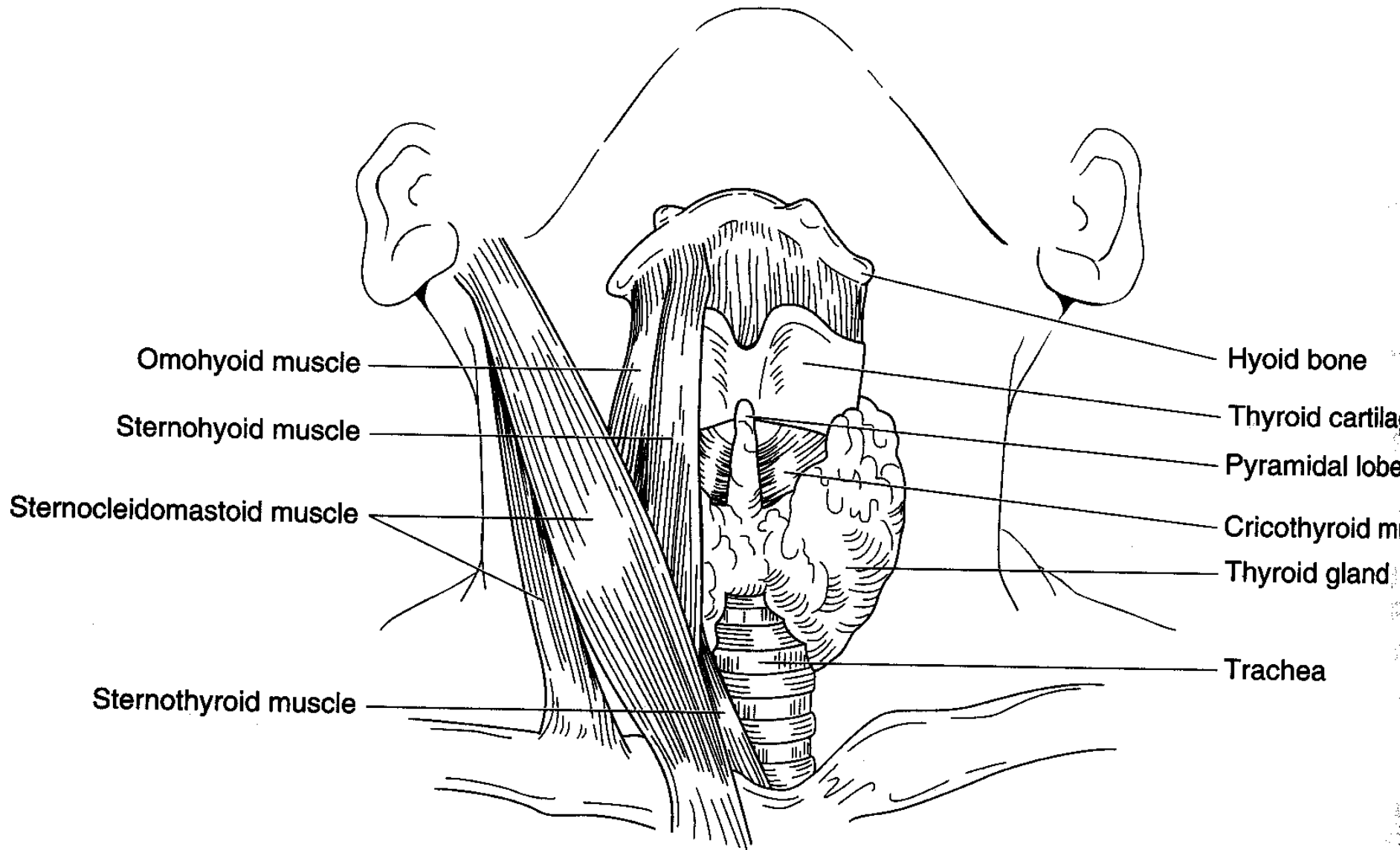


Thyroid Gland Disease

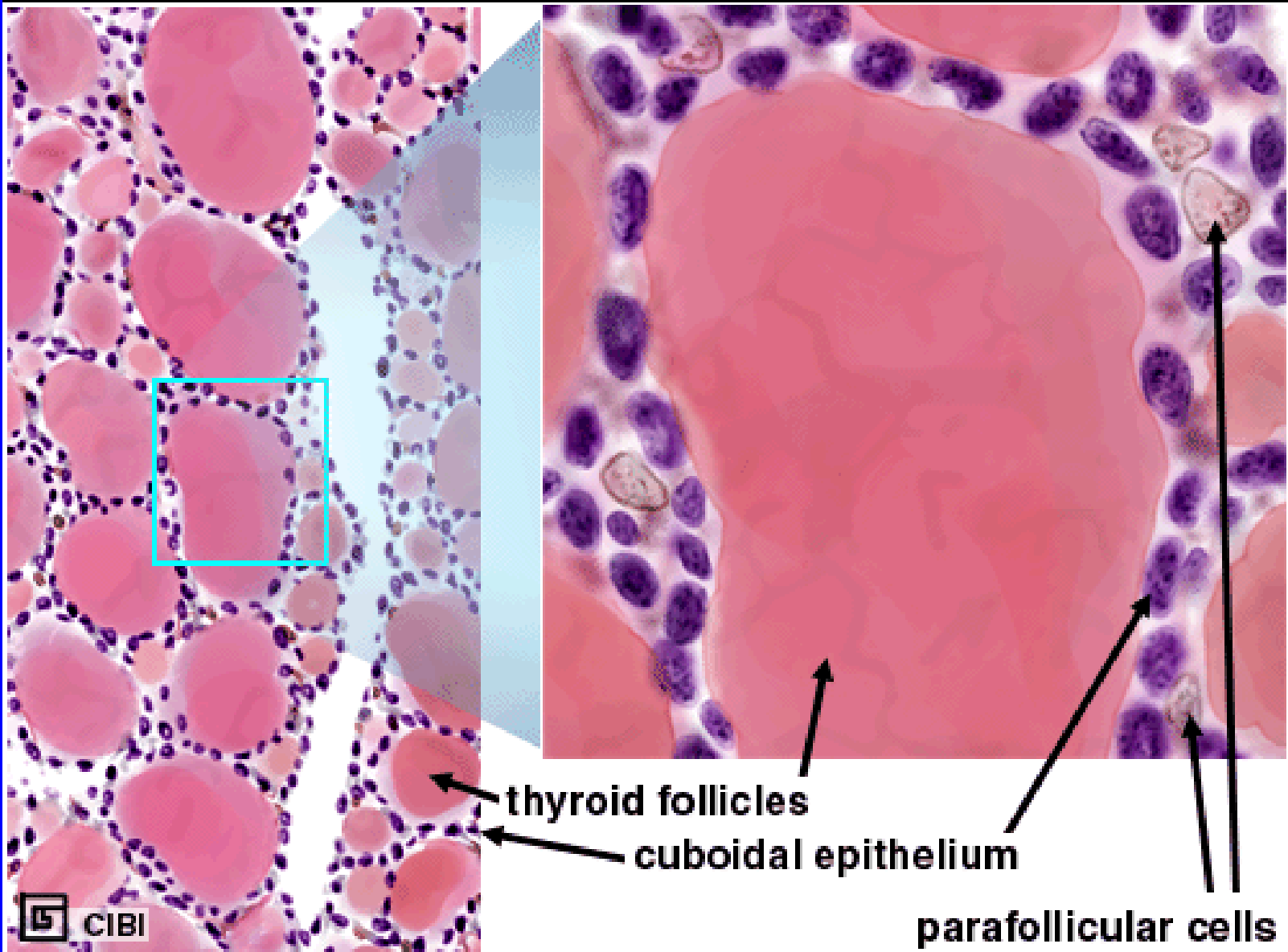
Zdeněk Fryšák

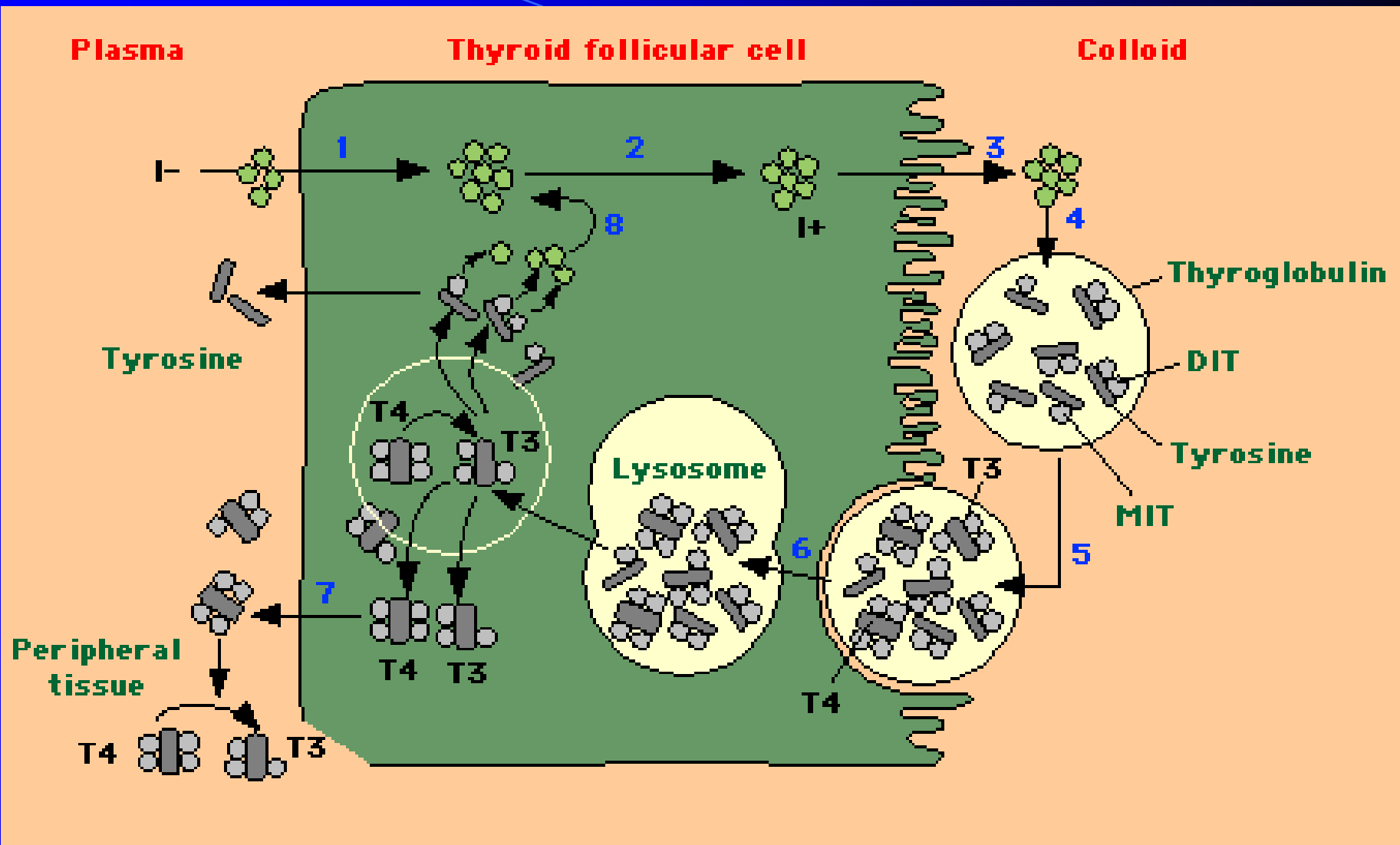
III. Interní klinika FN a LF UP

Olomouc



