Hyperthyroidism

and Hypothyroidism

Gilbert H. Daniels M.D.

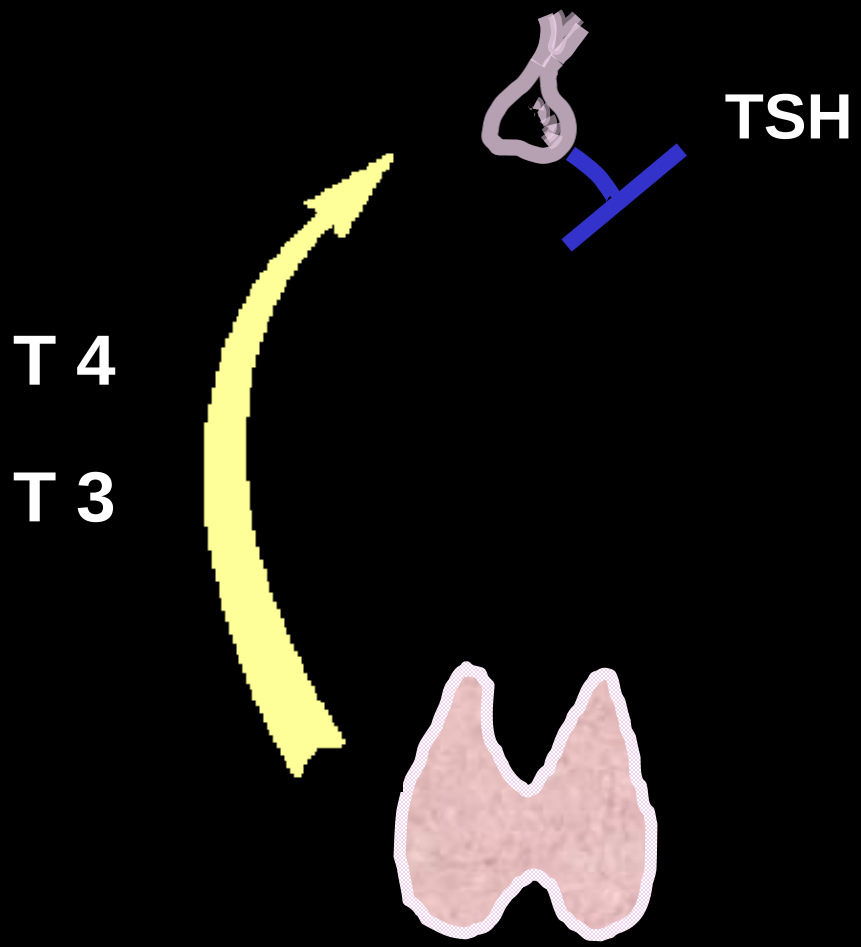
No Disclosures.

Gilbert H. Daniels M.D.

