THYROID/ADRENAL OPTIMIZATION

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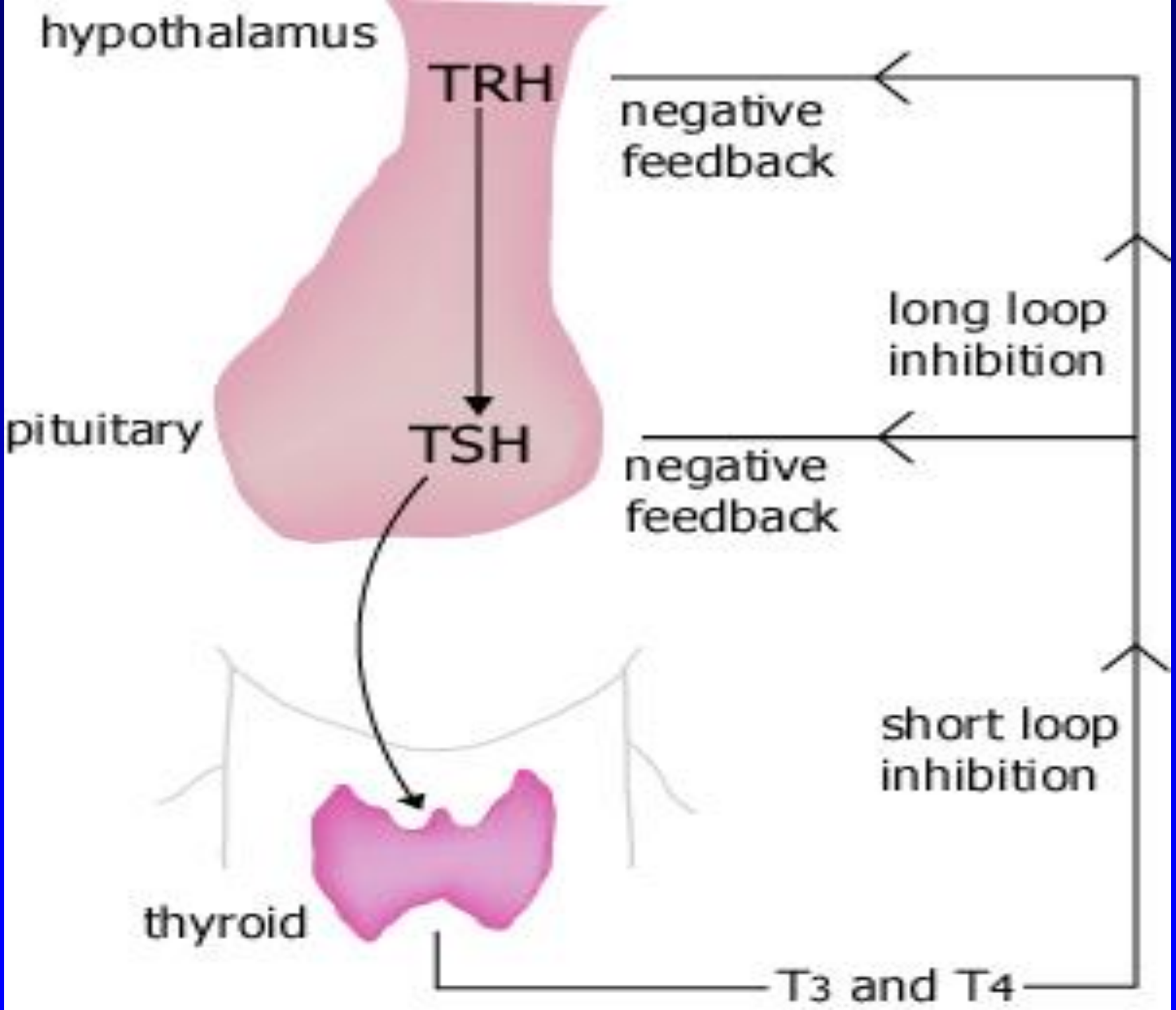

hypothalamus
TRH
negative
feedback
long loop
inhibition
pituitary
TSH
negative
feedback
short loop
inhibition
thyroid
T3 and T4

