

38 YEAR OLD WOMAN ON THYROID HORMONE

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CHICAGO
MEDICINE

Endorama

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HISTORY OF PRESENT ILLNESS

- 33 year old woman who was self-referred to Endocrine Clinic for “resistance to thyroid hormone.”
 - Progressive deterioration since age 19.
 - Physical and mental incapacitation to the point of not being able to work or function.
 - Finally found to have TSH of 9.
 - Tried on levothyroxine, desiccated thyroid, and liothyronine.
 - Felt best on combination of levothyroxine and sustained release liothyronine.
 - Increased thyroid hormone doses every 6 months.
 - Presented on levothyroxine 200 mcg BID and liothyronine 85/85/30 mcg daily.
 - Sleeping better. No cognitive problems. Improved memory.

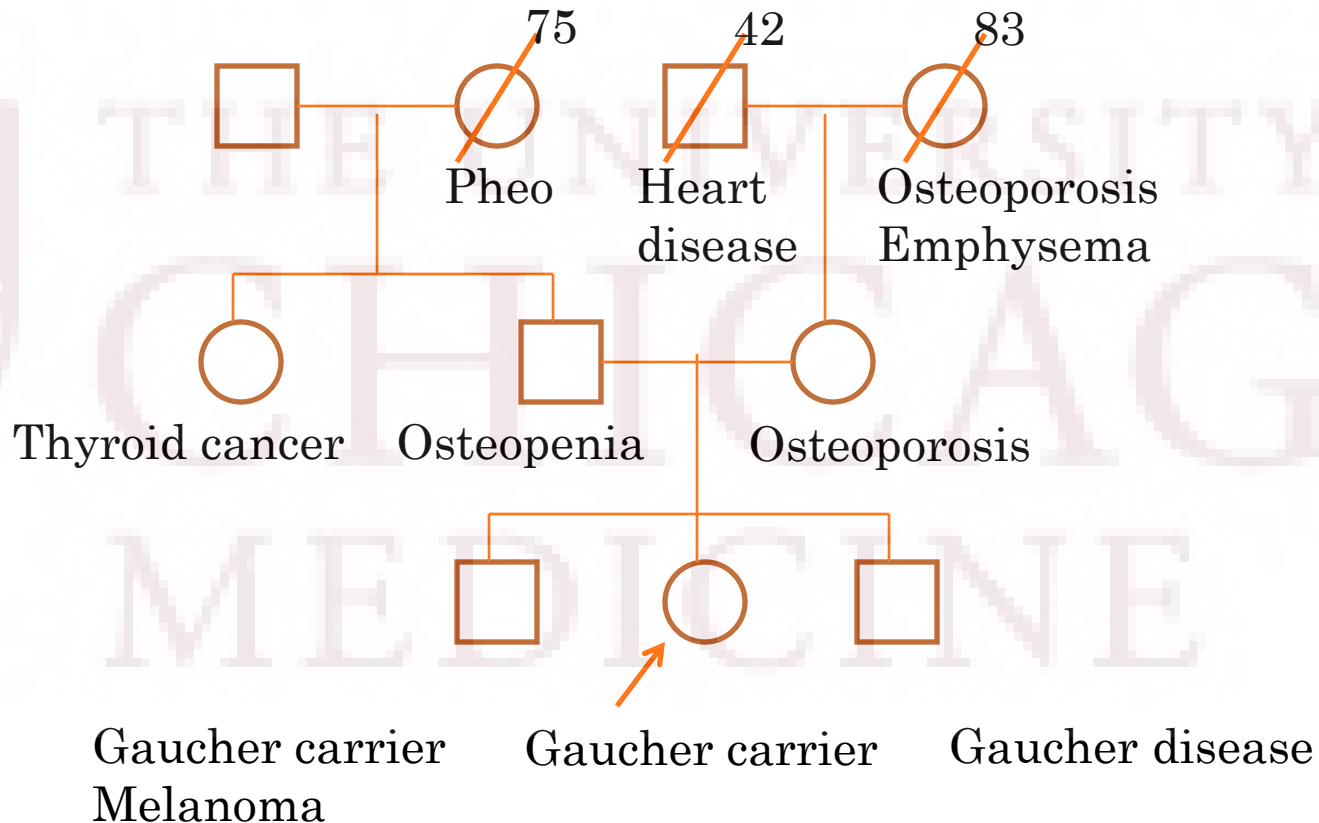


HISTORY CONT.

- Past Medical History:
 - “RTH”
 - Fibromyalgia
 - Recurrent urinary tract infections
 - Thyroid nodule, 2 mm
- Medications:
 - Levothyroxine 400 mcg daily
 - Liothyronine 200 mcg daily.
 - Fluconazole 200 mg bid
 - Nystatin powder BID
 - Progestin (Camila)
 - Lunesta
 - Cyclobenzaprine
 - Metoprolol
- Social History:
 - C student until high school
 - Attending Kent law school
 - No tobacco use
 - 1 glass of wine per week
- ROS:
 - Cold intolerance
 - Constipation
 - Mild depression



FAMILY HISTORY



HISTORY CONT.