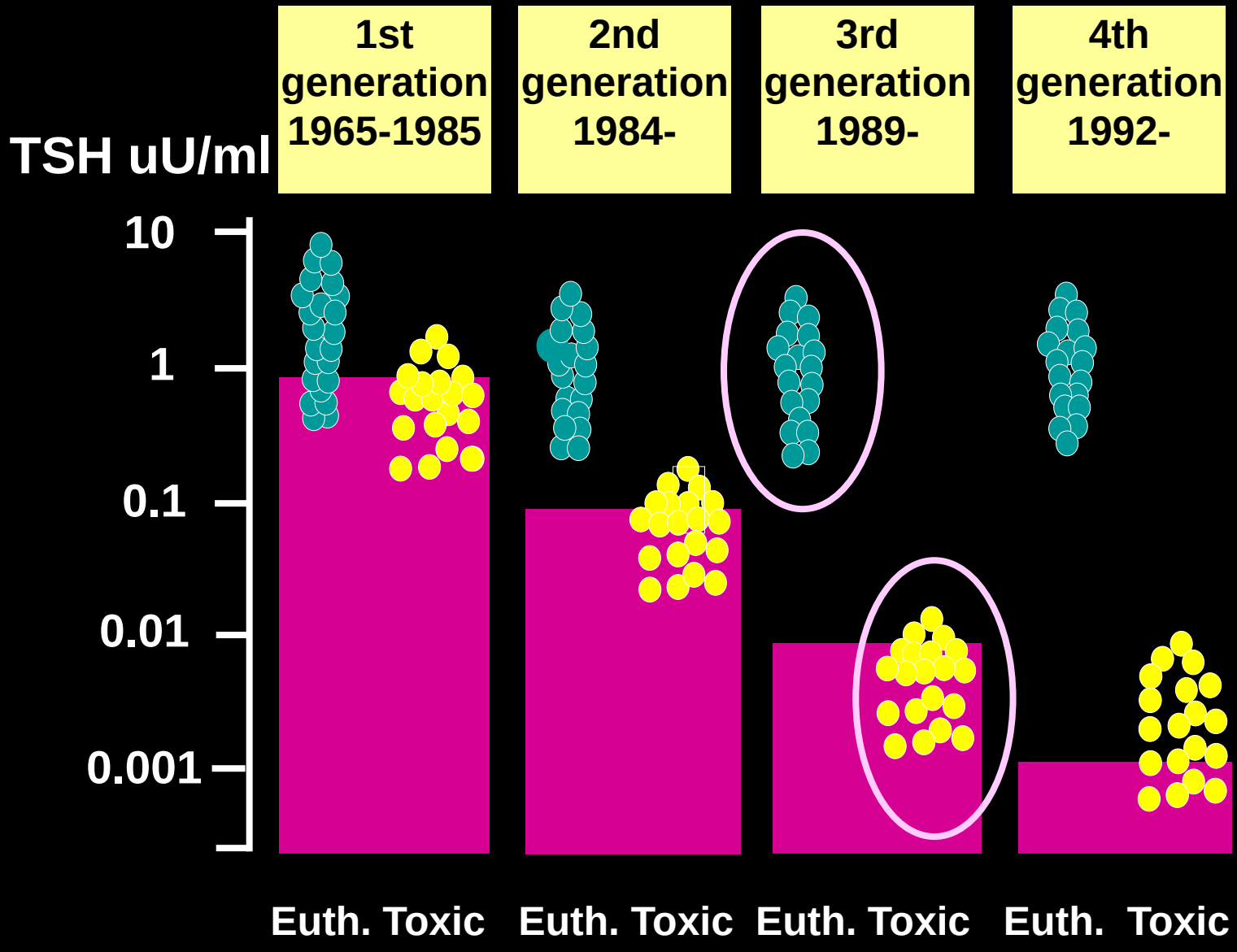
Objectives

- To understand the differential diagnosis of hyperthyroidism
- To understand the growing role of drug-induced thyroid dysfunction
- To appreciate the significance of subclinical hyper and hypothyroidism
- To understand what causes a change in L – T4 dosing.
- To understand the T4/T3 controversy for hypothyroidism

Hyperthyroidism



TSH Assays


1st generation 1965-1985
2nd generation 1984-
3rd generation 1989-
4th generation 1992-
TSH uU/ml
10
1
0.1
0.01
0.001
Euth.
Toxic
Euth.
Toxic
Euth.
Toxic
Euth.
Toxic

Hyperthyroidism - High or Normal RaI U

- Hot Nodule
- Toxic Nodular Goiter
- Graves Disease
- TSH Induced Hyperthyroidism
- HCG Induced Hyperthyroidism

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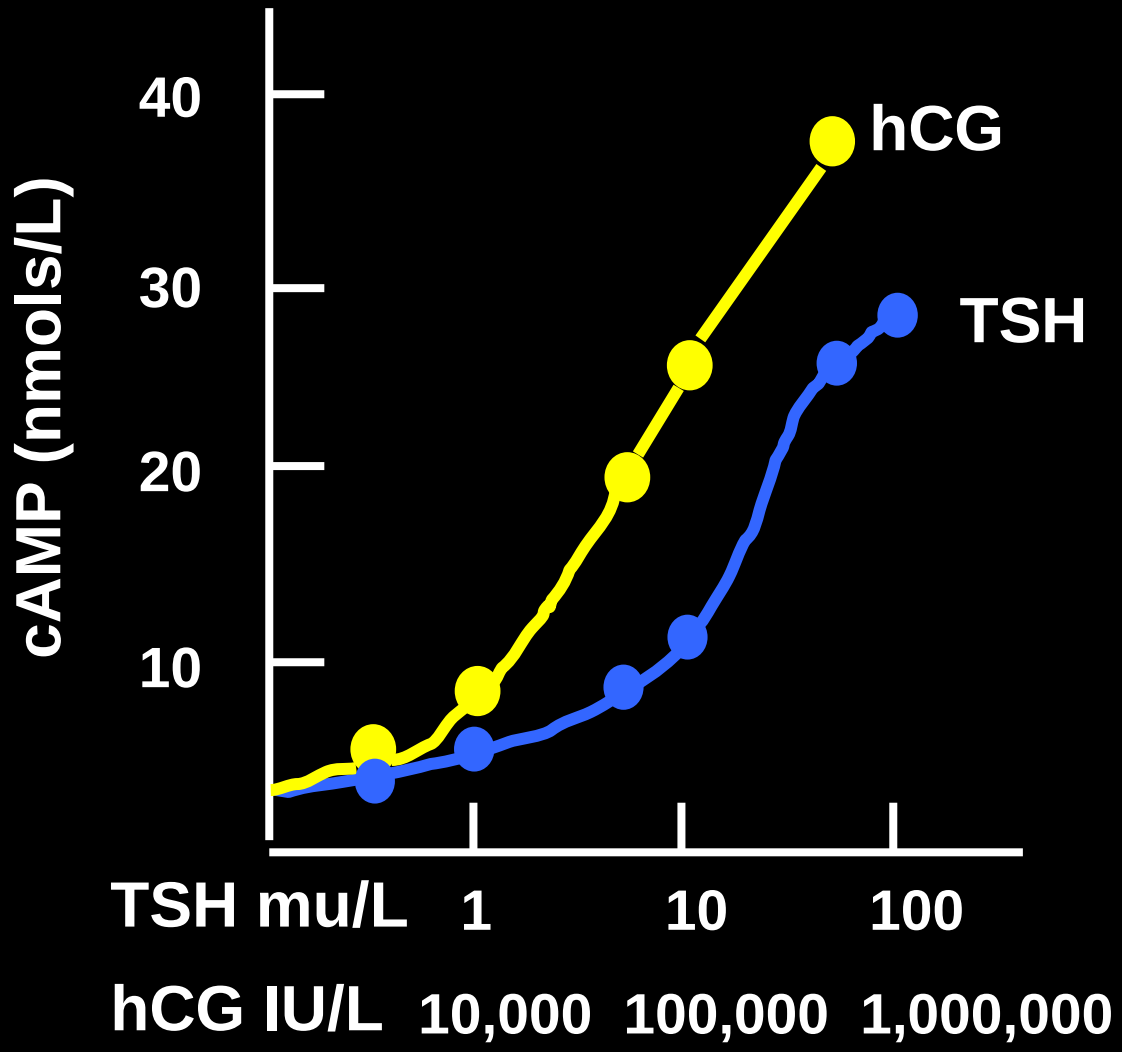
HCG vs. TSH