HYPOTHYROIDISM--Causes

- **Primary**—Thyroid gland failure. TSH increased
- **Secondary**—Low thyroid hormones. Low TSH
- **Tertiary**—Hypothalamic failure. Low TRH
- **Receptor uptake failure—Thyroid** resistance
  --may be iodine deficiency
- **Poor T4>T3 conversion**
- **High(er) Reverse T3**
- **Adrenal Fatigue/Failure**—Affects thyroid hormone production, conversion, uptake

HYPOTHYROIDISM--Symptoms

- Fatigue
- Weakness
- Cognitive decline
  --"brain fog"
- Insomnia
- Constipation
- Menstrual irregularity
- Depression
- Anxiety
- Headache
- Increased pain sensation
- Decreased libido
- Poor disease resistance
- Cold hands/feet

HYPOTHYROIDISM--Signs

- Low, Low-normal Labs
  --high(er) Reverse T3
- Dyslipidemia
- Infertility
- Low body temperature
- Weight gain
- Dry skin
- Allopecia
  --lateral 1/3 eyebrows
  (Hertoghe's Sign)
  --overall
- Other hormonal issues

Issues to OPTIMIZED Thyroid Replacement Therapy

- **Strict reliance on T4 only treatment**
- **Strict reliance on "normal range" as sufficient treatment goal**

  --vast differences across range

  --patient must be only 5% out of population!
- **Strict reliance on TSH as treatment goal**

  --"normal range" set too high

  --does not reflect Free T3 level or Reverse T3

  --NO danger in suppressing TSH

Thyroid Hormones

- Thyroxine (T4)

  --most highly produced (80%)

  -- production about 100mcgs per day

  --prohormone (storage) for >T3

- Triiodothyronine (T3)

  -- production about 30mcgs per day

  -- 20% produced by thyroid gland

  -- **most produced peripherally**

  -- 4 X as potent as T4

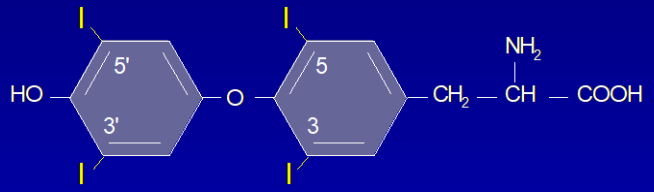
“Euthyroid Sick Syndrome”

FT3	low normal
FT4	normal
rT3	high
TSH	normal

Reverse T3

- shunts T4 from T3
- Antagonizes (blocks) T3 receptor
- slows metabolism
- adds bodyfat
- causes fatigue
- lowers body temperature
- impairs cognitive function
- increases pain sensation
- rT3 supports its own production!

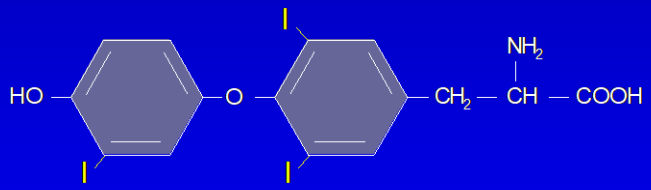
Thyroid Activation and Inactivation Catalyzed by Human iodothyronin deiodinases (D)



3,5,3',5'-tetraiodoL-thyronine (thyroxine, T_4)

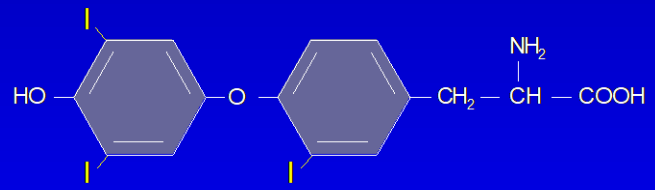
5' Deiodinase = D1

D3 = 5 Deiodinase



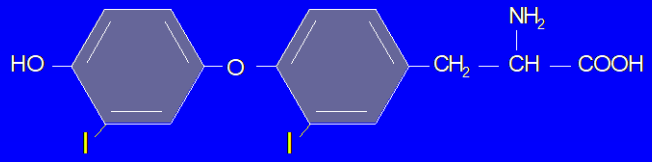
3,5,3'-triiodoL-thyronine (T_3)

