THYROID
CASES & FAST FACTS

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Hyperthyroidism (T-tox)

1. Autoimmune disease
    1. Graves
    2. Postpartum
    3. Hashimotos
2. Nodular disease
    1. Toxic adenoma
    2. Toxic nodular goitre

3. Drugs/other
    1. Amiodarone (Type 1 and 2)
    2. De Qervains
    3. Excess thyroid hormone
    4. TSH-oma, TH resitance

Presentation /clinic

- **Graves**
  - Ophthalmopathy
  - Female (10:1)
  - Rapid onset
  - Severe toxicosis
  - Associated AID
- **TN or TNG**
  - T3 toxicosis
  - Sub-clinical
  - Slow onset
  - Older
  - Palpable nodules

? FHx, Drug Hx, Pain over the thyroid, pregnancy

Presentation /clinic

- **Hashimotos**
  - Lymphocytic infiltration
  - AB positive (TG> TPO AB)
  - Transient toxicosis
  - Tri-phasic response
  - Hypothyroidism
  - Low uptake at Scintigram
- **Post-partum**
  - < 6/12 post partum
  - 50% Graves
  - 50% PP-thyreoditis
  - Tri-phasic response
  - Generally spontaneous recovery

Investigations

- TFT's (fT3, fT4, TSH)
- TPO AB
- TG AB
- TSH receptor AB
  (Thyroid stimulating IG)

1. **Who needs US?**
2. **Who should request US?**
3. **Who needs Scinthigram ?**

1. Autoimmune disease
   1. Graves
   2. Postpartum
   3. Hashimotos
2. Nodular disease
   1. Toxic adenoma
   2. Toxic nodular goitre
3. Drugs/other
   1. Amiodarone (Type 1 and 2)
   2. De Qervains, Riedels, ...

Investigations

- **Ultrasound**
  - thyroid nodule
  - euthyroid
  - thyroid cancer ?
- **Scinthigram**
  - Thyreotoxicosis
  - ? Thyreoditis
  - ? Toxic nodule vs. Graves

Treatment

- **Carbimazole**
- **Propylthiouracil**
- **Radioiodine**
- **Watch and wait**

Other issues

- Management post radioiodine?
- Management of thyroid cancer ?
- The suspicious thyroid nodule

Hypothyroidism

Causes

With goitre

- Hashimotos
- Iodine deficiency

Without goitre

- Atrophic thyreoditis
- Other thyreoditis
- Congenial

Pituitary/hypothalamic

Iatrogenic

- Radioiodine
- Surgery
- Drugs (iodine, lithium)

Hypothyroidism and pregnancy

- Treatment adjustment
- Target TSH ?
- What to follow?

Hypothyroidism

- **Target TSH?**
- **Subclinical hypothyroidism ?**
- **TSH vs. symptoms**
- **Thyroxine absorption**
  - Food
  - Drugs
  - Medical conditions

How much Thyroxine ?

- Age
- Gender
- Cause of hypothyroidism (remaining thyroid function)
- Difference of replacement vs THS suppression Rx for thyroid cancer
- Approximate Dose T4:
  - Male: 1.5 mcg/kg
  - Postmenopausal woman: 1.7 mcg/kg
  - Premenopausal woman: 2.2 mcg/kg

L-thyronine (T3)

- BTA (UK)
- Patient interest groups
- Evidence
- Clinical approach
- Who can get it
- How to use T3
- Safety
- When not to use T3
- Long acting T3
- Armour thyroid