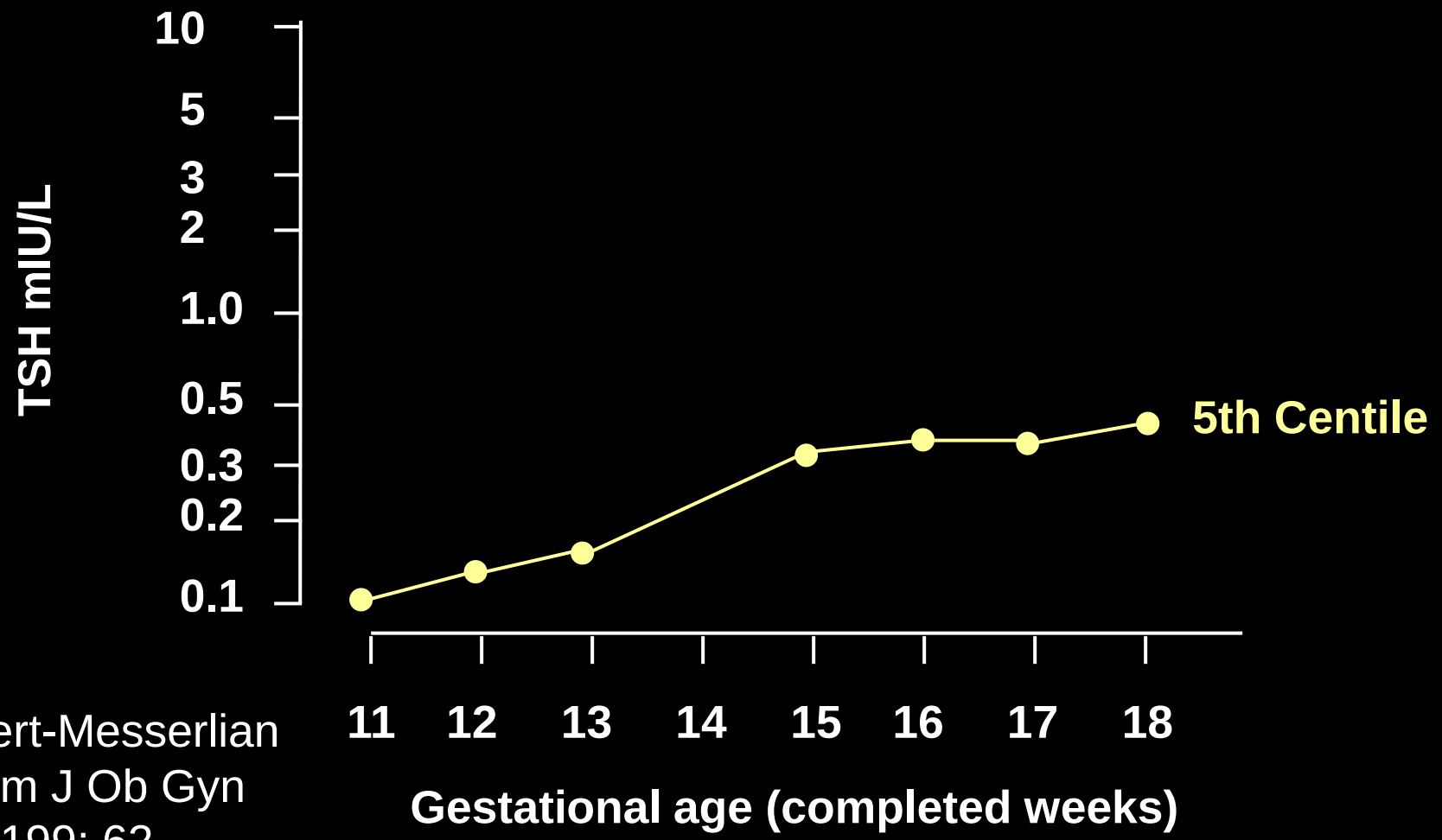


Yoshikawa et al

JCEM 1989; 69: 891

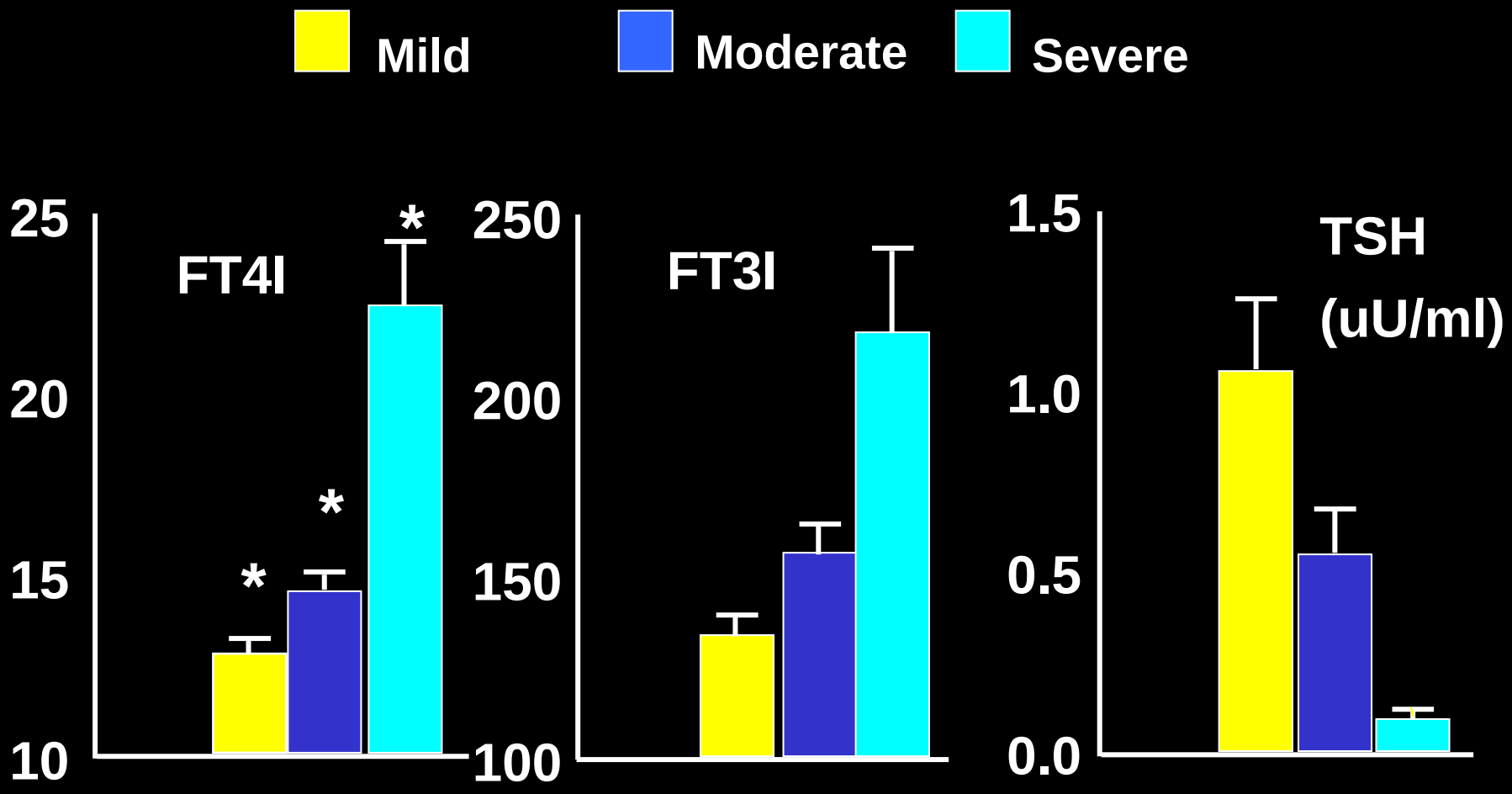
Pregnancy: TSH

9562 women - excluding hypothyroidism



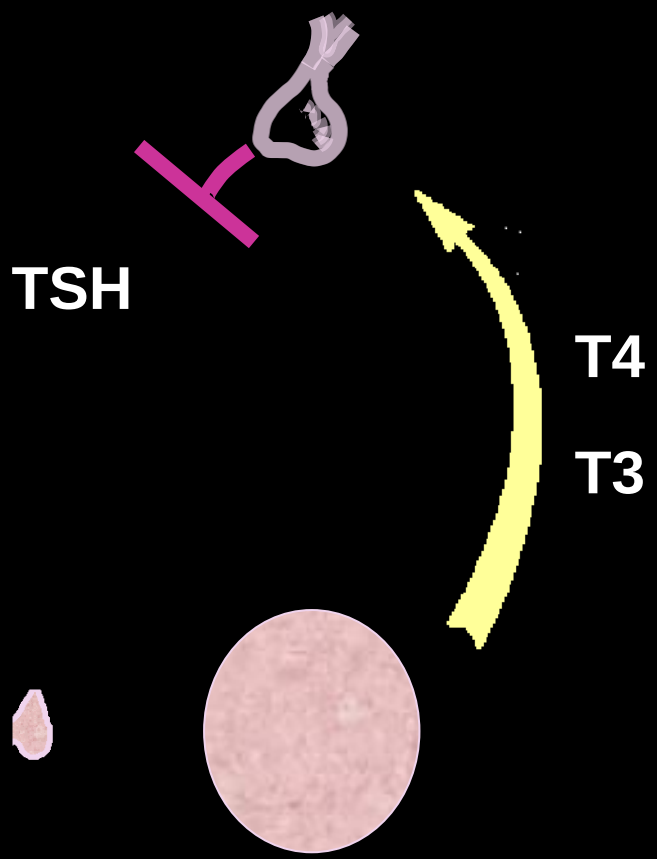