D3



3,3',5'-triiodoL-thyronine (reverse T_3)

D1



3,3'-diiodothyronine (T_2)

↓Enzyme D1/D3, ↓ T4>T3

- Increases in ReverseT3/T3
- D1/D3 (T4>T3) inhibited by:

  --stress

  --severe caloric restriction

  --nutritional deficiencies (zinc, selenium, iodine, etc)

  --acute and chronic illness

  --drugs (beta blockers, amiodarone, etc)

New (old) Thyroid Concepts

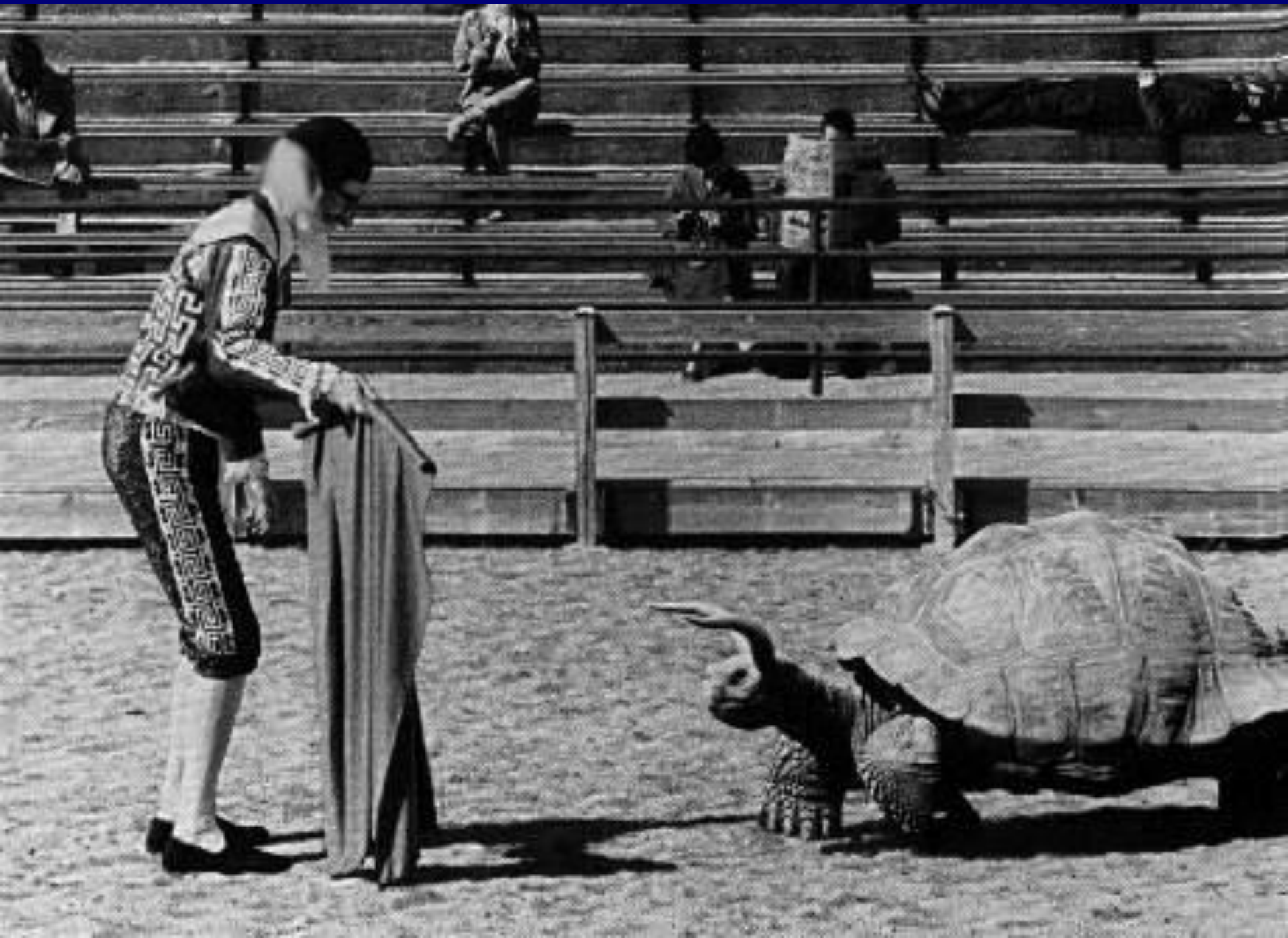
- T3 is the hormone of action
- Unless you monitor it, you have no idea of thyroid function
- Reverse T3 reverses T3
- Due to resistance/absorption issues?
- TREAT THE PATIENT!
- T4/T3 therapy is USUALLY better than T4 alone