○ Physical Exam:

- Ht 5'3", Wt 107.3 lbs
- BP 94/60, HR 78
- Nonpalpable thyroid gland.
- No lid lag.
- No tremor.

○ Laboratory Tests:

- TSH <0.01
- FTI 20 (6-10.5)
- T4 14.2 (5.0-11.6 mcg/dL)
- T3 359 (80-195 ng/dL)
- rT3 499 (145-300 pg/mL)
- Thyroglobulin 4 ng/mL
- Tg Ab, TPO Ab neg

- BMD:
 - L-spine T-score -1.1
 - Femoral neck T-score -1.0



HISTORY CONT.

- Returned for follow up 3 years later.
- Felt well on her current dose:
 - Levothyroxine 800 mcg daily
 - Liothyronine 420 mcg daily
- Had an episode of abdominal pain and collapse on levothyroxine 1200 mcg daily and liothyronine 560 mcg daily.
- Fibromyalgia symptoms had improved on higher doses of thyroid hormone.
- Physical exam: HR 104, fast DTRs, fine tremor of hands and tongue
- Labs: TSH <0.006, fT4 4.23 (0.8-1.77), T3 19.9 (2.0-4.4)



HISTORY CONT.

- Returned for follow up 2 years later.
- Interested in becoming pregnant.
- Currently on levothyroxine 500 mcg daily and liothyronine 210 mcg daily.
 - With attempts to titrate down, she develops severe fatigue, irritable bowel, myalgias, sore throat, hair loss, and cold intolerance.
 - Overall felt well. Only complained of difficulty losing weight, palpitations controlled on metoprolol, mild tremor.
 - Regular menses until 3 months ago.
 - Responded to progesterone.
 - Started seeing a fertility specialist.



PAST MEDICAL HISTORY UPDATED.

- “RTH”
- Thyroid nodule:
 - Follow up thyroid ultrasound 1 month ago showed growth of her thyroid nodule from 2 to 5 mm.
- Osteopenia
- Fibromyalgia
- Chronic Lyme and Babesiosis
- Medications:
 - Levothyroxine 500 mcg daily
 - Liothyronine 210 mcg daily
 - Metoprolol 50 mg daily
 - Atovaquone 150 mg q week
 - Azithromycin 250 mg q 2 weeks
 - Cefuroxime 250 mg q week
 - Lunesta 1.5 mg QHS



PHYSICAL EXAM

- Vitals: Ht 5'3", Wt 123 lbs, BP 121/70, HR 72, RR 18
- HEENT: Conjunctivae clear. EOMI. PERRL.
- Neck: Small thyroid. No nodule noted.
- CV: RRR. No murmur appreciated.
- Pulm: CTAB.
- Abd: Normoactive BS. Soft, nontender, nondistended.
- Neuro: Normal DTRs. Tremor on outstretched arms.



LABORATORY TESTS

- T3
- rT3
- fT4
- T4
- Follow up BMD pending

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PLAN

- Counseled on risk of losing pregnancy on current doses of thyroid hormone.
- Reasonable goal would be thyroid hormone levels within 20% of upper limit of normal.
- Decrease levothyroxine by 25 mcg every month and liothyronine by 10 mcg every month.
- Follow up in 6 months.



My Questions:

- How is this person alive (and functional)?
- What are the consequences on the heart and bone?
- How will this affect the fetus?



Effects of thyroid hormone excess on clinical status and thyroid indices

- Desiccated thyroid was administered to male prisoners, increased progressively from 3 to 25 grains over 3 months.

2500 mcg T4 +
625 mcg T3!!!

Table 1.—Frequency of Symptoms during the Ingestion of Desiccated Thyroid*

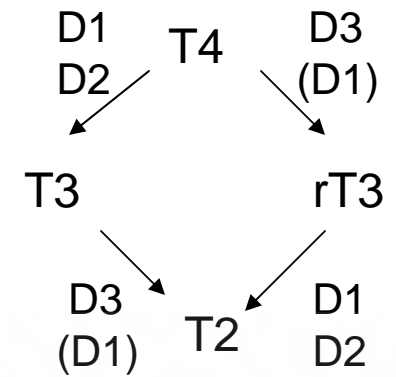
| Dosage: | None | 3 grs./d.† | 10 grs./d. | 15 grs./d. | 20 grs./d. | 25 grs./d. |
|-------------------|------|------------|------------|------------|------------|------------|
| Nervousness | 29 | 50 | 67 | 72 | 80 | 78 |
| Irritability | 7 | 43 | 50 | 32 | 50 | 56 |
| Sweating | 22 | 7 | 56 | 50 | 80 | 78 |
| Palpitation | 7 | 43 | 56 | 90 | 60 | 78 |
| Chest pain | 0 | 14 | 40 | 50 | 50 | 78 |
| Strength | 7 | 57 | 56 | 80 | 70 | 78 |
| Appetite increase | 7 | 22 | 24 | 64 | 90 | 50 |
| Nocturia | 0 | 7 | 8 | 8 | 0 | 0 |
| Diarrhea | 0 | 14 | 16 | 24 | 50 | 22 |
| Constipation | 7 | 7 | 8 | 0 | 50 | 22 |