Lambert-Messerlian et al Am J Ob Gyn 2008; 199: 62

Hyperemesis Gravidarum



Goodwin et al Am J Ob Gyn 1992;167:646

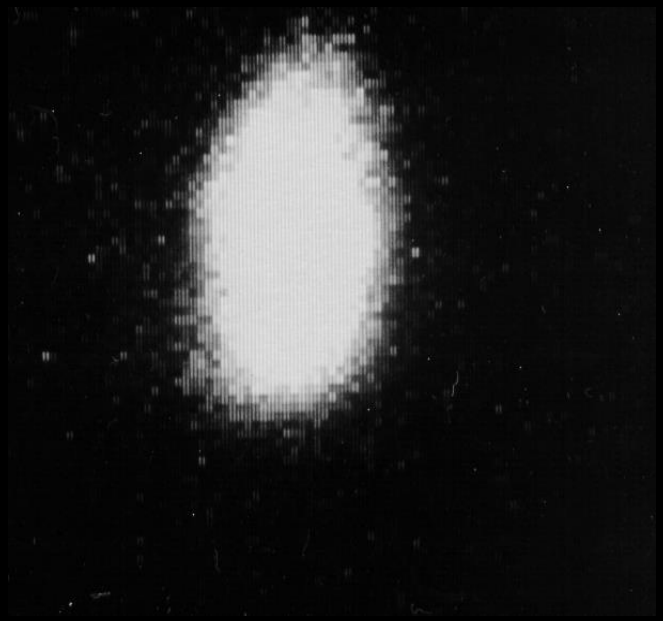
Hot Nodule



Mutations in:

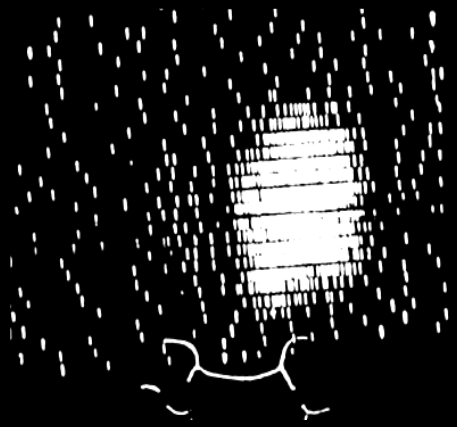
- TSH Receptor
- Gsα

Hot Nodule



Hot Nodule : Radioactive Iodine Therapy

3-17-59

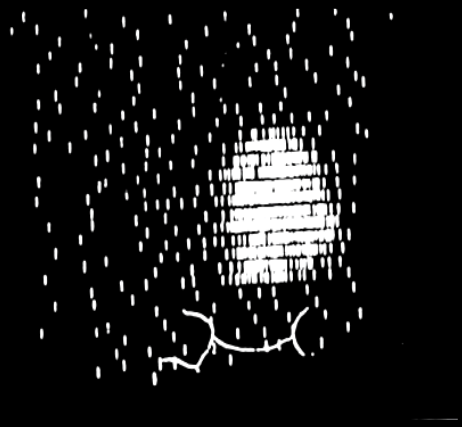


RaI U 51 %

PBI 10.4

Rx 8 mCi ^{131} I

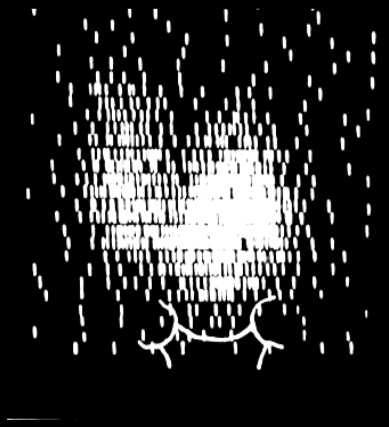
7-28-59



RaI U 32 %

PBI 4.0

4-14-60

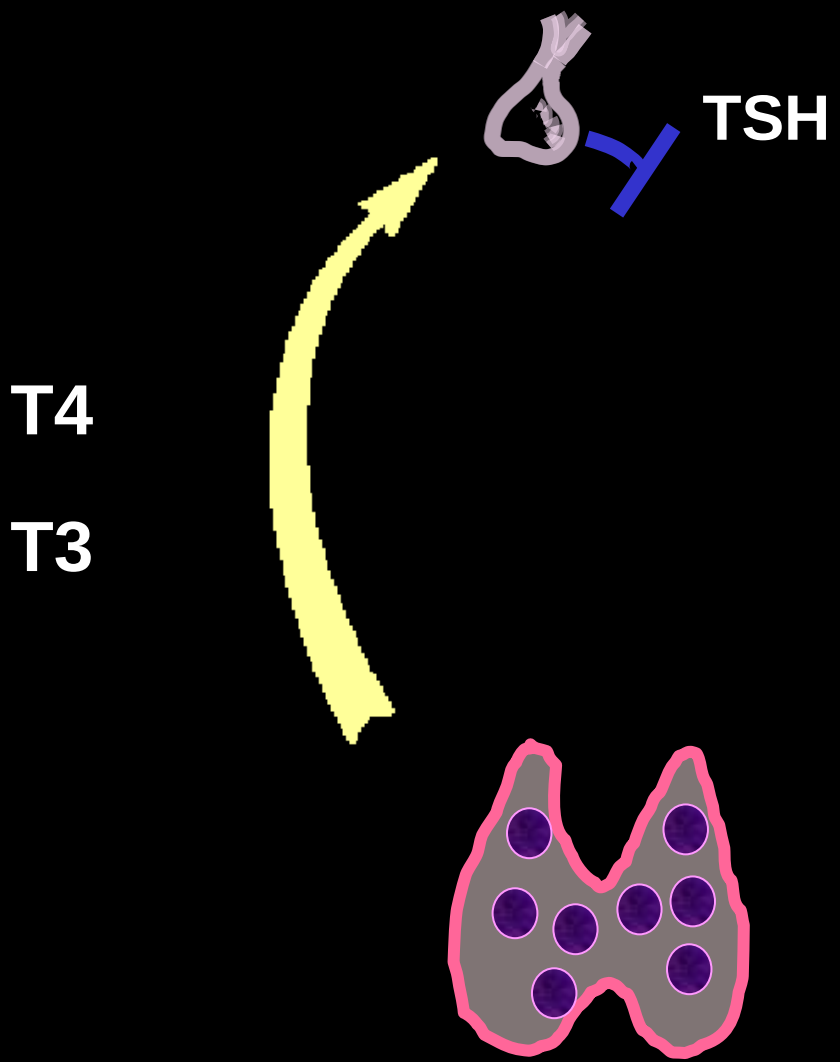


RaI U 35 %

PBI 4.2

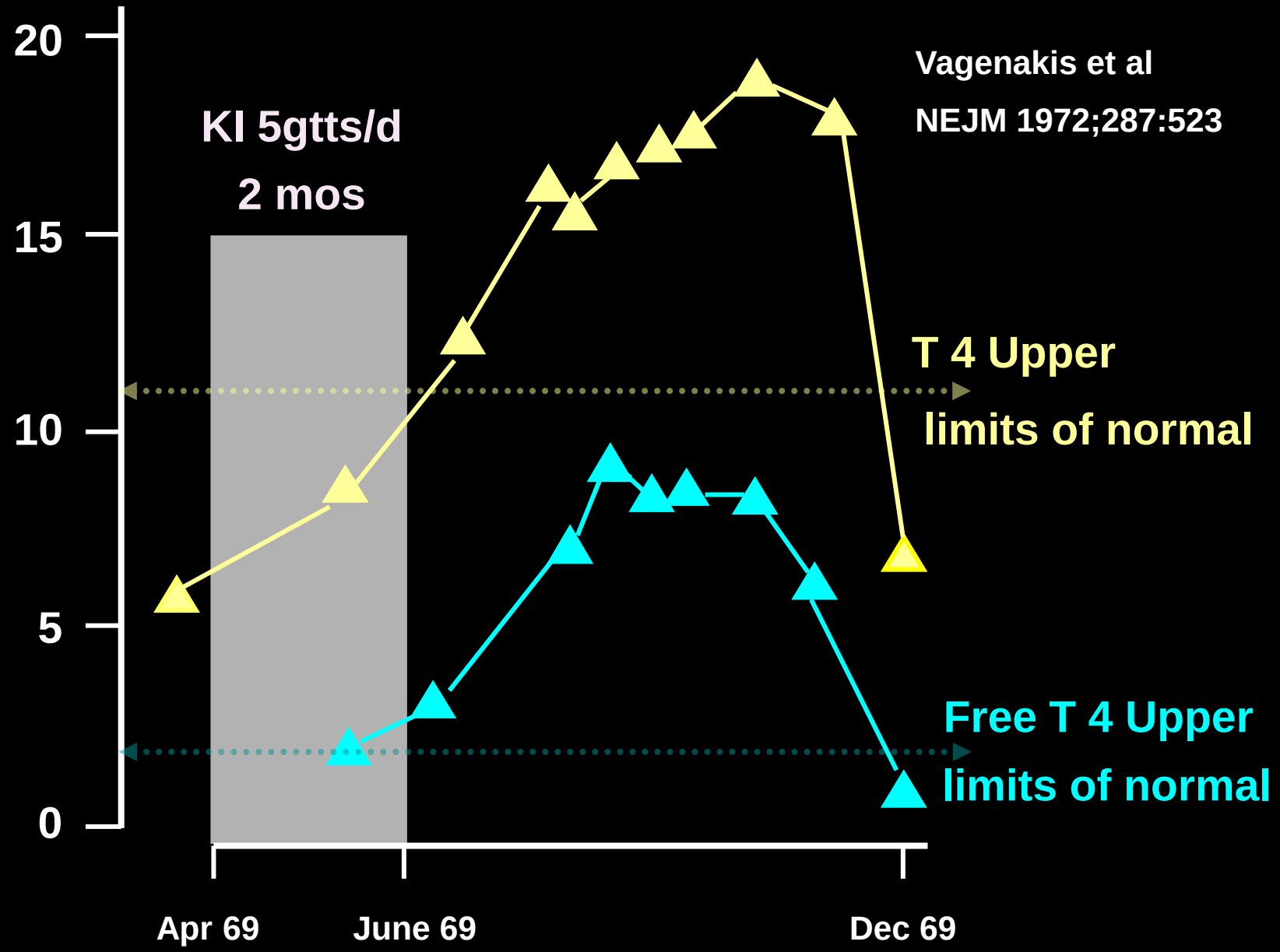
Hypothyroid : 5 % in our experience