Thyroid Function Tests in Pregnant Women

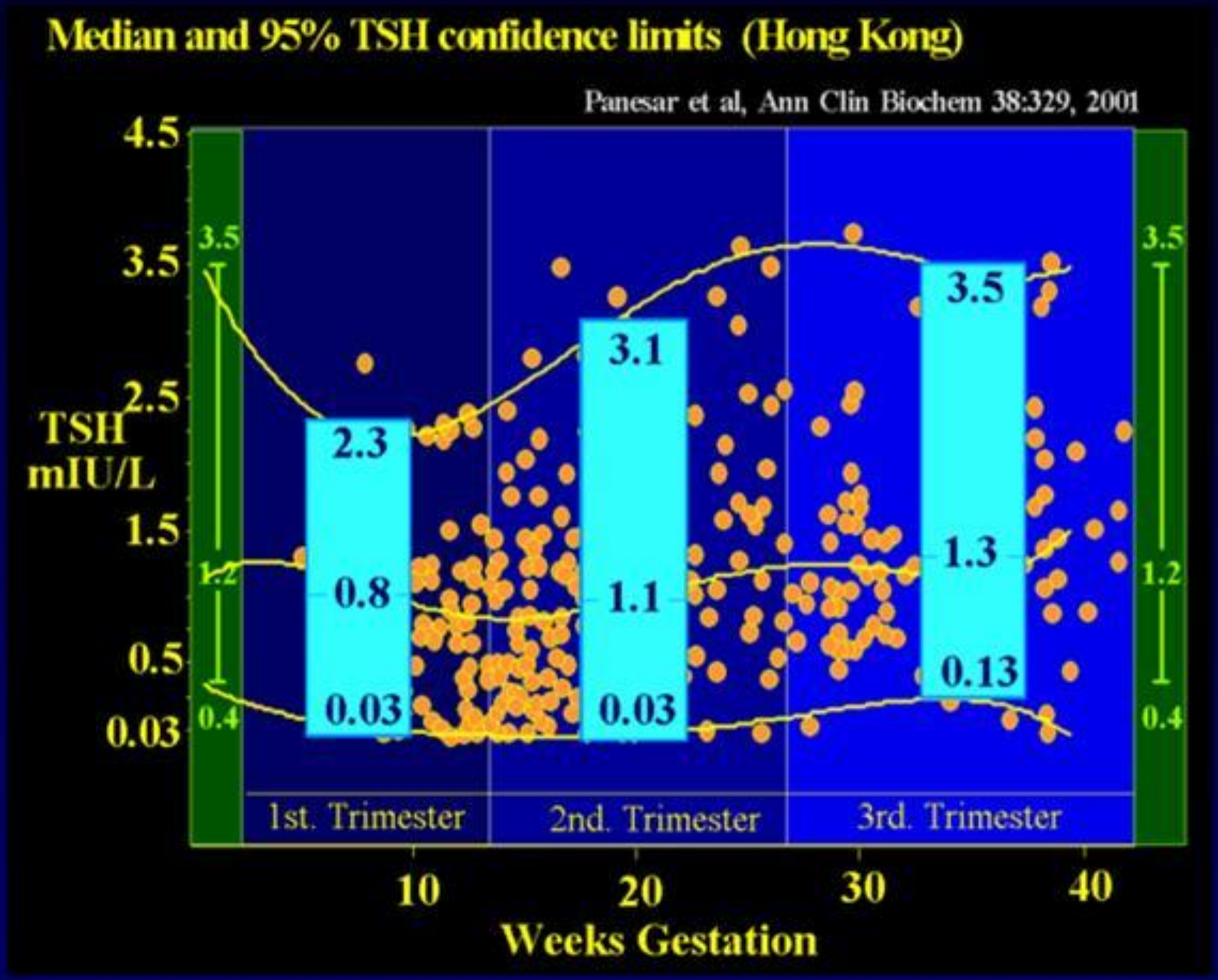
30 y/o woman

- 12 weeks gestation
- No thyroid history, negative exam
- Free T4 1.6 ng/dL (0.8-1.8)
- TSH 0.13 mIU/L (0.5-4.5)