*Percentage of subjects with symptoms during one or more inquiry during each treatment course.

- 7/10 could not complete the study.



Changes in thyroid hormone metabolism with TSH-suppressive levothyroxine therapy



| | Time 1 | Time 2 | |
|----------------------|------------------|----------------|--------|
| Time since RAI (yrs) | 0.15 (0.07-0.74) | 7.6 (5.1-10.2) | |
| LT4 dose | 174±42 | 171±44 | 0.62 |
| Free T3 (pg/L) | 6.8±1.1 | 5.2±0.8 | <0.001 |
| Free T4 (pg/L) | 27.7±2.8 | 26.6±4.3 | 0.06 |
| Total T3 (nM) | 2.25±0.42 | 1.75±0.32 | <0.001 |
| Total T4 (nM) | 169±31 | 151±24 | <0.001 |
| Total rT3 (ng/mL) | 0.45±0.12 | 0.48±0.13 | 0.2 |
| Total T4/total T3 | 76.3±13.2 | 88.1±15.1 | <0.001 |
| Total T4/rT3 | 396±93 | 333±76 | <0.001 |
| Total T3/rT3 | 5.40±1.77 | 3.96±1.38 | <0.001 |
| TSH | 0.07±0.06 | 0.04±0.05 | <0.001 |

Suppressive doses of thyroid hormone and ANS function

- 25 patients on >10 year TSH suppressive therapy after thyroidectomy for DTC.
 - Randomized to maintenance (TSH <0.4) and intervention (TSH target 0.4-4.8) for 6 mo.
- Restoration to euthyroidism:
 - No change in urinary excretion of NE, DOPA, and VMA.
 - No change in overall heart rate variability.
- May indicate irreversible changes or adaptation during long-term exposure to excess thyroid hormone that is not remedied by 6-month euthyroidism.

Suppressive doses of thyroid hormone and BMD

- 22 patients on supraphysiological doses of LT4 for affective disorders
 - 4 premenopausal women, 12 postmenopausal women, and 6 men; mean age of 51 ± 7 years
 - Dose of 380 ± 108 mcg of LT4/day
 - Mean duration of 5.8 ± 3.3 years
 - TSH of 0.06, fT4 24.97 (9-19), TT3 1.74 (0.8-2.0)
 - No sig. decrease in BMD, compared to reference population
- RCT on TSH suppressive therapy on PTC patients.
 - 144 v. 127 patients; mean age 50.2 ± 13.3 v. 52.3 ± 14.4
 - TSH of 0.07 ± 0.10 v. 3.14 ± 1.69
 - Sig. decrease in T-score within 1 year (seen in patients ≥ 50 years old) v. 5 years

Ricken et al. [J Affect Disord.](#) 2012 Jan;136(1-2):e89-94.

Sugitani et al. [Surgery.](#) 2011 Dec;150(6):1250-7.

Hyperthyroidism and bone loss

- TSH has been proposed to be a direct negative regulator of bone turnover.
- Unclear if T3 acts directly on osteoclasts or via osteoblasts.
- Bone biopsies show an increased frequency of bone remodeling cycle initiation and shortened cycle duration.
 - 10% loss of bone per cycle.
- Associated with negative calcium balance.



Potential complications in uncontrolled hyperthyroidism

○ Maternal:

- Pregnancy-induced hypertension
- Preterm delivery
- Congestive heart failure
- Thyroid storm
- Miscarriage
- Placenta abruptio
- Infection

○ Fetal:

- Hyperthyroidism
- Neonatal hyperthyroidism
- Intrauterine growth retardation
- Small-for-gestational age
- Prematurity
- Stillbirth



Fetal loss associated with excess TH exposure

- >200 members of an Azorean family with RTH
- Per pregnancy rates of miscarriage:
 - Affected mothers: 23.7%
 - Affected fathers: 6.7%
 - Unaffected first degree relatives: 8.8%
- Delivery of children:
 - Affected mothers: 65% affected children
 - Affected fathers: 56% affected children
- Birth weights:
 - Unaffected infants born to affected mothers: -1.79 ± 0.86
 - Affected infants born to affected mothers: -0.06 ± 1.11

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