THYROID FUNCTION TESTING

- TSH
- Free T4
- Free T3
- Reverse T3
- Thyroid Ab's (Hashimoto's?)

  --Thyroid peroxidase TPO (detects Ab's to TPO)

  --Anti-thyroglobulin Ab



Always use "Free"
thyroid hormone tests
to remove
Thyroid Binding Globulin
effects.
But Total T4 can tell you how much is being absorbed while on treatment.

Thyroid Test Goals

- HAPPY, HEALTHY PATIENT
- Free T4

  --midrange or higher
- Free T3

  --AT LEAST upper half of range

  --Children have fT3 of 7
- Reverse T3

  --lower half of range

IF Thyroid RT (T4-only) makes symptoms WORSE:

- Reverse T3 too high
- Check iron (Ferritin)
- Adrenal Fatigue

T3 Therapy

- Where T4 is adequate, but T3 lacking
- Where other assays are good, but rT3 increased
  --adding T3 combats rT3
- When Body Temperature is low in spite of adequate lab numbers
  --hormone levels not high enough for that Pt
- Keep in mind D1/D3 will increase, so too will T3/rT3 as patient gets healthier as T4>T3↑
- But T3--only does not provide T4 for D1

T3 Therapy

- Start low: 5mcgs QD-BID
- Short half life - around 7 hours
- Take 2nd dose sublingual b/c of lunch
- Increase by 5mcgs, every three days
- Watch for hyperthyroid symptoms
- Once you have driven rT3 down, it may stay down…
- …and T3 can be withdrawn.
- This Tx does not provide T4 for DI

Natural Dessicated Thyroid [NDT]

- Pig thyroid glands
  --numerous brands
  --grain fed "contented" pigs
  – 38 mcg T4 + 9 mcg T3 per grain (60 mg)
  – supplied in ¼, ½, 1, 1 ½, 2 , 3, 4, 5 grain
  --also provided by Compounding Pharmacies
- To convert from Levothyroxine (T4)
  – T4 + (4 x T3)
  – but probably higher dose would be optimal
- Best clinical response AND least side effects

Take Thyroid Before Testing?

- Taking thyroid medication before testing shows how much is being absorbed
- Compare hormone level to clinical response
- TEST THEM WHERE THEY LIVE
- NOT taking med before labs removes daily dose of T3 from test
- Less chance of freaking out other doctors

Thyroid RT levels above range are NOT "hyperthyroidism"

- Hyperthyroid is defined as **clinical symptoms**
- TREAT THE PATIENT
- High(er) levels in non-treated patients are NOT the same!