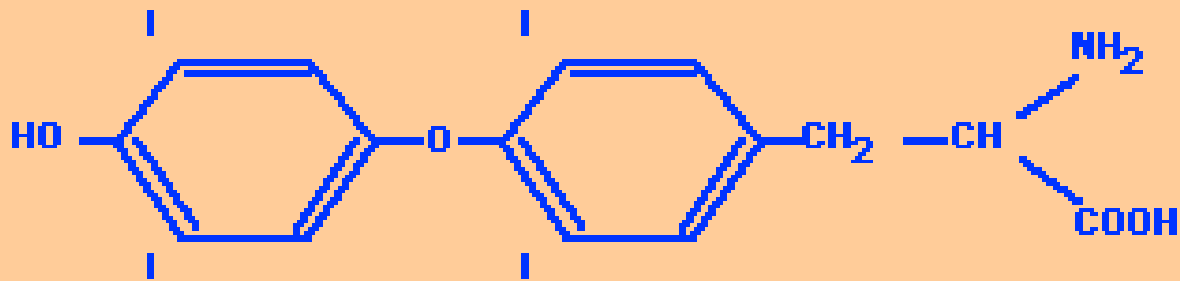
Thyroid Gland: Histology





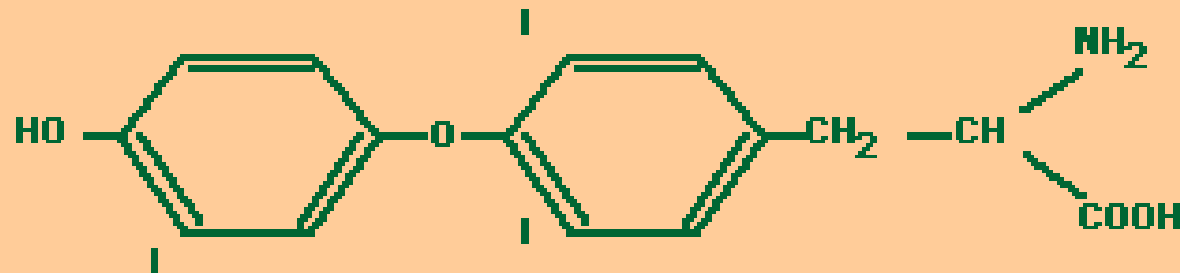
Structures of the Thyroid Hormones

Thyroxine (T_4)



$t_{1/2} = 5-7d$

3,5,3'-Triiodothyronine (T_3)