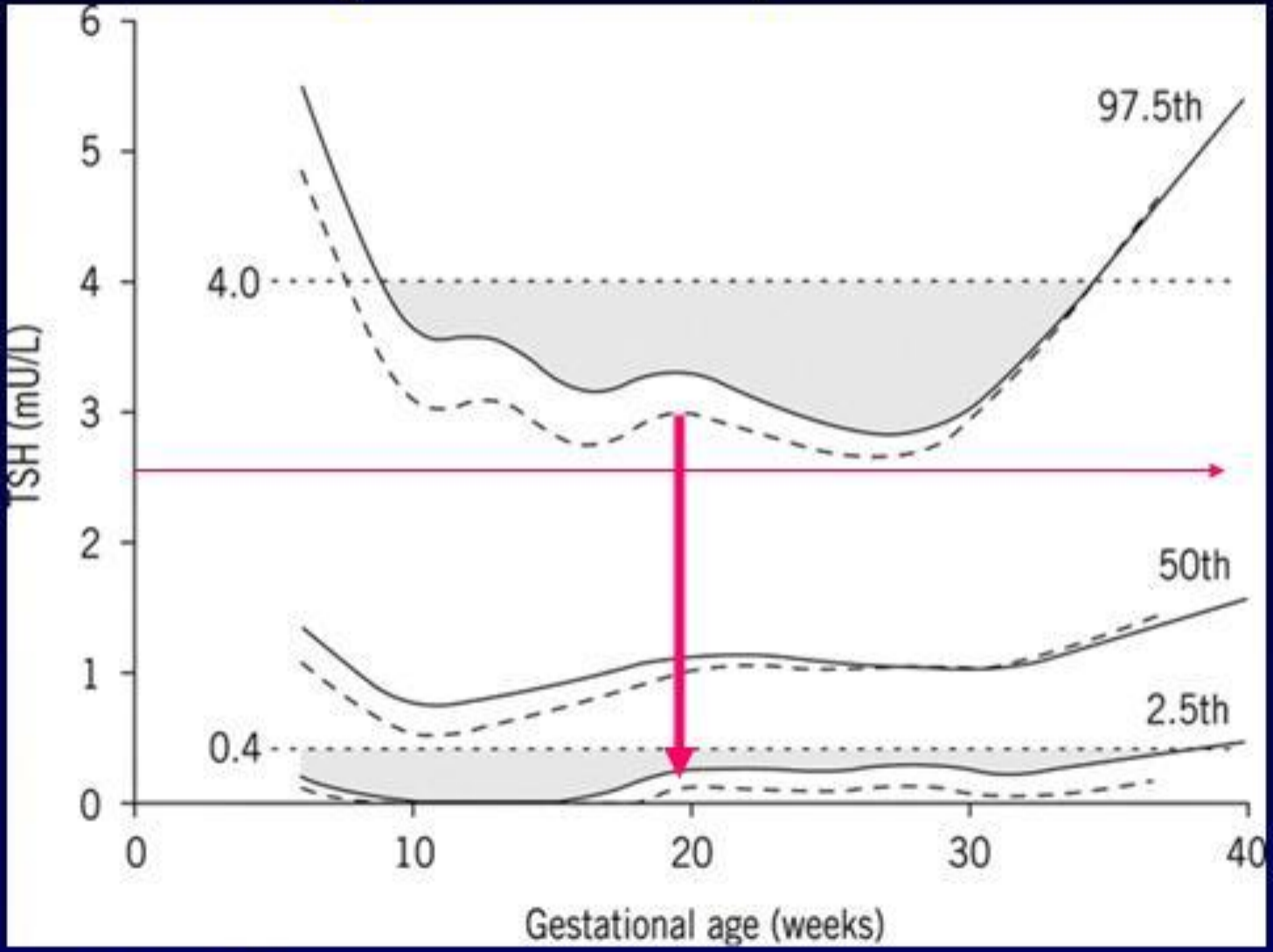
- How do you explain these test results?
- What would you do?
- (Should she have had TFT's checked?)

