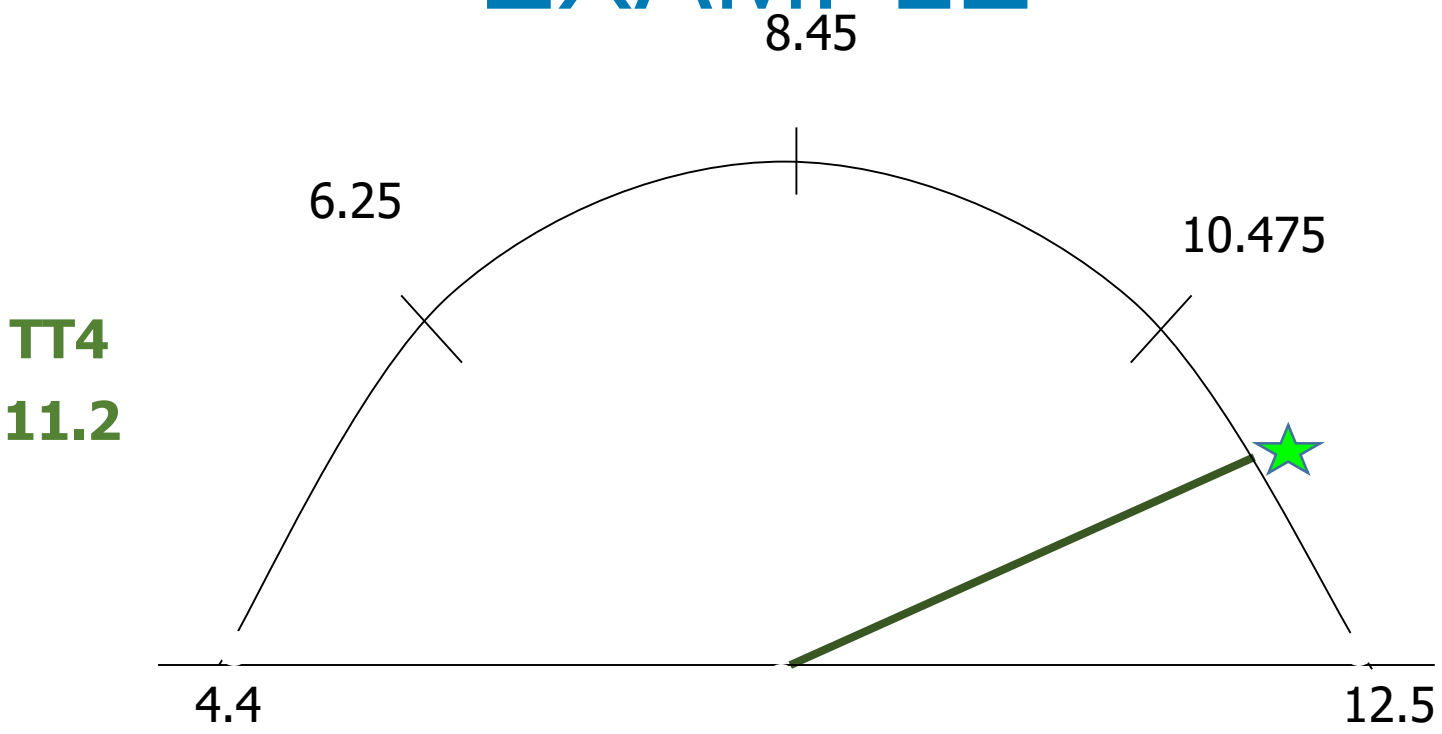
    high T3 uptake = low T3 (lots of spaces available)
- Free Thyroxine Index (FT4I)
  - *Calculation based on an estimate* of serum free T4
    - Multiple T4 by T3 uptake
  - Calculated from total T4 and thyroid hormone binding ratio
- T3 uptake and FTI cheaper than measuring actual free T3 and rT3 hormone levels