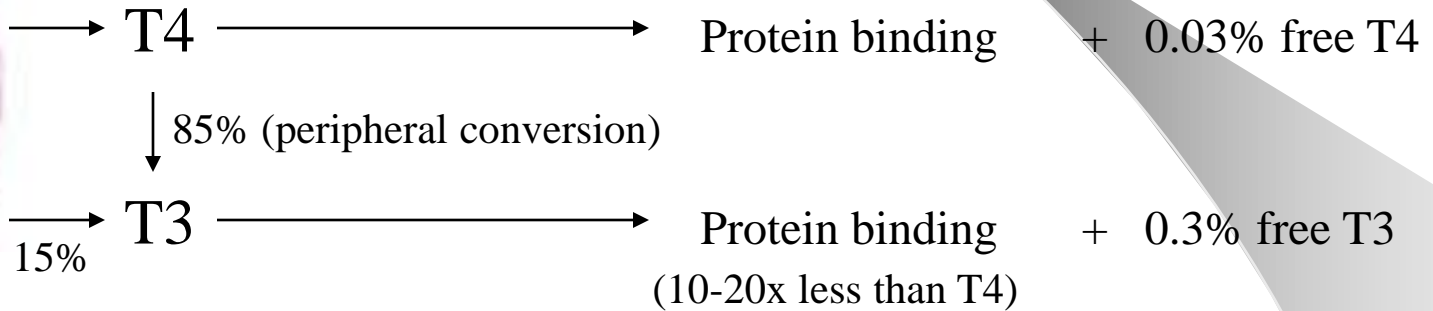
$t_{1/2} = < 24 \text{ hrs}$

Normal Daily Thyroid Secretion Rate:

T4 = 100 ug/day

T3 = 6 ug/day

(ratio T4:T3 = 14:1)



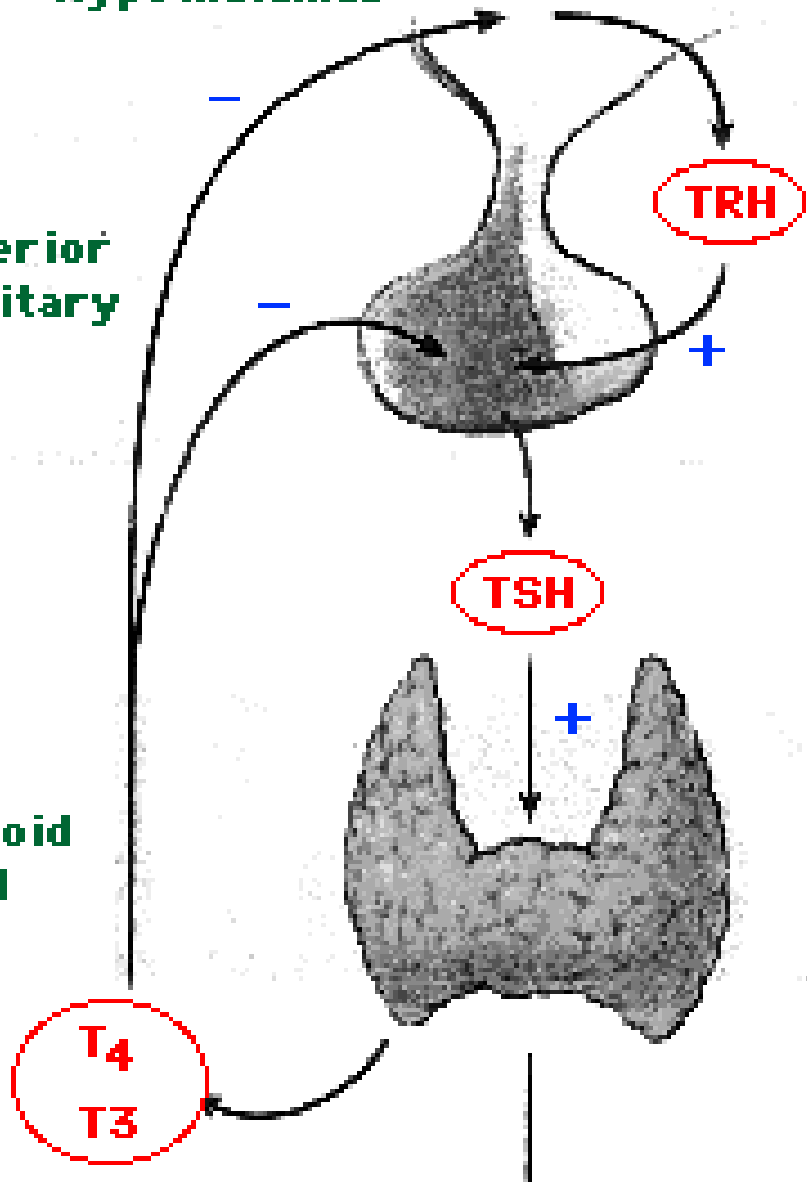
	<u>T4</u>	<u>T3</u>
Potency	1	10
Protein Bound	10-20	1
Half-Life	5-7d	< 24h
Secreted by thyroid	100 ug/d	6 ug/d

Hypothalamus

Anterior
pituitary

Thyroid
gland

Serum

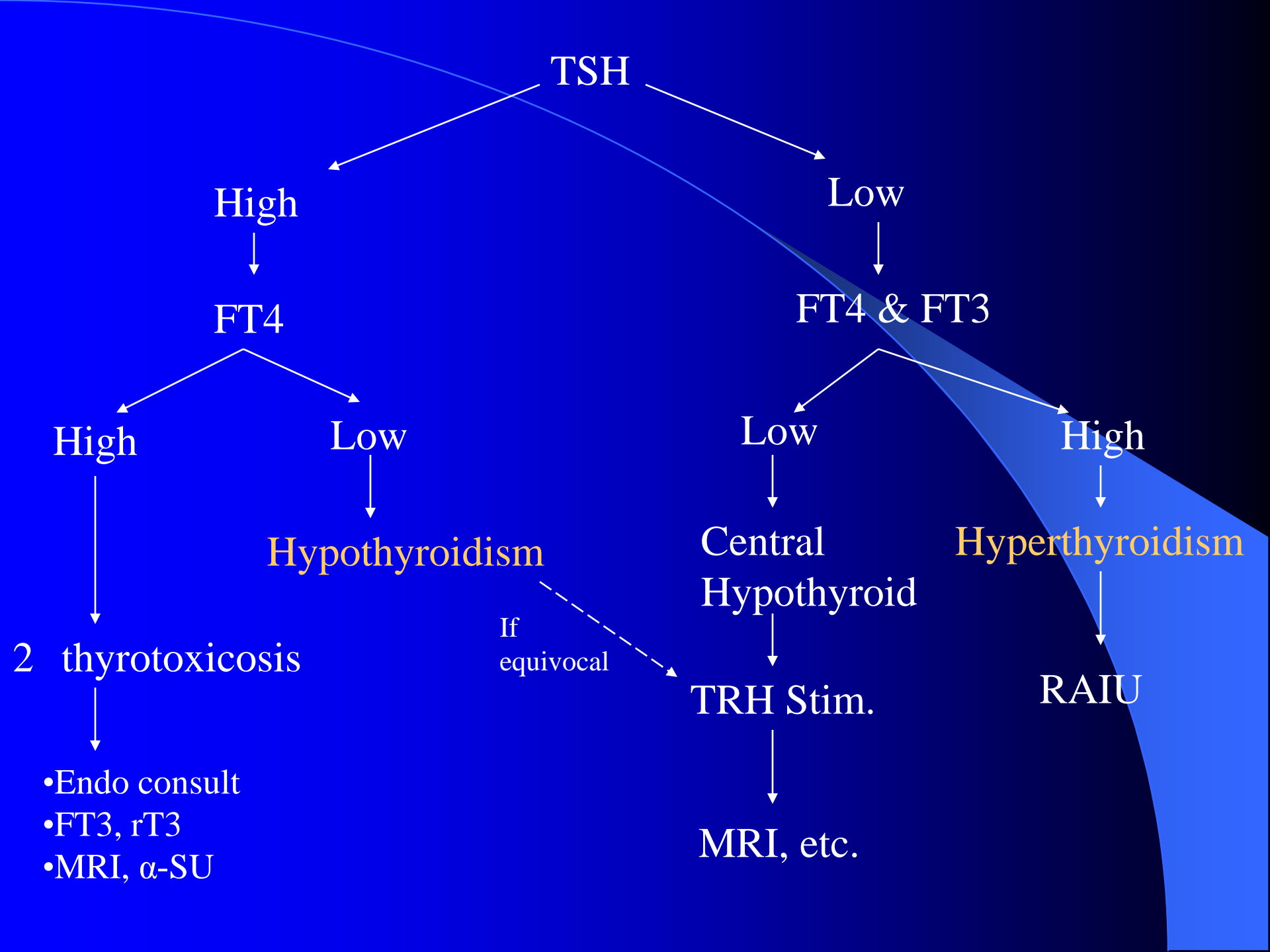


Thyroid Function: blood tests

TSH	0.4 – 5.0 mU/L
Free T4 (thyroxine)	9.1 – 23.8 pM
Free T3 (triiodothyronine)	2.23-5.3 pM