Changes in Thyroid Tests during Gestation

Courtesy of Dr. C. Spencer

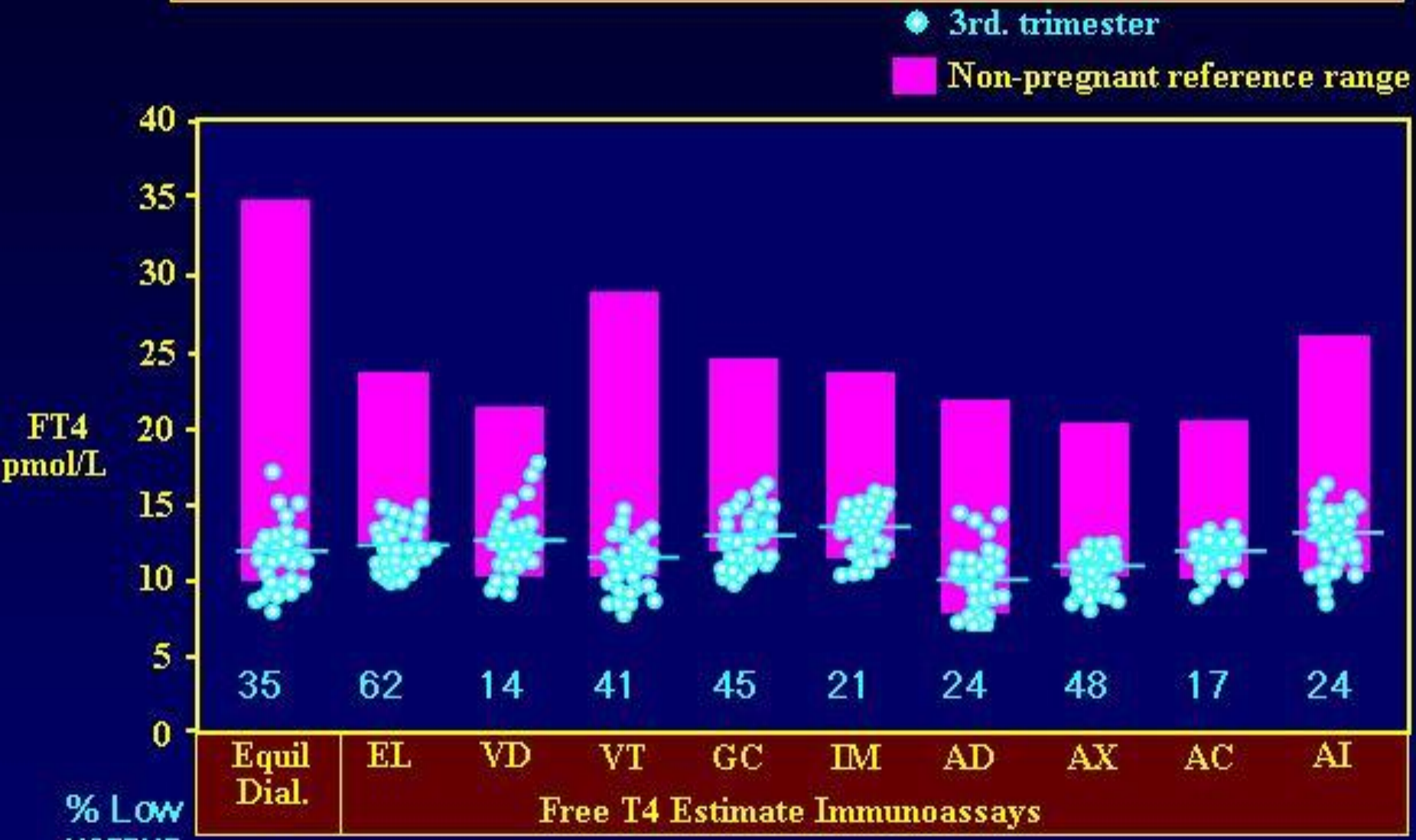

Median and 95% TSH confidence limits (Hong Kong)
Panesar et al, Ann Clin Biochem 38:329, 2001
4.5
3.5
2.5
1.5
0.5
0.03
TSH mIU/L
3.5
1.2
0.4
2.3
0.8
0.03
3.1
1.1
0.03
3.5
1.3
0.13
1st. Trimester
2nd. Trimester
3rd. Trimester
10
20
30
40
Weeks Gestation

Median, 5th, 95th, and 97.5th %ile of TSH by week of gestation in 17,298 women



Casey et al. 2005

3rd. Trimester Free T4 - Analyzed by Different Methods



Sapin et al Clin Lab 50:581, 2004

slide courtesy of Carole Spencer

Case 4

48 y/o man

- fatigue and cold intolerance
- decreased libido and erectile function
- thyroid not enlarged
- TSH = 2.2 mIU/L (0.3-5.0)
- fT4 = 0.6 ng/dL (0.8-1.8)

How do you explain these test results? What would you do?