THYROID GRADIENT LEVELS

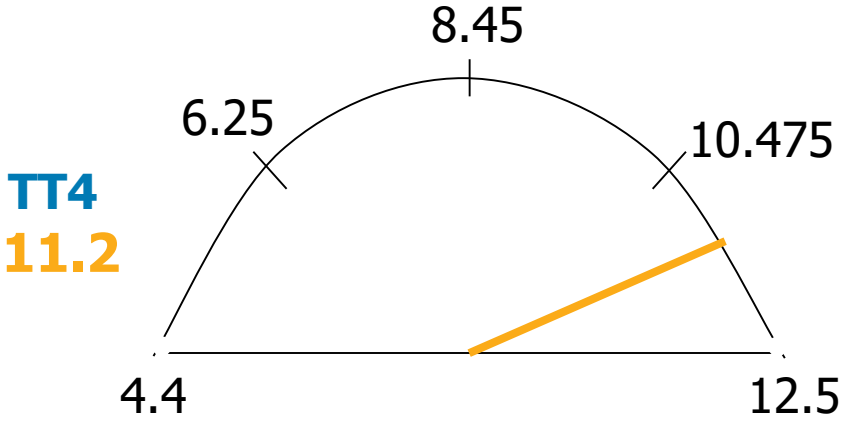


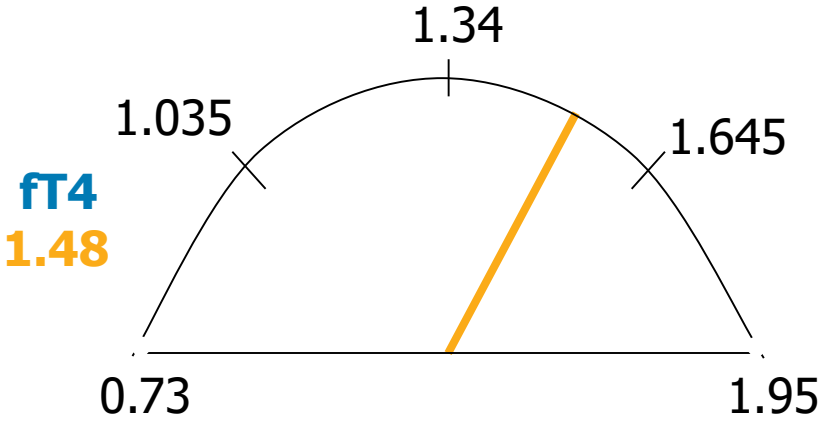
TEST	RESULTS	UNITS	EXPECTED RANGE
T3 UPTAKE	32.8	%	20.0-38.5
T3 TOTAL	141	NG/DL	90-200
T4 (THYROXINE)	11.2	UG/DL	4.4-12.5
FREE T4	1.48	NG/DL	0.73-1.95
FREE T3	2.5	PG/ML	2.3-4.2
REVERSE T3	317	PG/ML	90-350