  --patient pools in studies polluted by Graves Dz
- NO association of patients Tx'd with Thyroid, w/o hyperthyroid Sx, and:

  --Afib

  --Bone mineral loss

Educate Patients: Thyroid Excess

- Palpitations
- Nervousness
- Feeling hot and sweaty
- Fine tremor
- USUALLY only temporary
- Decrease dose for a few days
- Watch symptoms

Adrenal Fatigue, Subclinical Hypoadrenia, non-Addison's Hypoadrenia, Adrenal Exhaustion, Neurasthenia, Pumpkin Pie

ADRENAL FATIGUE

- Differentiate from common Addison's Disease

  --4/100,000, severity, drugs and dosage requirements
- High percentage of hypothyroid patients
- Affects ALL body systems
- Actually a failure of the HPAA

  --naysayers discredit as claim of primary adrenal failure only

ADRENAL FATIGUE
Causes

- Extended periods of unrelenting stress
  --emotional, physical, biological
- Nutritional deficiencies
- Undiagnosed or undertreated hypothyroidism
  (hypothyroidism Tx w/T4 only)
- Toxic metal exposure
- Halogens (fluoride, chlorine, bromine)
- Sleep apnea
- Chronic Fatigue Syndrome? Fibromyalgia?

DIAGNOSIS

1 RULE:

The diagnosis of Adrenal Fatigue is based purely upon symptomology. IF the patient produces the symptoms, they have the disease state.

DIAGNOSIS

#2 RULE

All laboratory assays can be COMPLETELY normal, yet the patient (+) for Adrenal Fatigue

The “Therapeutic Test”

IF the patient is symptomatic, AND responds positively to HC, they HAVE the disease.

The “Stages” of Adrenal Fatigue

- Intended to demonstrate a general degeneration of the body’s ability to adapt to stress
- No clearly defined “stages”
- No set time intervals
- Some degenerate rapidly, especially after a catalyzing event

STAGES OF ADRENAL FATIGUE
Stage I

- Alarm Reaction “Fight or Flight”
- Stress → ↑cortisol
- Normal response
- Sustained stress response:

  -- increased caffeine inTAKE

  -- increased sugar inTAKE

  -- “I can TAKE it”

STAGES OF ADRENAL FATIGUE
Stage II

- Resistance Response
- Adrenals still able to keep up—but at a cost
- Onset of serious symptoms:
  -- fatigue
  -- sugar/salt cravings
  -- depression
  -- weight gain
  -- female hormonal irregularities
  -- hypothyroidism
- Caffeine, sugar intake ↑↑
- Usual first presentation to physician

STAGES OF ADRENAL FATIGUE
Stage III

- Adrenal Exhaustion
- Adrenal hormone (HPAA) production declines
- Cortisol drops; aldosterone may, too
- Patient is no longer able to effectively function in life
- Extreme difficulty in arising from bed in AM
- Exercise Intolerance/ Chronic Fatigue
- Patients cannot deal with stress in any form