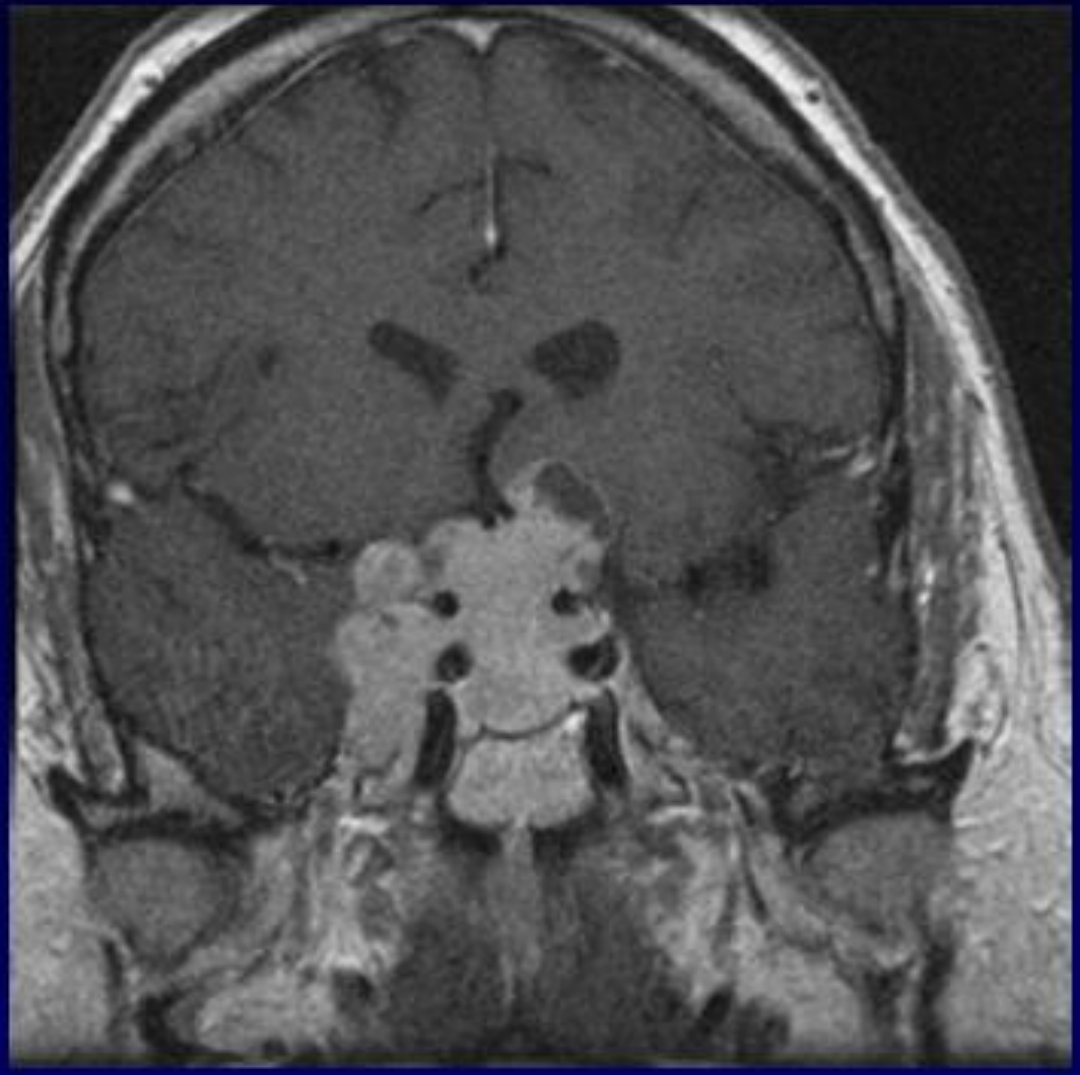
Case 4

- 48 y/o man
  - TSH = 2.2 mIU/L (0.3-5.0)
  - fT4 = 0.6 µg/dl (0.8-1.8)

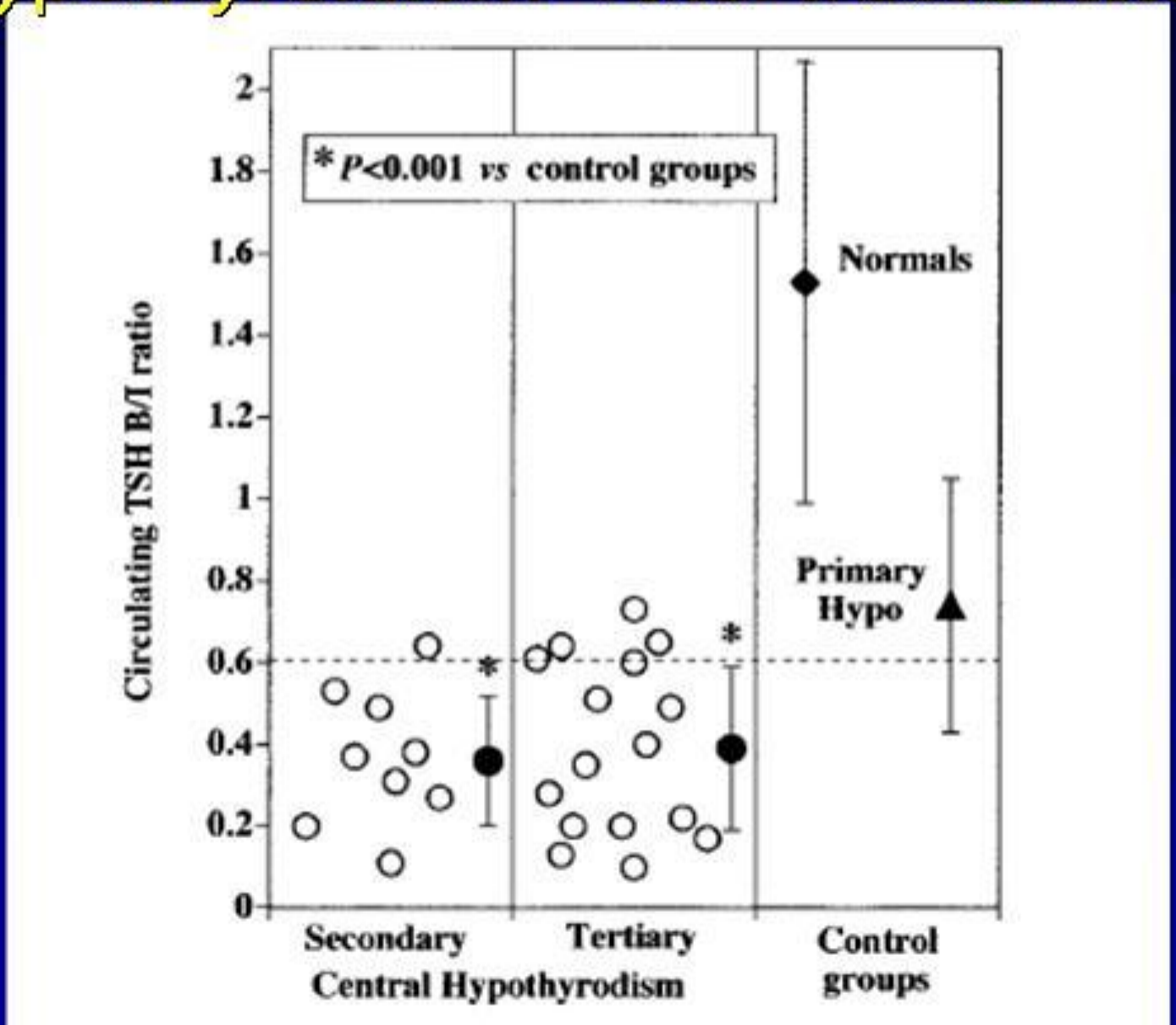
  - Testosterone 10 µg/dl (250 - 900)
  - LH/FSH = normal
  - AM cortisol = 14 µg/dl (7-22)
  - Prolactin = 6800 ng/dl (< 20)