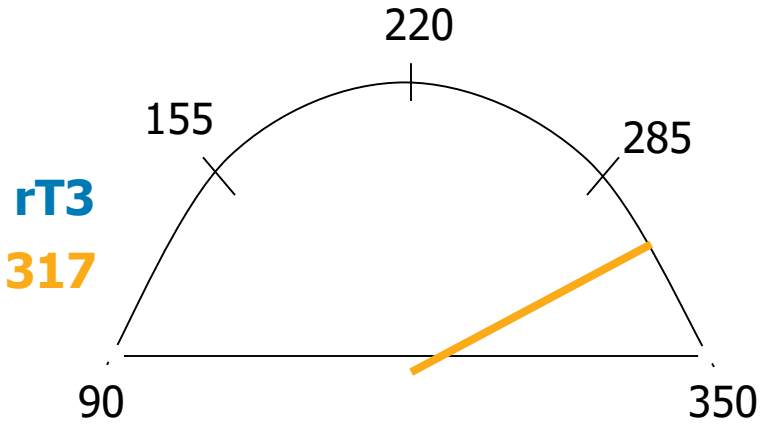
THYROID GRADIENT LEVELS EXAMPLE

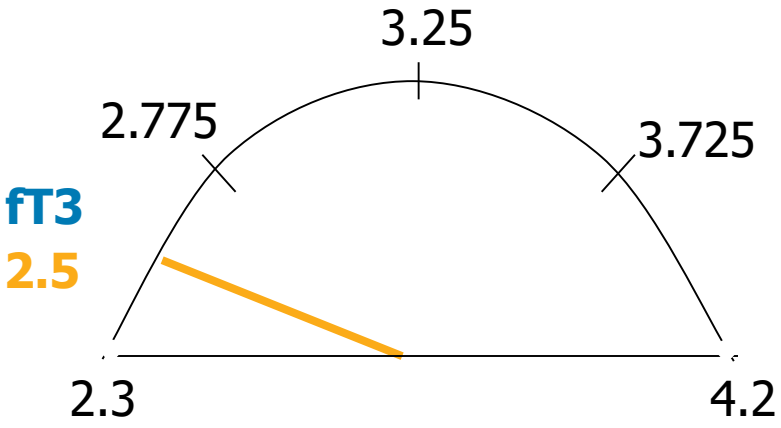


THYROID GRADIENT LEVELS EXAMPLE





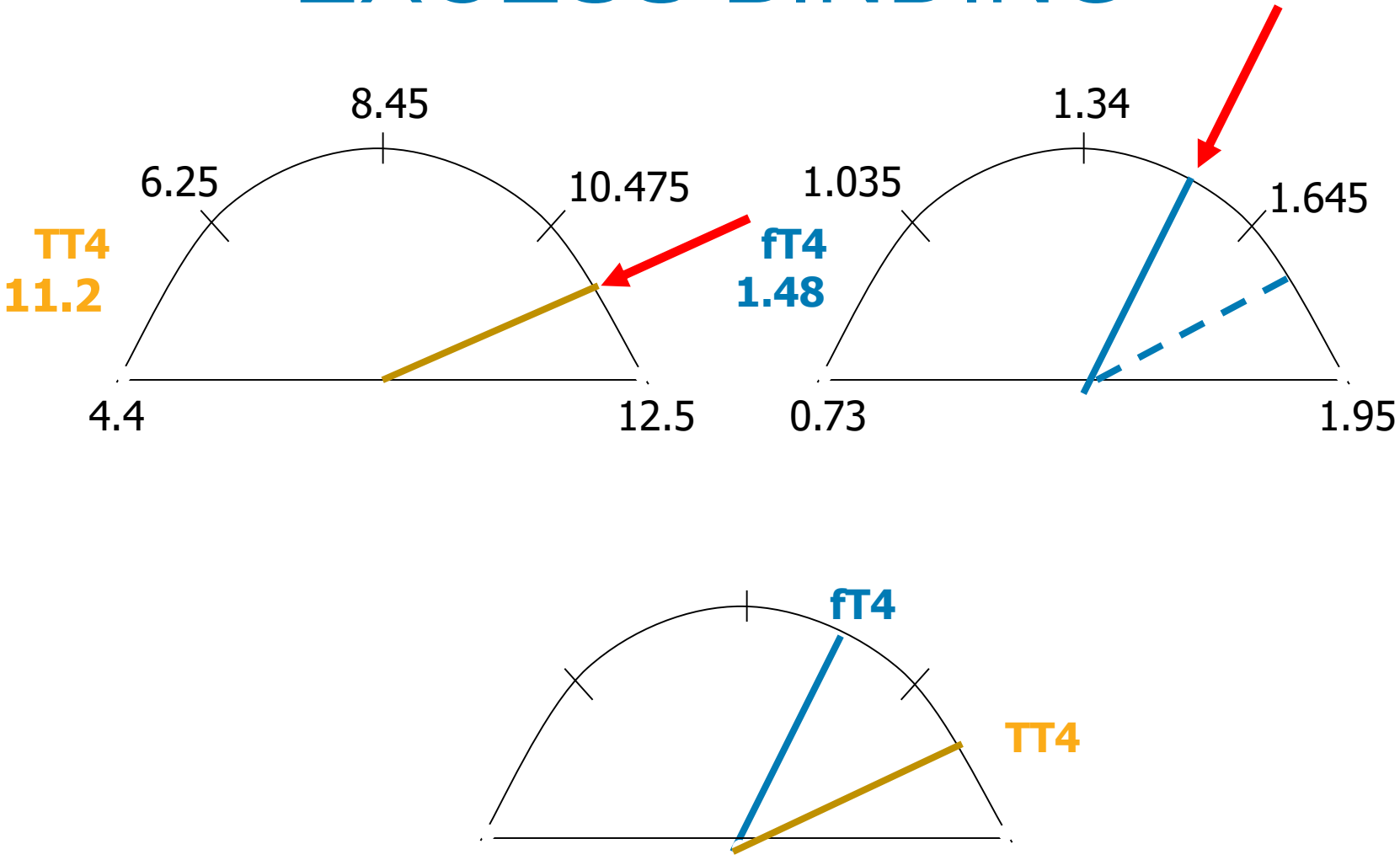




EXCESS BINDING

- Imagine these gradients curves as the upper portion of a clock.
- If the binding were normal, TT_4 & FT_4 as well as TT_3 & FT_3 should be about the same position on the clock.
- As you can see, they are not. This indicates excessive binding which may be secondary to excess estrogen or T_4.