Thyroid Disease

- Hypothyroidism
- Hyperthyroidism
- Thyroid Cancer
 - Thyrogen (recombinant human TSH)



Hypothyroidism

- Decreased thyroid hormone levels
 - Low T4
 - Possibly Low T3 too.
 - Raised TSH (unless pituitary problem!)

Major Symptoms and Signs of Hypothyroidism

Mechanism

Symptoms

Signs

Slowing of metabolic processes

Fatigue and weakness
Cold intolerance
Dyspnea on exertion
Weight gain
Cognitive dysfunction
Mental retardation (infant)
Constipation
Growth failure

Slow movement and slow speech
Delayed relaxation of tendon reflexes
Bradycardia
Carotenemia

Accumulation of matrix substances

Dry skin
Hoarseness
Edema

Coarse skin
Puffy facies and loss of eyebrows
Periorbital edema
Enlargement of the tongue

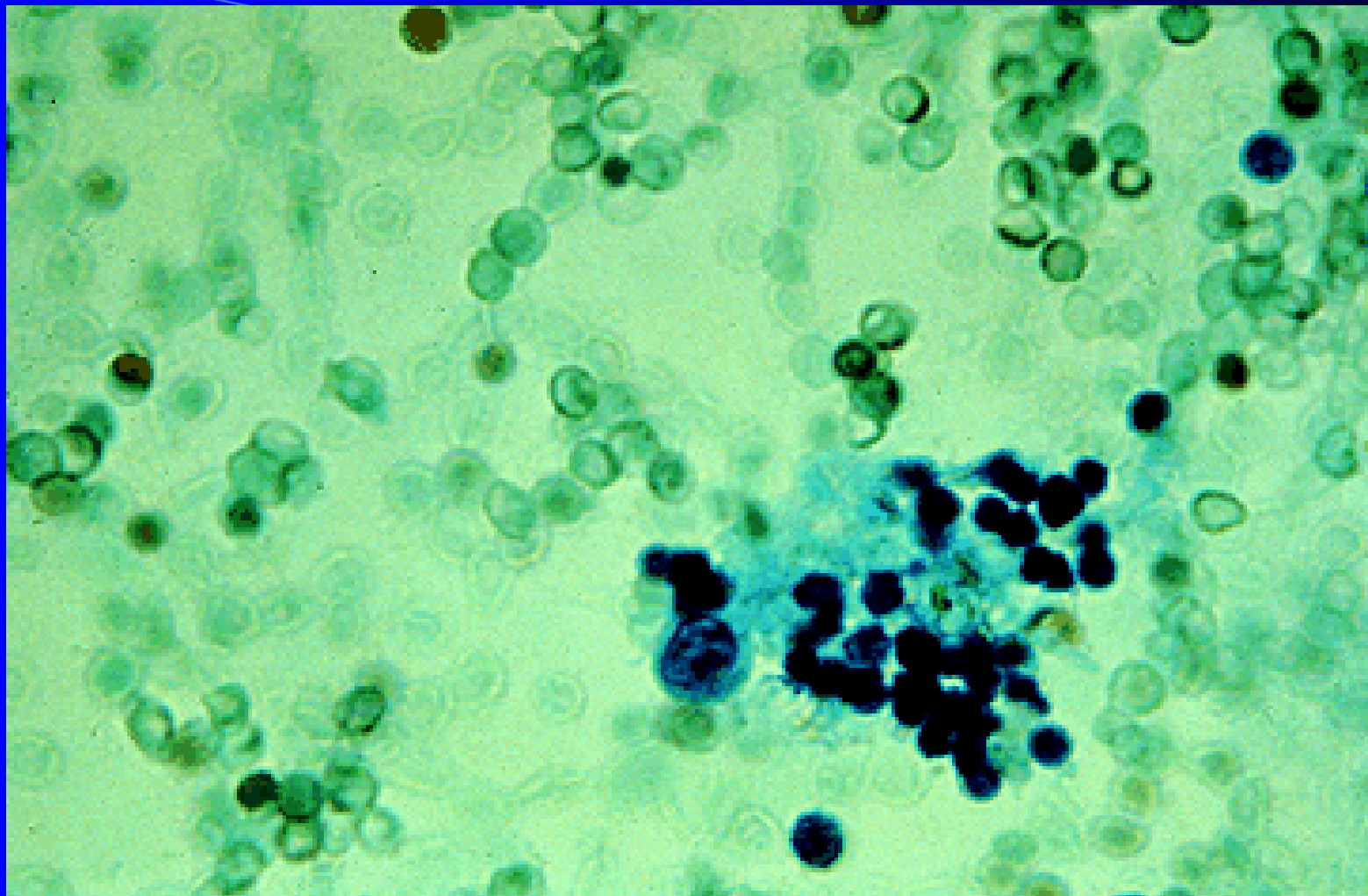
Other

Decreased hearing
Myalgia and paresthesia
Depression
Menorrhagia
Arthralgia
Pubertal delay