Case 4

Giant Prolactinoma



TSH Bioactivity in Central Hypothyroidism Persani et al JCEM 2000



Sheehan's Syndrome

Atmaca et al. Thyroid 2007

72 patients with Sheehan's syndrome:

- 56 (85%) had normal TSH levels
- 4 (6%) had low TSH levels
- 6 (9%) had sl. Elevated TSH levels

TABLE 1. COMPARISONS OF CHARACTERISTICS OF THE GROUPS[a]

Groups	*CH0* (n = 56)	*CH1* (n = 10)	*Euthyroid* (n = 6)	*Control* (n = 10)
Age (yr)	54.3 ± 10.9 (29–75)	52.2 ± 8.4 (38–65)	50.02 ± 12.3 (31–63)	49.0 ± 9.1 (32–67)
Duration of the disease (yr)	17.2 ± 8.4 (4–36)	21.0 ± 9.4 (5–39)	18.6 ± 10.5 (6–30)	
fT_3 (N; 2.2–4.7 pg/ml)	0.96 ± 0.77 (0.03–3.05)	1.81 ± 0.81 (0.24–2.90)	2.61 ± 1.00[b] (0.86–3.30)	
fT_4 (N; 8–20 pg/ml)	3.10 ± 2.30 (0.10–7.80)	10.3 ± 3.02 (8–16)	11.6 ± 4.30[b] (8.30–19.7)	
TSH (N; 0.2–4.5 μIU/ml)	2.09 ± 1.71 (0.10–6.80)	0.96 ± 1.03 (0.01–2.90)	2.43 ± 1.81 (0.29–4.79)	1.33 ± 0.53 (0.35–2.0)

Case 4

Pearls

- If suspicion of thyroid dysfunction is more than minimal, always measure T4 (total or free) with TSH
- TSH is “normal” in hypopituitarism (much of the time)
- Also true for other pituitary hormones (LH/FSH, PRL, GH, ACTH)

25 year old male, Hx of congenital heart disease, developed AF

treated with electrical cardioversion. Sinus rhythm has been maintained with oral amiodarone treatment, 200 mg daily, given in association with oral anticoagulation therapy (dosage adjusted following regular INR testing). Biochemical testing before the start of amiodarone treatment documented a serum TSH level of 2.1 mIU/L and a serum free T_4 level of 1.2 ng/dL (15.4 pmol/L).

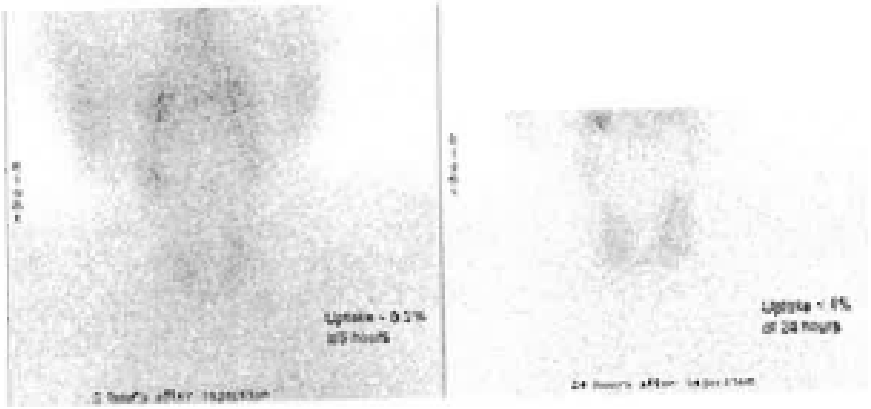
The patient has no personal history of thyroid disease and has not been the recipient of any iodine-containing contrast reagents recently. His family history is negative for thyroid disorders.