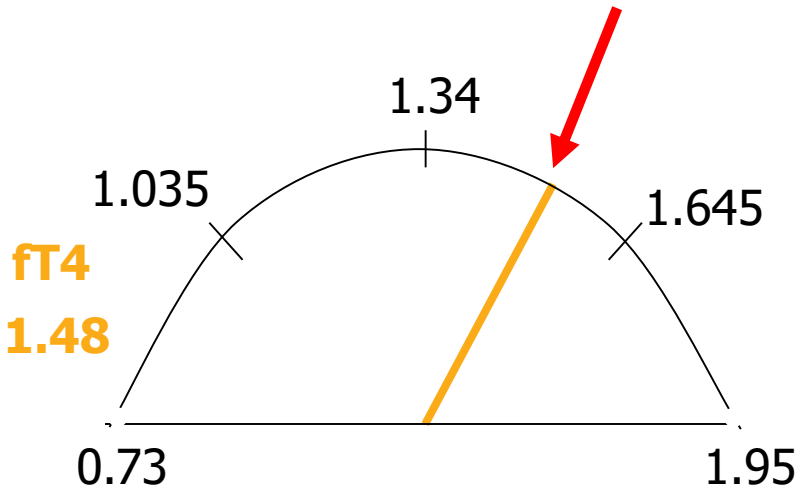
EXCESS BINDING

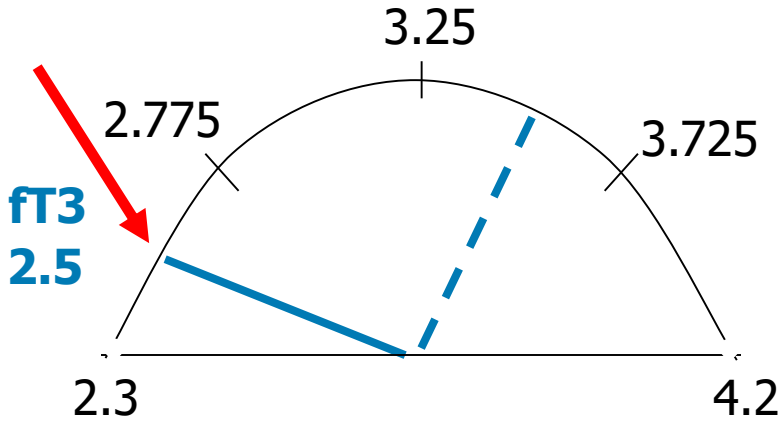


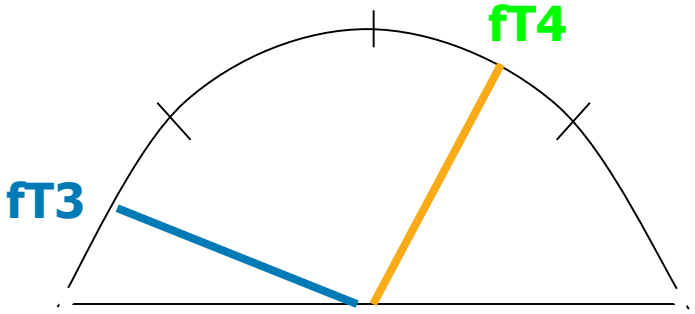
DECREASED CONVERSION OF T4 TO T3

- If there is proper conversion of FT4 to FT3, both FT4 & FT3 should be at the same position on the clock.
- As you can see, they are not.
- This represents a conversion problem. Now you must try to find the etiology by looking at the many causes of poor conversion.