Diastolic hypertension
Pleural and pericardial effusions
Ascites
Galactorrhea

Hashimoto's Disease

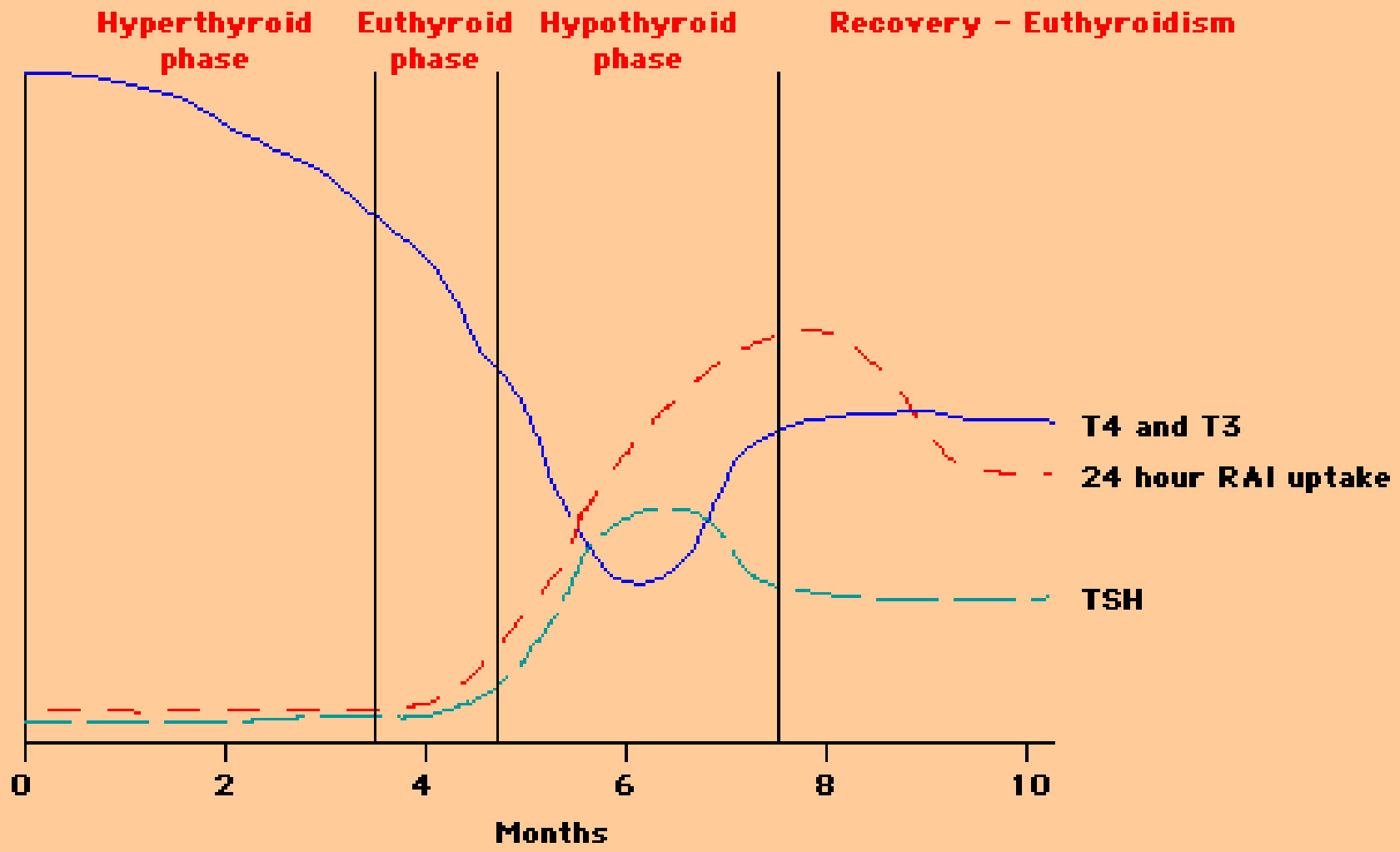
- Most common cause of hypothyroidism in North America (iodinated salt)
- Autoimmune lymphocytic thyroiditis
- Antithyroid antibodies:
 - Thyroglobulin Ab
 - Microsomal Ab
 - TSH-R Ab (block)
- Females > Males
- Runs in Families!



Hashimoto's thyroiditis Fine needle aspirate of the thyroid in Hashimoto's thyroiditis. Lymphocytes are predominant, sometimes surrounding rare follicular cells. No formed follicles are seen. Some colloid is present in the background.

Subacute (de Quervain's) Thyroiditis

- Preceding viral infection
- Infiltration of the gland with granulomas
- Painful goitre
- Hyperthyroid phase → Hypothyroid phase



Treatment of Hypothyroidism

- Iodine only if iodine deficiency is the cause
 - Rare in Czech Republic!
- Replacement thyroid hormone medication:
 - T4?
 - T3?
 - T4 + T3 Mixture?
 - Thyroid Hormone from “natural sources” ?

Levothyroxine (T4)

- Synthetically made
- 50 ug white pill → no dye (hypoallergenic)
- Most commonly prescribed treatment for hypothyroidism
- No T3 (but 85% of T3 comes from T4 conversion)
- All patients made euthyroid biochemically
- Most (but not all) patients feel normal

Levothyroxine (T4)

- Average dose 1.6 ug/kg
- Age > 50-60 or cardiac disease: must start at a low dose (25 ug/d)
- Recheck thyroid hormone levels every 4-6 weeks after a dose change
- Aim for a normal TSH level

Levothyroxine (T4)

- Medical situations where T4 medication may be affected.
- Estrogen: Pregnancy, OCP, HRT
 - Need to increase T4 dose!
- Drugs that interfere with T4 absorption
 - Iron, Calcium
 - Cholestyramine (cholesterol resin Rx)
 - At least 4h between T4 and these drugs!

“I still don’t feel normal on levothyroxin even though my blood tests are normal.”

- Free T4, Free T3
 - wide range of normal
- TSH (0.4 –5.0 mU/L)
 - Narrow range of normal, but still a range!
 - Adjust dose for a lower TSH still in the normal range?
- Tissue levels versus circulating levels?
 - No human studies
 - Rodents: High T4 and normal T3 tissue levels

Liothyronine (T3)

- Liothyronine
- Shorter half-life
 - Fluctuating levels (i.e. need a slow-release pill)
 - Twice daily dosing often needed
- 10x more potent: palpitations & other cardiac side effects
- High T3 levels, low T4 levels (not physiologic either!)

T3/T4 Thyreotom

- Thyreotom
- Combo pill of T3 and T4
- Ratio of T4:T3 = 4:1 (not 14:1)
- T3 still not slow release
- Few small studies showing benefit
 - 1999 NEJM study 33 patients
 - Benefit: mood & cognitive function

TABLE 4. RESULTS ON VISUAL-ANALOGUE SCALES AT THE END OF EACH TREATMENT PERIOD.*

SCALE	AFTER THYROXINE (N= 33)	AFTER THYROXINE PLUS TRIIODOTHYRONINE (N= 33)	P VALUE†
Mood			
Sad	40 ± 24	26 ± 19	<0.001
Confused	34 ± 24	23 ± 20	<0.001
Fearful	30 ± 29	20 ± 22	0.001
Irritable	39 ± 28	27 ± 22	0.002
Tense	42 ± 29	28 ± 23	0.007
Angry	32 ± 28	25 ± 20	0.02
Tired	49 ± 26	39 ± 28	0.04
Agitated	39 ± 30	34 ± 26	0.18
Physical symptoms			
Feel cold	37 ± 27	23 ± 24	0.004
Blurred vision	30 ± 29	22 ± 27	0.01
Nauseated	22 ± 23	13 ± 17	0.02
Sleepy	39 ± 29	29 ± 27	0.09
Light-headed	35 ± 26	31 ± 28	0.22
Drowsy	36 ± 27	31 ± 25	0.29
Feel hot	24 ± 21	25 ± 27	0.80

*On every scale, a lower score represents a more favorable state. Scores of 0 or 100 are theoretically possible but are rarely encountered. Plus-minus values are means ±SD.

†P values were calculated by paired t-tests.

Desiccated Thyroid (obsolete)

- Desiccated powder derived from thyroids of slaughtered pigs or cows
 - Vegetarian?
 - Mad Cow Disease?
- Contains T4 and T3
- Still no slow-release of T3
- Ratio of T4:T3
 - Variable
 - Still not physiologic, often too high in T3 (T4:T3 = 3:1)

“In an ideal world...”