Toxic Nodular Goiter



Toxic Nodular Goiter

Iodine-induced Hyperthyroidism

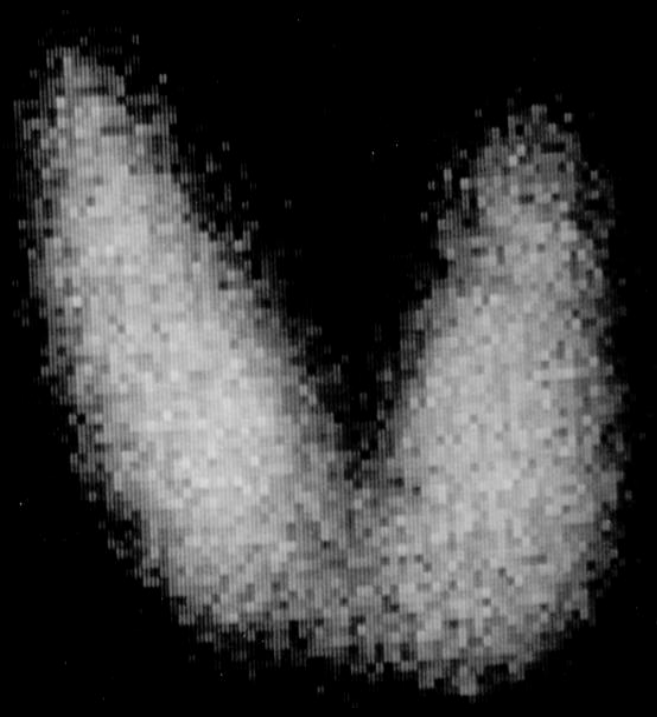


Therapy for Hot Nodule and TMNG

- **Untreated non-iodine-induced hyperthyroidism will persist !**
- **Traditionally we often recommended definitive therapy with RaI, surgery or other ablative techniques.**
- **However, long-term anti-thyroid drugs may be used for toxic nodular goiters and are quite effective.**