CONVERSION OF T4 TO T3



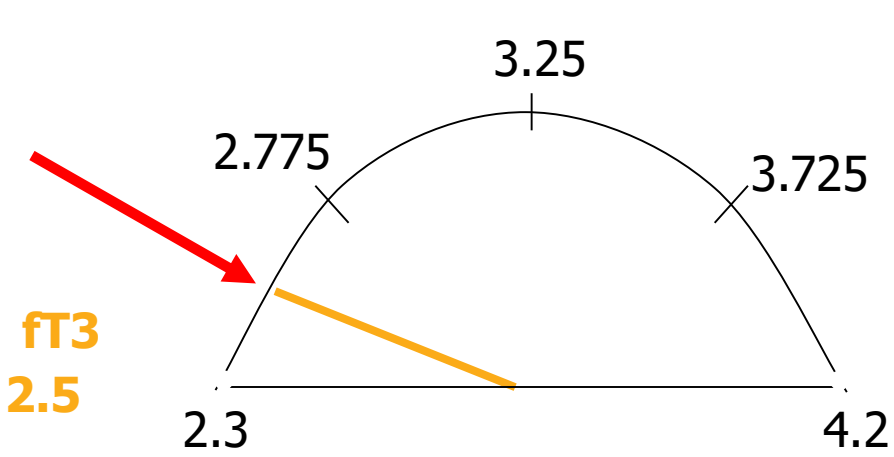


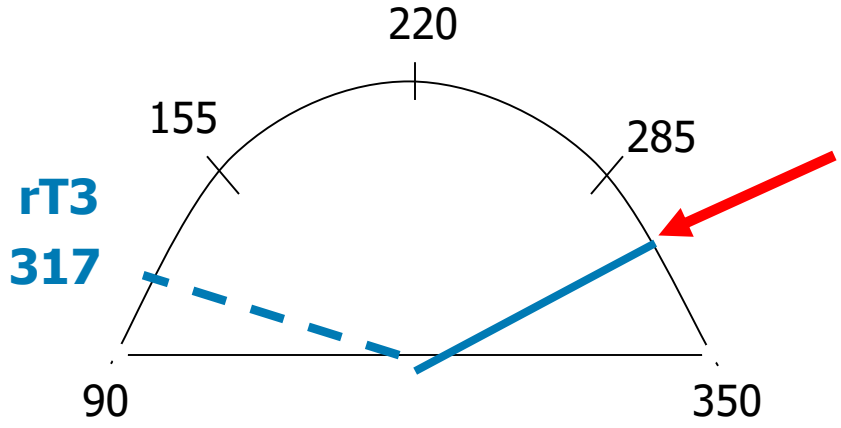


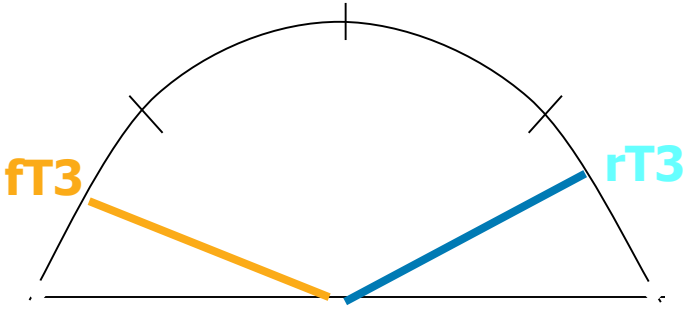
Free T_3 and rT_3

- If the conversion of T4 to FT3 and rT3 is normal, FT3 and rT3 should have about the same position on the clock.
- Even though rT3 is within the normal range for this laboratory, it is in excess of FT3.
- Since FT3 and rT3 occupy the same receptor and FT3 will activate the receptor and rT3 will not, if the patient has excess rT3 they will have symptoms of tissue hypometabolism despite all the laboratory tissue falling within the normal range.