- Mixed compound with T4:T3 = 14:1
- T3 component slow release formulation
- Resultant:
 - Normal circulating TSH, FT4, FT3
 - Normal tissue levels of T4 and T3
- Good, large studies (RCTs) demonstrating clear benefit over T4 alone
- Doctor's *don't* like to experiment on their patients

Hyperthyroidism

- Heat intolerance
- Weight loss (normal to increased appetite)
- Hyperdefecation
- Tremor, Palpitations
- Diaphoresis
- Lid retraction & Lid Lag
- Decreased menstrual flow

Graves' Disease

- Most common cause of thyrotoxicosis
- TSH-R antibody (stim)
- Goitre, Orbitopathy, Dermopathy



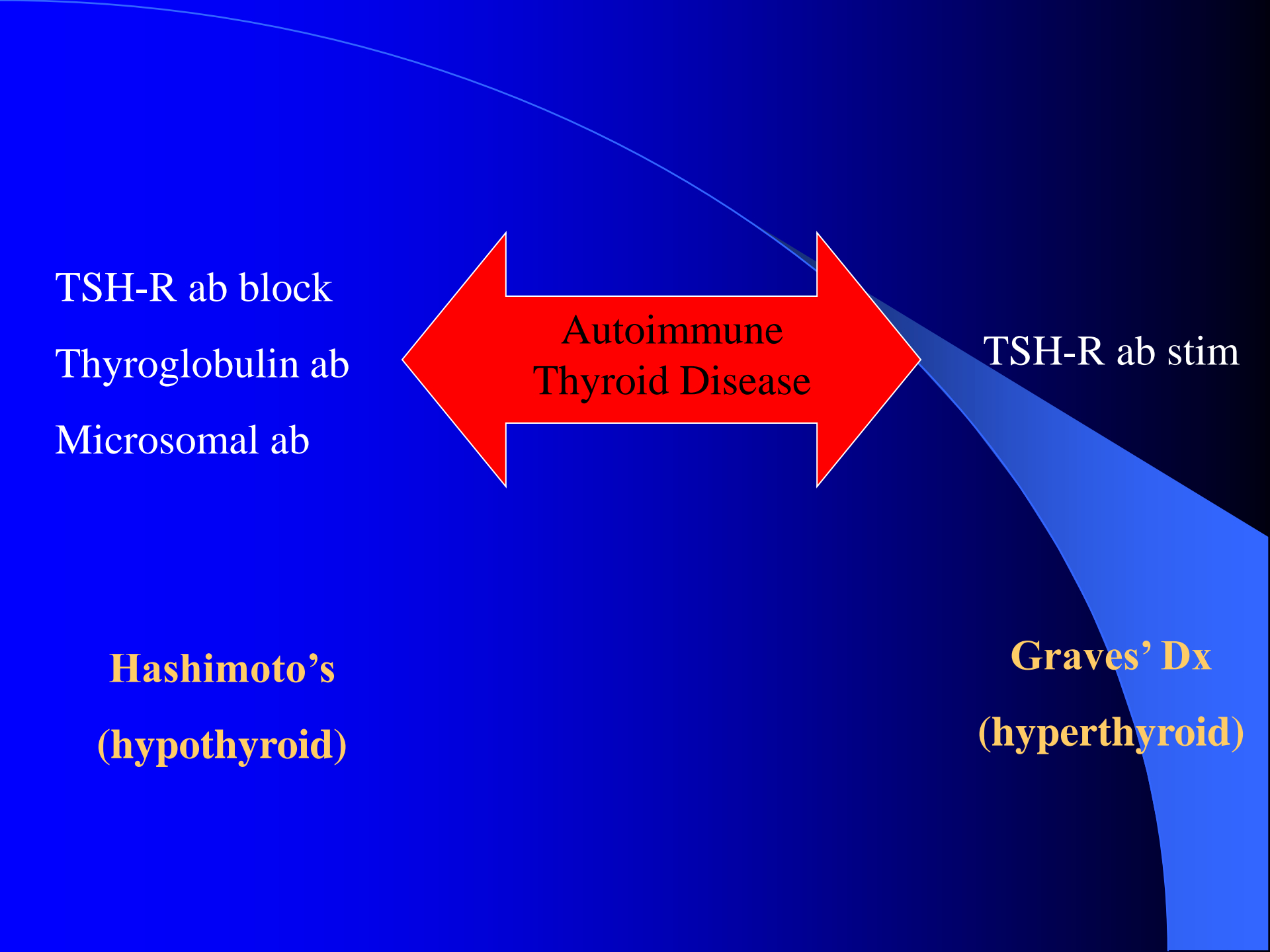
Autoimmune
Thyroid Disease

TSH-R ab block
Thyroglobulin ab
Microsomal ab

TSH-R ab stim

Hashimoto's
(hypothyroid)

Graves' Dx
(hyperthyroid)



Hyperthyroidism: Treatment

- Beta-blockers (hyperadrenergic symptoms)
- Hyperthyroidism:
 - Anti-thyroid Drugs
 - Thiamazol, Propylthiouracil (PTU), Methimazole
 - Surgical Thyroidectomy
 - Radioiodine Ablation
- Thyroiditis:
 - ASA, NSAIDS, +/- corticosteroids
- Iodine (high doses → Wolff Chaikoff effect)

Thyroid nodules & cancer

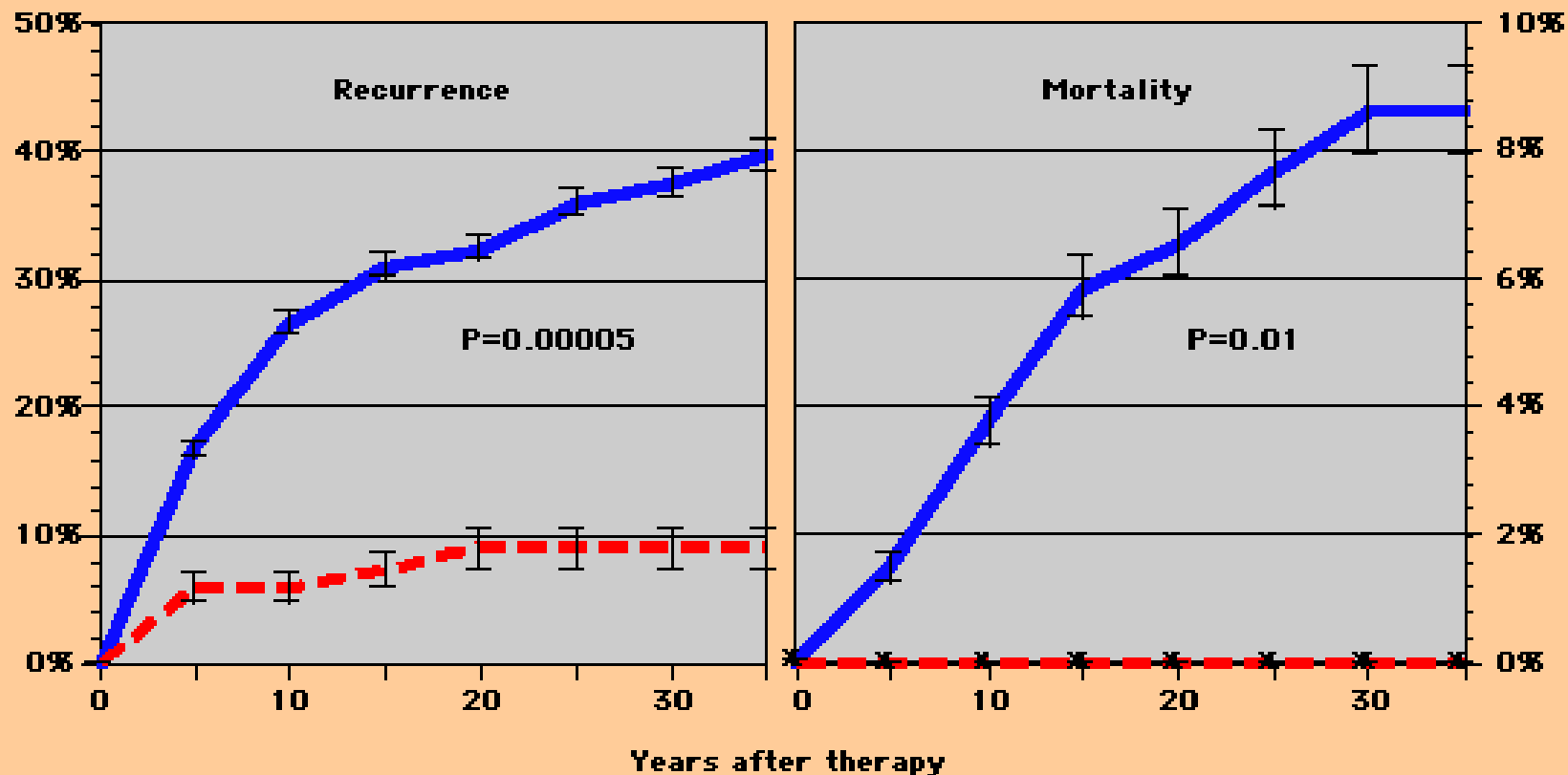
- **Thyroid nodules are common**
 - 4% of adults (6.4% women, 1.5% men)
 - U/S: 20% of women have nodules
 - U/S: 50% of women > 50 y.o. have nodules
- **Most thyroid nodules are benign**
 - Only 5 - 6.5 % are cancer (4 % women, 8 % men)
 - 92 % Differentiated thyroid cancer
 - only 0.5 % chance of serious thyroid cancer