STAGES OF ADRENAL FATIGUE
Stage IV

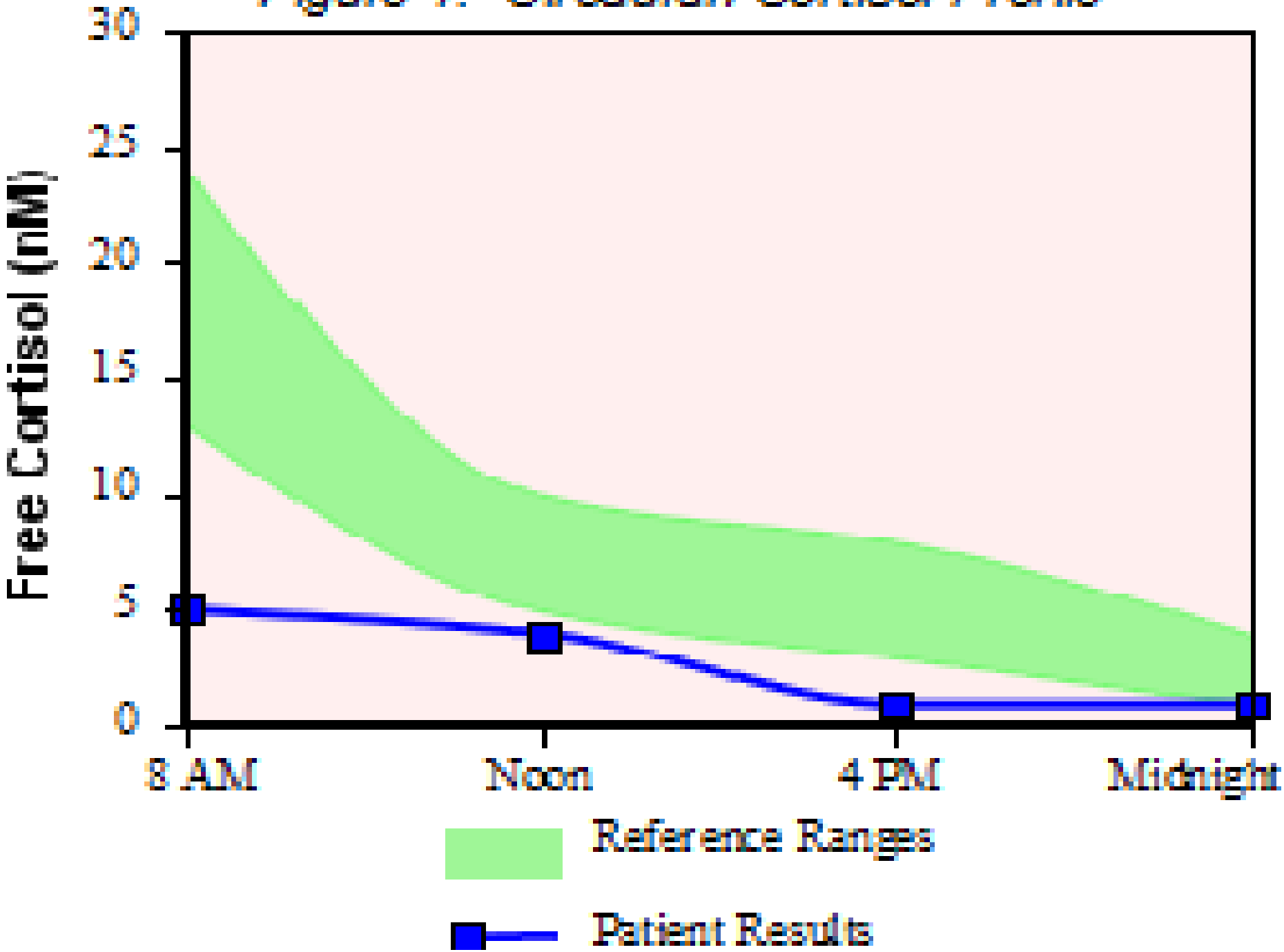
- Adrenal Failure
- Addison's Disease
- Death risk

LABORATORY TESTING
Saliva

- The best single laboratory test for AF
- Noninvasive
- Three or four samples during day

  --8AM, noon, 5PM, 11PM
- Cortisone and PROG preparations can falsely elevate results
- Be careful of contaminating specimen
- Hydrate normally prior to test day

Figure 1. Circadian Cortisol Profile



TREATMENT

- “Tincture of Time”
- Stress relief
- Nutritional
- Sea salt (1/4-1/2tsp RO H2O BID)
- Hydrocortisone
- Florinef

  --when hypotensive

  --Tx for aldosterone deficiency

NUTRITIONAL SUPPORT
Vitamin C

- Intrinsic to adrenal hormone production cascade
- Boosts immune function
- Adrenal hormone production-> free radicals
- Humans cannot glucose -> Vit C
- MUST also include bioflavonoids (not just ascorbic acid)
- 1 gram BID

NUTRITIONAL SUPPORT
Vitamin E

- Works with enzymes in adrenal hormone cascade
- Making adrenal hormones -> free radicals
- d-alpha-tocopherol is NOT “natural Vit E”

  --easiest to manufacturer

  --most profitable

  --suppresses other forms
- Therefore must provide MIXED tocopherols
- 400iu BID MIXED tocopherols (alpha, beta, delta, gamma)

NUTRITIONAL SUPPORT
B Vitamins

- B-1 Thiamine BID
- B-2 Riboflavin BID
- B-3 Niacin 25-50mg BID
- B-5 Pantothenic acid 750mg BID
- B-6 Pyridoxine 50-100mg BID
- B-12 methyl cobalamin 100-200 mcgs BID