FT3 AND RT3 RATIO







ETIOLOGY AND CORRECTION OF EXCESS RT3

- Excess rT3 will further inhibit conversion from T4 to T3.
- Since rT3 is derived from T4, you must lower T4.
- If the patient is on a T4 preparation, give slow release T3 and discontinued T4 preparation (slowly over time to control TSH).
- If the patient is not on a T4 preparation, still give slow release T3
  - This will decrease TSH and the production of T4 from the thyroid gland and its inappropriate conversion to rT3.

ETIOLOGY AND CORRECTION OF EXCESS RT3

Excess cortisol blocks T4 to T3 conversion and increases T4 to rT3:

- Check 4 point salivary levels of cortisol and correct appropriately
- Correct the reasons for poor conversion – nutritional deficiencies, medications, etc.

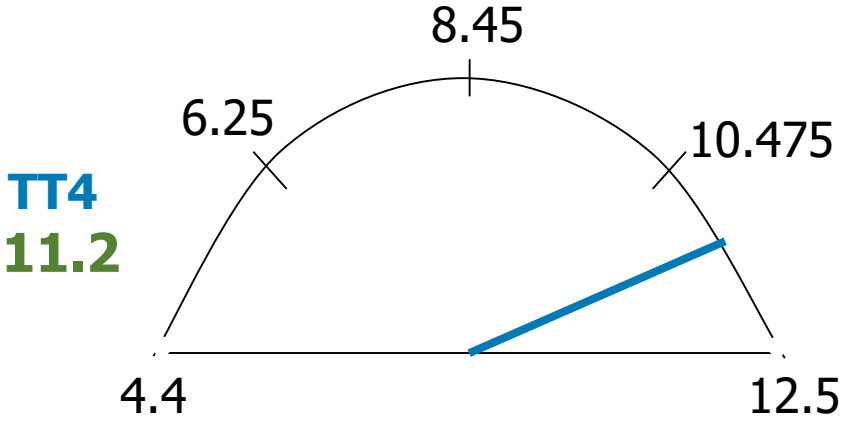
Growth Hormone increases T3 production

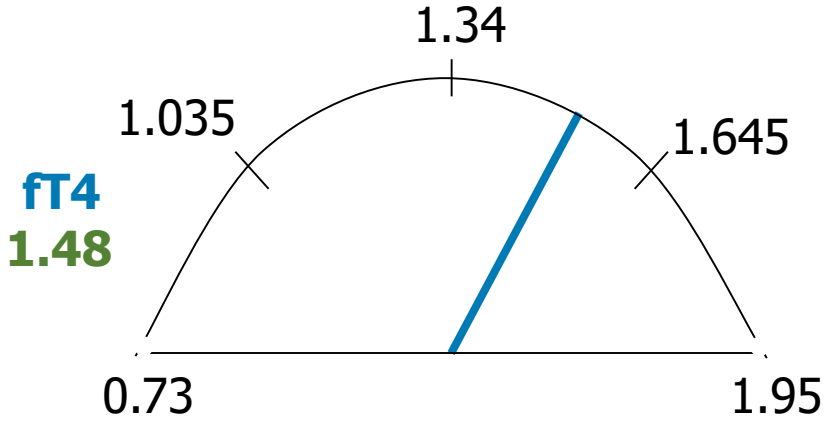
- Oral estrogen inhibits growth hormone; change to transdermal if appropriate.
- Modify lifestyle (exercise, sleep) and nutrition to increase natural growth hormone production.