Thyroid Cancer

	Papillary	Follicular	Medullary	Anaplastic
% of thyroid cancers	76 %	16 %	4 %	1 %
% die from thyroid Ca	6 %	24 %	33 %	98 %
Treatment	Surgery RAI LT4	Surgery RAI LT4	Surgery	Surgery +/- XRT

Treatment: DTC

- Surgery
 - RLN injury 2 %, SLN 4-6 %
 - Hypocalcemia: temp 40 %, permanent 2 %
- RAI
 - High dose (100 mCi or more)
 - Doses > 29.9 mCi as outpatient
 - Need TSH to be high
 - Hold LT4 for at least 4-6 weeks
 - Hold T3 (Cytomel) for at least 2 weeks
- Levothyroxine (LT4)
 - Suppress TSH



Radioiodine ablation reduces recurrence and mortality in stage II and stage III thyroid cancer Long-term development of recurrent disease (left panel) or death (right panel) from thyroid cancer in patients without distant metastases at presentation, who received either ^{131}I ablation (red dashed lines) or no ablation (blue solid lines). (Data from Mazzaferri, EL, Jhiang, SM, Am J Med 1994; 97:418.)

DTC: monitoring

- Serum Tg, WBS
- Need serum TSH levels being highly suppressed
- Hold LT4 for 4-6 wk (cytome1 2 wk)
- Thyrogen
 - Recombinant human TSH injections

Thyrogen[®] (thyrotropin alfa for injection) Testing Schedule

(To be filled out by my doctor or nurse)