NUTRITIONAL SUPPORT
Minerals

- Mg+ magnesium 800mg QD (divided doses)
- Ca+
- Trace Minerals:

  Iodine, zinc, copper, manganese, chromium, selenium, molybdenum

NUTRITIONAL SUPPORT
Others

- **Phosphatidyl serine 300mg QHS (incr sensitivity of HPAA)**
- **Adrenal extracts (HC, nutritional components)**
- **Licorice root (and other Adaptogens)**

--Glycyrrhizic acid component

--many healthful benefits (immune function, indigestion, etc, etc, etc)

--MAY raise BP—IF you eat a ton of it

--↑ adrenal hormone production

--↓ adrenal hormone metabolism

--inhibition of 11β-Hydroxysteroid Dehydrogenase (11β-HSD), which converts cortisol→ cortisone

<u>NOTE</u>: this enzyme also affects other hormonal conversions!

Hydrocortisone

- “Gentle” corticosteroid
- Bioidentical
- Administered at ***physiologic*** doses (nonsuppressive at ≤ 40mg QD)
- Be aware AF induces absorption issues

  --increasing HC dose may increase thyroid replacement absorption, aka “thyroid dump”
- Increase dose for acute stress, hypoglycemia or impending illness
- If nausea w/ dose-> take with food

Hydrocortisone is to prednisone as a glass of wine is to a fifth of liquor



Evening HC Dosing

- If patient awakens at 2AM “jacked up”
- Body systems compensate for each other
- NE increased to compensate for lack of cortisol
- → QHS low dose HC (usually not after 5PM)

NUMBER ONE TREATMENT:

LAUGHING!!!



CASE STUDY

36yo ♀ Accountant presents w/ CC: "I'm always tired". c/o of mood swings, irregular periods. "My hair is breaking off and falling out". Dry skin. Constipation. Anxious and irritable. "I just can't think". Lack of libido. "My hands are always cold, when no one else's are". "I just feel weak". "*Things just hurt*".

MEDICAL HISTORY

- Hypothyroidism
- Depression
- Anxiety
- Alopecia
- Chronic Fatigue Syndrome?

MEDICATION LIST

- Levothyroxine sodium) (T4) 50mcgs po QD
- Fluoxetine (refused)

PREVIOUS LABS (on T4)

TSH 4.2 (0.5-4.5)

T4 5.4 (4-11)

Thyroid Ab's --WNL

CBC –WNL

Lipid Profile –needs work!

NONE of the patient's symptoms went away!

MEDICATION LIST

- Synthroid 100mcgs po QD

The patient's symptoms got worse!

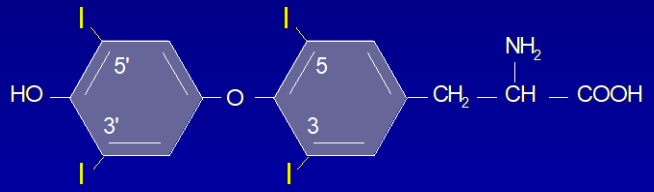
NOW she comes to you.

WHAT IS GOING ON?

Same Patient—New Labs

- TSH 2.4 (0.5-4.5)
- T4 8.2 (4-11)
- Free T4 1.1 (0.7-2.0)
- Free T3 2.5 (2.3-4.2)
- Reverse T3 22 (<24)

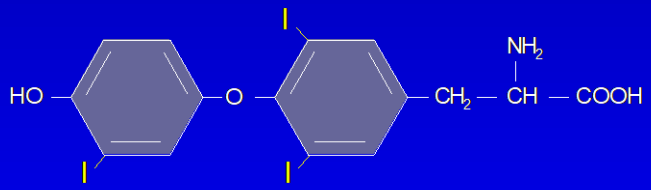
Thyroid Activation and Inactivation Catalyzed by Human iodothyronin deiodinases (D)