On physical examination, weight is 172 lb (78.2 kg) and height is 72.5 in (184.2 cm) (BMI = 23 kg/m^2). Pulse rate is 94 beats/min in a regular rhythm, and blood pressure is 128/74 mm Hg. He has a mild tremor of the outstretched hands. His thyroid gland is not increased in volume, nor is it tender. No discrete nodules are palpable, and there is no bruit on auscultation. He has no signs of Graves ophthalmopathy.

Laboratory test results:

- Serum TSH = <0.01 mIU/L
- Serum free T_4 = 5.05 ng/dL (65.0 pmol/L)
- Serum free T_3 = 9.6 pg/mL (14.7 pmol/L)
- Erythrocyte sedimentation rate = 18 mm/h
- Hemoglobin = 16.2 g/dL (162 g/L)
- White blood cell count = 8200/μL (8.2 × 10^9/L)
- Platelet count = 340 × 10^3/μL (340 × 10^9/L)

The results of a ^{123}I uptake scan are shown.



Which of the following investigations would be the most useful to establish the underlying cause of thyrotoxicosis?

A. Measurement of thyroglobulin antibodies, TPO antibodies, and TSH receptor antibodies
B. Measurement of urinary iodine excretion
C. Thyroid technetium-99m 2-methoxyisobutyl isonitrile scintigraphy (Tc-99m-MIBI)
D. Measurement of interleukin 6 and C-reactive protein
E. High-resolution and color-flow Doppler ultrasonography

69 A 32-year-old woman presents to the emergency department with a 2-day history of a sore throat, general malaise, anorexia, and a high fever associated with rigors. Severe Graves hyperthyroidism was diagnosed 2 months earlier, and she has since been treated with methimazole, 30 mg daily, and propranolol, 80 mg twice daily. She had lost 15.5 lb (7 kg) before Graves hyperthyroidism was diagnosed, and she has regained 2.2 lb (1 kg) since starting methimazole therapy.

On physical examination she is an ill-appearing woman. Weight is 138.5 lb (63 kg) and height is 66 in (167.6 cm) (BMI = 22.4 kg/m^2). Her temperature is 102.9°F (39.4°C), pulse rate is 80 beats/min, and blood pressure is 124/76 mm Hg. There is a white exudate overlying the tonsils and a small mouth ulcer. She has signs of mild Graves ophthalmopathy, and a moderately enlarged, soft, diffuse goiter is palpable in her neck. Findings on systems examination are otherwise unremarkable.

Urgent laboratory evaluation is performed:

- Hemoglobin = 14.2 g/dL (142 g/L)
- White blood cell count = 2300/μL (2.3 × 10^9/L)
- Neutrophil count = 100/μL (0.1 × 10^9/L)
- Platelet count = 210 × 10^3/μL (210 × 10^9/L)
- Serum electrolytes, normal
- Alanine aminotransferase = 56 U/L (0.94 μkat/L)
- Aspartate aminotransferase = 68 U/L (1.14 μkat/L)
- Erythrocyte sedimentation rate = 80 mm/h
- Serum TSH = <0.01 mIU/L
- Serum free T_4 = 5.59 ng/dL (71.9 pmol/L)

90 A 39-year-old woman with Hashimoto hypothyroidism returns for follow-up after adjustment of her levothyroxine dosage. Hypothyroidism was diagnosed at age 31 years in the postpartum period. She had a high titer of TPO antibodies and did not recover normal thyroid function. She ultimately developed a serum TSH concentration of 70 mIU/L before levothyroxine was prescribed at a dosage of 112 mcg daily. Her levothyroxine dosage was gradually increased to 150 mcg daily. She had been clinically and biochemically euthyroid while taking this dosage for several years, with her serum TSH concentration being between 1.0 and 3.0 mIU/L.

Over the past 6 months, she has unintentionally lost 8.8 lb (4 kg). She describes being more irritable, having modest heat intolerance, and having a diminished exercise capacity. You have had her return 3 times in the last 6 months for thyroid hormone testing and on each occasion her TSH was suppressed. Thus, her levothyroxine dosage was reduced to 50 mcg daily (her current dosage).