Patient's Name

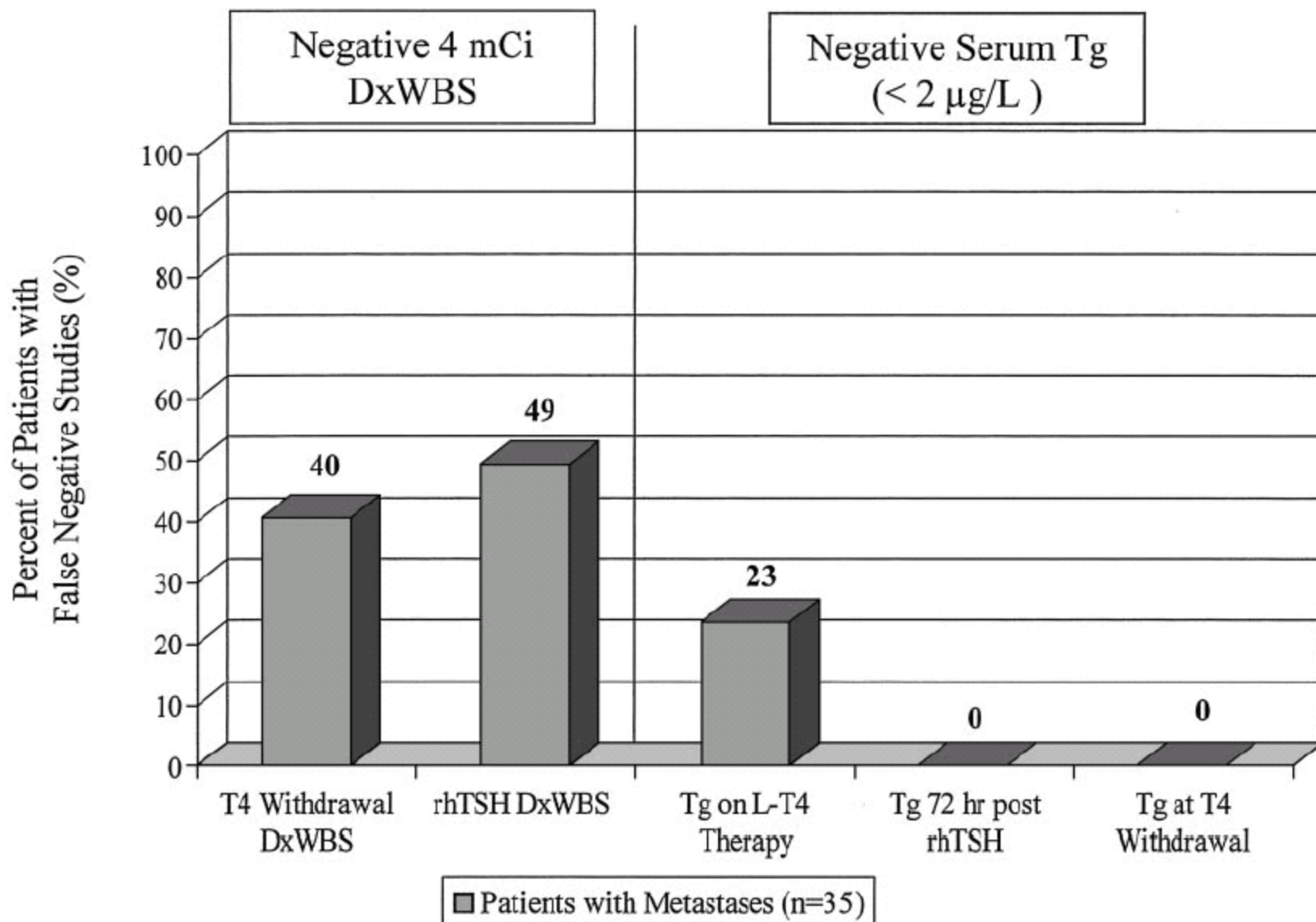
Physician's Name

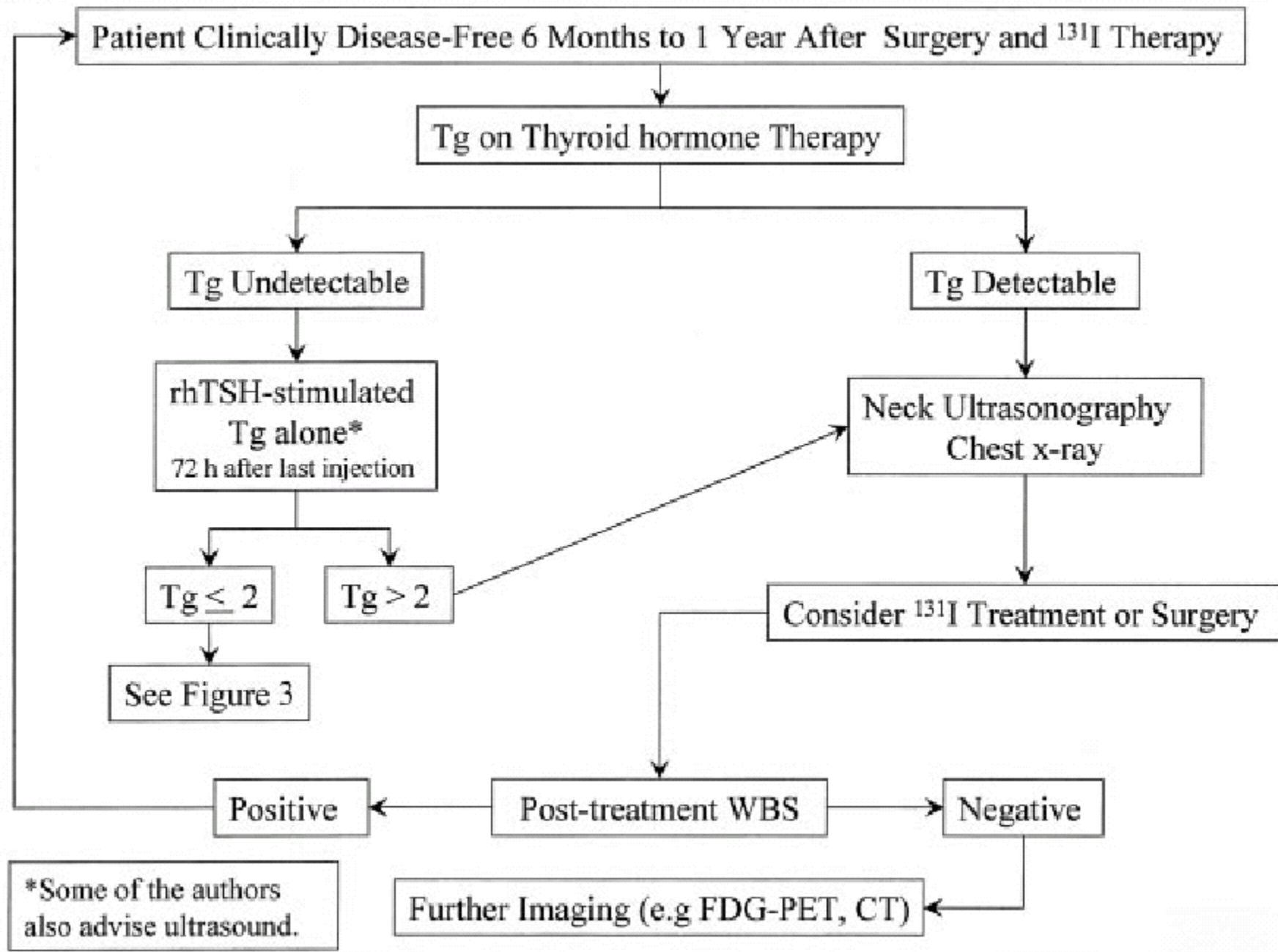
- I am having **only** a thyroglobulin (Tg) blood test with Thyrogen.
- I am having **both** a thyroglobulin (Tg) blood test and a whole body scan with Thyrogen.
- I must go on a low-iodine diet for 2 weeks before my whole body scan.

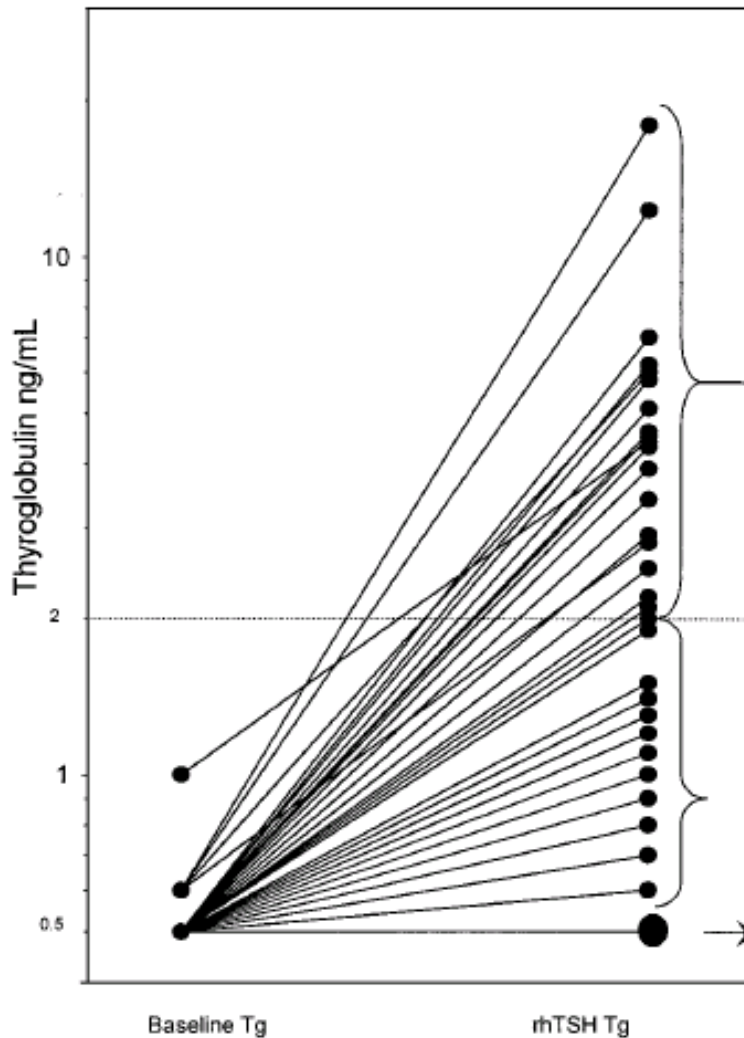
- I will be receiving **two** Thyrogen injections. My appointments are listed below.

When		What	Where
Day	Date/Time	Check applicable items	Write in location
1		<input type="checkbox"/> Thyrogen injection #1	
2		<input type="checkbox"/> Thyrogen injection #2	
3		<input type="checkbox"/> Radioactive iodine dose	
4			
5		<input type="checkbox"/> Whole body scan <input type="checkbox"/> Thyroglobulin (Tg) blood test	

Percent of False Negative Studies in Patients with Metastases on RxWBS







Tg > 2 $\mu\text{g/L}$
~20%-25%

Prompt
Evaluation

Tg 0.6-2.0
~15%-20%

Periodic
rhTSH - Tg
Until no rise

No Rise
Tg 0.5
~60-70%

Annual
THST - Tg

Thyrogen

- Cost \$ 1,470
- ODB covered (Ltd. Use #368)
- Trillium
 - 1-800-575-5386
 - 416-326-1558
- Thyrogen Reimbursement Helpline
 - 1-866-401-8323

The image features a dark blue background that transitions into a lighter blue gradient on the right side. A thin, light blue curved line starts from the top left and curves downwards towards the center. The word "END" is written in a bold, yellow, sans-serif font, positioned in the center of the image. The overall composition is minimalist and modern.

END