3,5,3',5'-tetraiodoL-thyronine (thyroxine, T_4)

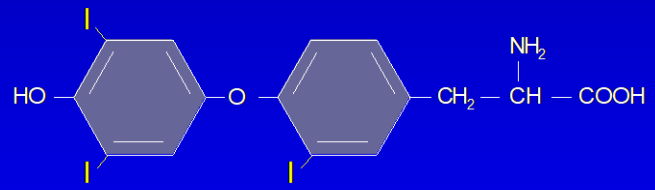
5' Deiodinase = D1

D3 = 5 Deiodinase



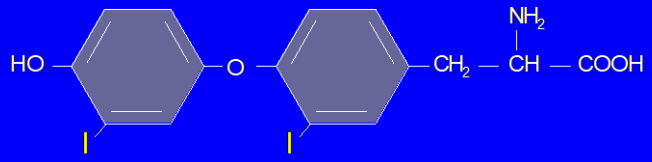
3,5,3'-triiodoL-thyronine (T_3)

D3



3,3',5'-triiodoL-thyronine (reverse T_3)

D1



3,3'-diiodothyronine (T_2)

ORDERS

- d/c T4
- Natural Dessicated Thyroid [NDT]

  --1 grain QAM/1 grain QPM

  --1 grain=60mg
- T3 5mcg BID
- Labs one month

F/U LABS

- TSH 0.9 (0.5-4.50)
- Total T4 9.6 (4-11)
- Free T4 1.9 (0.7-2.0)
- Free T3 5.8 (2.3-4.2)
- Reverse T3 11 (<24)

“I feel great! I sure am glad I didn’t take that antidepressant”

Three years later…


Worth1000.com

CASE STUDY

39yo. female Accountant presents

CC: “constant fatigue”--irrespective of number of hours of sleep. “This is way worse than before.”

Reports extreme difficulty arising from bed in AM, hypoglycemic episodes, surprisingly positive energy levels in PM when compared to AM, salt craving, “dizziness” upon standing quickly, greatly increased consumption of caffeine “but I can fall asleep right after an energy drink”. Also c/o awakening at 2AM “jacked up”.

CASE STUDY
Subjective Report (con't)

c/o anxiety, depression, nervousness, labile emotions to wide swings, nausea, irritability, lack of libido, feeling of doom or panic, inability to focus, inability to recover from even minor physical stressors, headache, "all over body ache", exaggerated startle reflex, frequent sighing, AFTERNOON CRASH, increased menopausal symptoms, increased allergies, photophobia, "flulike" symptoms and--"it takes me forever to get over EVERYTHING"

PHYSICAL EXAM

- Temp 97.2 (1400hrs)
- BP 105/60
  + Postural hypotension
- +Rhinitis
- + Asthenocoria
- + Sergent's White Line
- "unmotivated" affect

Rx: NDT 1gr AM/1gr PM

CIRCADIAN FLIPS

- **Circadian Flip Objective**

  --lower cortisol in AM

  --higher cortisol in PM

- **Circadian Flip (Subjective)**

  --lower energy in AM

  -- higher in PM

F/U LABS

- TSH 0.9 (0.5-4.50)
- Total T4 9.6 (4-11)
- Free T4 1.9 (0.7-2.0)
- Free T3 5.8 (2.3-4.2)
- Reverse T3 11 (<24)

HYDROCORTISONE
Dosing

- Start at 5mg upon arising, note any changes
- If no change in 15 minutes, add 5mg more
- Next day, 10mg AM, look for “crash”, take 5mg
- If 5mg aborts “crash”, set time for next day
- If not-> 5mg *more*. Now you know the 2nd dose for next day
- Continue, as for 3rd “crash”
- Do not go over 40mg QD. Few need more than 25mg QD
- Treat for (min.) 6 months—due to slow change in lifestyle, before attempting SLOW wean

Schedule F/U visit for one week, to D/W patient their SUBJECTIVE report— no need to run labs again.

Pt reports "I have not felt this good in years". "That last prescription was like magic". Body Temperature now 98.4F.