Azizi F. Thyroid 2019: 29: 62**5**

Graves' Disease



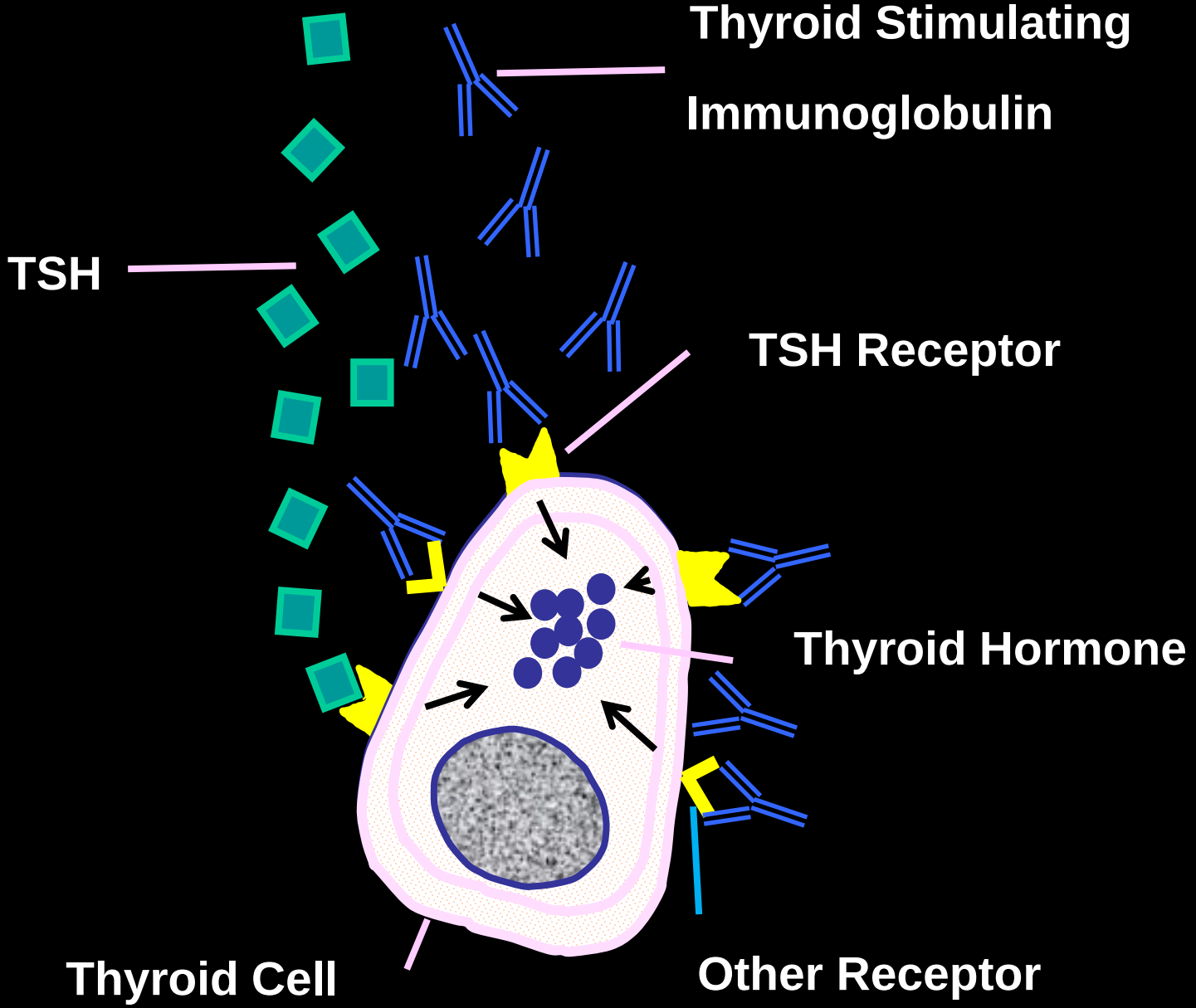
^{123}I Uptake 78 %

Graves' Ophthalmopathy

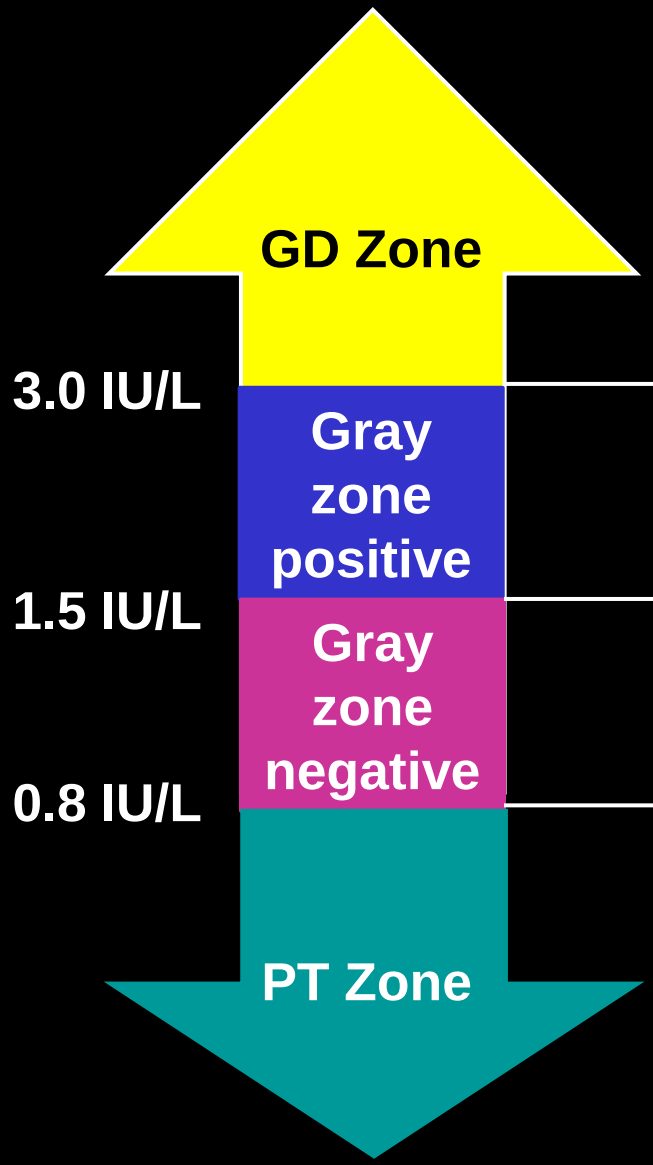
Teprotumamab: IGF-1 R Antibody Therapy

Thyroid Dermopathy: Pretibial Myxedema

Cheng CP et al NEJM 2005; 352: 918


Thyroid Stimulating
Immunoglobulin
TSH
TSH Receptor
Thyroid Hormone
Thyroid Cell
Other Receptor

Elecsys TRab



	Graves'Disease	Painless Thyroiditis