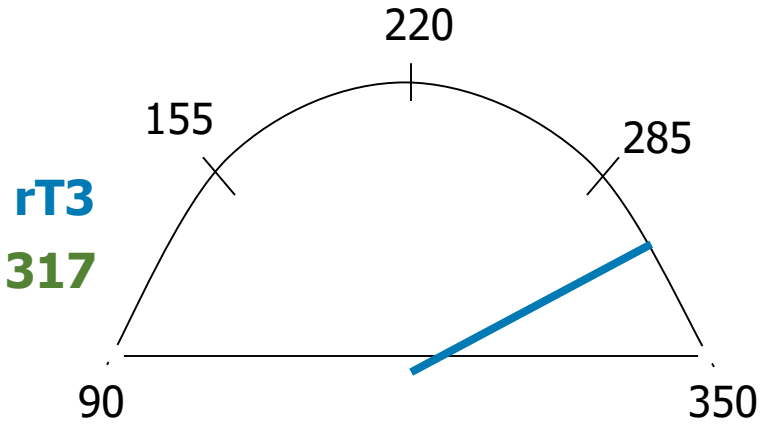
ETIOLOGY AND CORRECTION OF EXCESS RT3

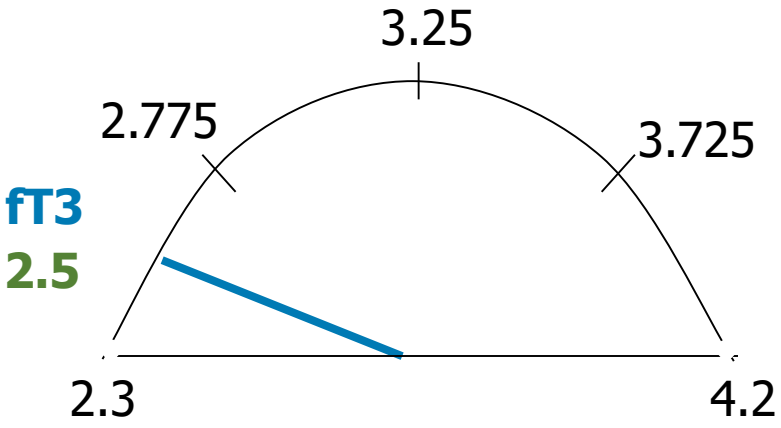
- The enzyme that converts T4 to rT3 is D3.
- D3 is increased in tissue hypermetabolism and decreased in tissue hypometabolism.*
- D3 is markedly induced by acidic and basic fibroblast growth factors as well as epidermal growth factor, platelet-derived growth factor, and cAMP analogs.*

THYROID GRADIENT LEVELS EXAMPLE

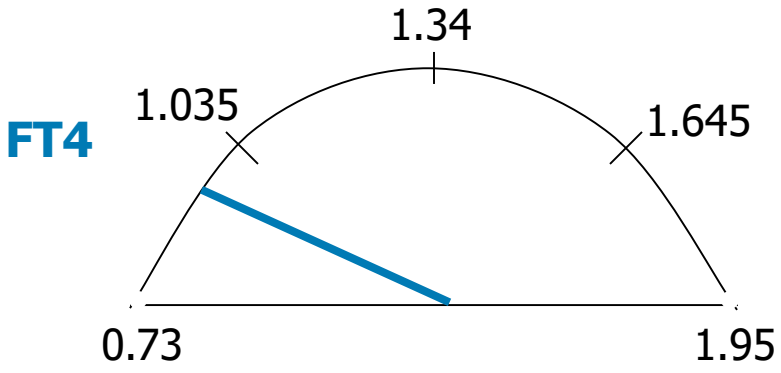


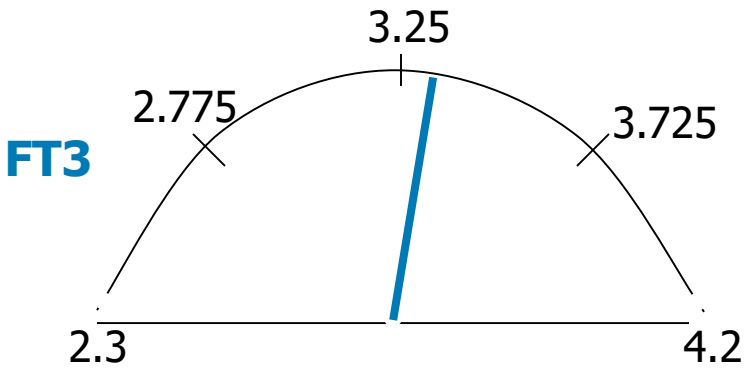






T3S HIGH RELATIVE TO CORRESPONDING T4S





THYROID TESTING

Baseline Testing

- Patients < 45 y/o and/or on thyroid replacement.
  - TT4, fT4, fT3, TPO, Vitamin D, Iodine, TSH
    - Antibodies are the most frequent cause of thyroid conditions.
    - Patient should be at complete rest for at least 15 minutes.
- Patients with chronic symptoms, non-responsive to therapy.
  - Add ferritin to list above.
  - Reverse T3?
- Patients with other autoimmune disorders or systemic symptoms possibly indicative of such, may wish to add TgAb.