On physical examination, height is 65.5 in (166.4 cm) and weight is 153 lb (69.5 kg) (BMI = 25.1 kg/m^2). Blood pressure is 124/74 mm Hg, and heart rate is 88 beats/min. Her thyroid gland is slightly enlarged and has an irregular texture. She has brisk patellar reflexes.

Thyroid function test results:

Serum TSH = 0.01 mIU/L

Free T_4 = 2.1 ng/dL (27.0 pmol/L)

She confirms that levothyroxine is her only prescription medication. She never takes extra tablets. You inspect the tablets in her levothyroxine pill container and find no error in the prescription. She takes no over-the-counter supplements. Your review of her history does not uncover any reason accounting for her decreased levothyroxine requirement.

Over several subsequent visits, and after further levothyroxine dosage adjustments, you discontinue her levothyroxine. Thyroid function testing 6 weeks later shows a TSH concentration of 2.1 mIU/L and a free T_4 concentration of 1.4 ng/dL (18.0 pmol/L). With this last blood test, you also measure a serum total T_3 level, a serum thyroglobulin concentration, and a spot urinary iodine concentration. Her total T_3 level is 120 ng/dL (1.8 nmol/L), her thyroglobulin concentration is 43 ng/mL (43 µg/L), and her random urinary iodine excretion is 177 µg/L (reference range, 28-544 µg/L).

Which of the following best explains euthyroidism after the discontinuation of levothyroxine in this patient?

A. Surreptitious ingestion of liothyronine
B. Ingestion of an over-the-counter supplement containing tiratricol
C. Ingestion of large amounts of nutritional supplements containing iodine
D. Autoimmune thyroid disease with current predominance of thyrotropin receptor–stimulating antibodies
E. Surreptitious ingestion of desiccated porcine thyroid extract

Case History

A 27 yo woman, 15 weeks pregnant, presents with nausea, dyspnea and palpitations. She has Graves' disease; admitted previously for similar symptoms.

Meds: PTU 200 mg QID, Propranolol 20 mg TID

PE: BP 154/70 P 125 T 101 Ht 5'7'' Wt 135 lb.

MS: agitated CV: no rales, no S3, no edema

Thyroid: diffuse (> 100 gm); + bruit

Lab: TSH: < 0.01 mU/L (nl: 0.5-5.0)

FT4 12.9 ng/dl (nl: 0.8-1.8) T3 958 (nl: 90-180)

Does she have thyroid storm?

How would you initiate treatment?

Thyroid Storm Score

Feature	Score	Feature	Score
Fever:		**Pulse:**	
99-99.9	5	99-109	5
100-100.9	10	110-119	10
101-101.9	15	120-129	15
102-102.9	20	130-139	20
103-103.9	25	>139	25
>103.9	30	Atrial fibrillation	10
CNS:		**CHF:**	
Absent	0	Absent	0
Mild (agitation)	10	Mild (edema)	5
Moderate (delirium)	20	Moderate (rales)	10
Severe (sz, coma)	30	Severe (pulm edema)	15
GI:		**Precipitant History:**	
Absent	0	Absent	0
N, V, D, Pain	10	Present	10
Jaundice	20		

Burch and Wartofsky, Endocrinology and Metabolism Clinics of North America, 1993.

Treatment of Thyroid Storm

Although PTU is traditionally preferred because of its effects on T4 to T3 conversion, there is no evidence that PTU is more efficacious than Methimazole in Thyroid Storm.

Use Either ATD in High Dose:
Methimazole 60-120 mg daily in Divided Doses
PTU 600-1200 mg daily in Divided Doses

Methimazole and PTU Can Be Given PO, NG Tube, or Rectally
Methimazole Can Be Given IV

Cooper D. N Engl J Med 2005;352:905-917
Hodak S, Thyroid 2006;16:691-5

Thyroid Storm Treatment

- **Reduce Thyroid Hormone Synthesis**
  - Propylthiouracil (PO, NG, Rectal): 200 mg Q 4-6 hours
  - Methimazole (PO, NG, Rectal): 20 mg Q 4-6 hours
- **Reduce Thyroid Hormone Release**
  - Sodium Iodide (IV): 1 gm over 24 hours
  - Potassium Iodine (PO): 5-10 drops TID [SSKI, Lugol's]
- **Reduce Heart Rate**
  - Esmolol (IV): 500 ug over 1 min, then 50-300 ug/kg/min
  - Metoprolol (IV): 5-10 mg Q 2-4 hours
  - Diltiazem (IV): 0.25 mg/kg over 2 min, then 10 mg/min, or (PO): 60-90 mg Q 6-8 hours
- **Support Circulation and Oxygenation**
  - Stress Dose Glucocorticoids IV
  - IV Fluids
  - Oxygen