THYROID TESTING

Follow-up testing

What do you really need?

- Will you change your course of action based on the test?

Recommended: fT4, fT3, TSH, TPO

- Add ons - where previous testing indicates need to monitor:
  - TT4
  - Ferritin
  - Vitamin D
  - Iodine

INTERPRETATION OF TESTING

- ✓ Timing of sample in relationship to last dose of TRT is critical to interpretation of results.
- ✓ For correlation of levels to TRT you want to avoid peaks and valleys.
- ✓ Keep timing consistent in follow up testing.

HALF LIFE VS. DURATION VS. LEVEL

It is claimed that T4 has a half life of 7 days……then why do we dose it every 24 hours?

- Studies have shown T4 could be given once a week?
- Levels drop to baseline in most in 18-20 hours.
- Duration of action stated as 24 hrs.
- Level is maintained approximately 20 hours.

It is claimed that T3 has a half life of 1 to 1.5 days, but is dosed up to 4 times a day.

- Duration of action stated as 4-6 hours.
- Level is maintained 4-6 hours.

INTERPRETATION OF TESTING

If 24 hours of more have passed since last dose of TRT, then resulting levels are not correlated to dose but show more of a baseline production from the thyroid gland.

INTERPRETATION OF TESTING

For T4, peak occurs 2-4 hours post dose and levels drop off in 18-20 hours.

- Test 4 to 18 hrs after dose for best correlation.

For T3 (IR) peak occurs in 1 to 2.0 hours and levels drop off after 4-6 hours.

- Test 2 to 4 hrs after last dose for best correlation.

For combination T4 and T3 IR products, test at 4 hours after last dose.

For any compounded SR preparation, best time to test is 4-8 hours after last dose.

THYROID REPLACEMENT THERAPY OPTIONS

WHAT'S IN YOUR THYROID?

- 1 Grain (60 mg) of "natural" Thyroid USP contains 38 mcg of T4 and 9 mcg of T3.
- T4 commercial products may contain lactose and have variable absorption problems.
- T3 commercial products limited in strengths and only available in immediate release dosage form.

- Levothyroxine Sodium USP (T4) Pentahydrate and Liothyronine Sodium USP (T3) are pure, bio-identical hormones.

THYROID USP (Desiccated Thyroid)

- 1 Grain (60 mg) of Thyroid USP contains only 38 mcg of T4 and 9 mcg of T3.
  - More than 99.9% of contents of thyroid USP are not the thyroid hormones T3 and T4.
- Ratio of T4:T3 is 4.2:1, which is *not* physiological.
- Ratio is fixed – doesn't allow for individual differences in metabolism or changes with time.

COMMERCIAL THYROID USP

- Thyroid Desiccated USP:
  - Derived from pork or beef
  - Armour® Thyroid
    - Porcine source
  - Thyroid USP (various manufacturers)
  - Thyroid Strong®
  - Thyrar® (bovine)
  - S-P-T® (pork thyroid suspended in soybean oil)

THYROID USP

- May also contain T2,T1, selenium, calcitonin
  - T2 & T1 may provide biological activity but overall contribution is considered minimal.
  - The amounts are not identified, quantified, or standardized.

- May contain lactose, sucrose, dextrose, starch or other “suitable” diluents.

HOW TO CHECK THE BASAL BODY TEMPERATURE

- Shake thermometer down at night
- In A.M., take axillary temperature before arising for 10 minutes
- Menstruating women should take their temperatures on days 2-4 of cycle
- Normal axillary temperature is 97.8-98.2

Thank You!

If you would like a copy of this presentation, please contact:

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