GD Zone	n = 382 (99.7%)	n = 1 (0.3%)
Gray zone positive	n = 25 (69.4%)	n = 11 (30.6%)
Gray zone negative	n = 7 (26.9%)	n = 19 (73.1%)
PT Zone	n = 0 (0%)	n = 218 (100%)

Kamijo et al. Endocr Journal 2010; 57: 895

Graves' Hyperthyroidism Therapy

- **Block Synthesis**

  Methimazole or PTU

- **Ablate or Remove the Thyroid**

  Radioiodine or Surgery

Anti-Thyroid Drugs

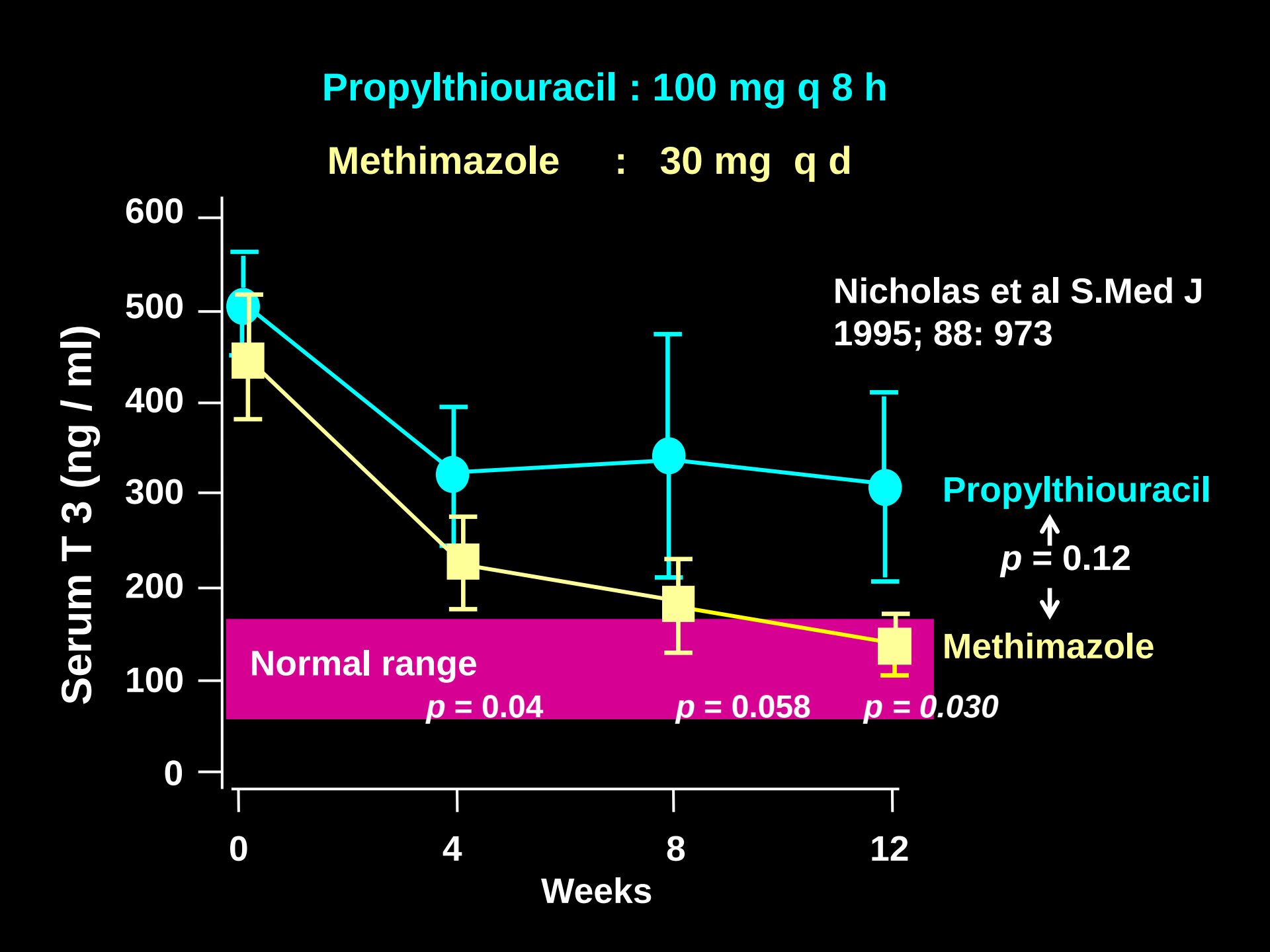
Minor Toxicity (5 %)

- Fever
- Rash
- Joint Pains

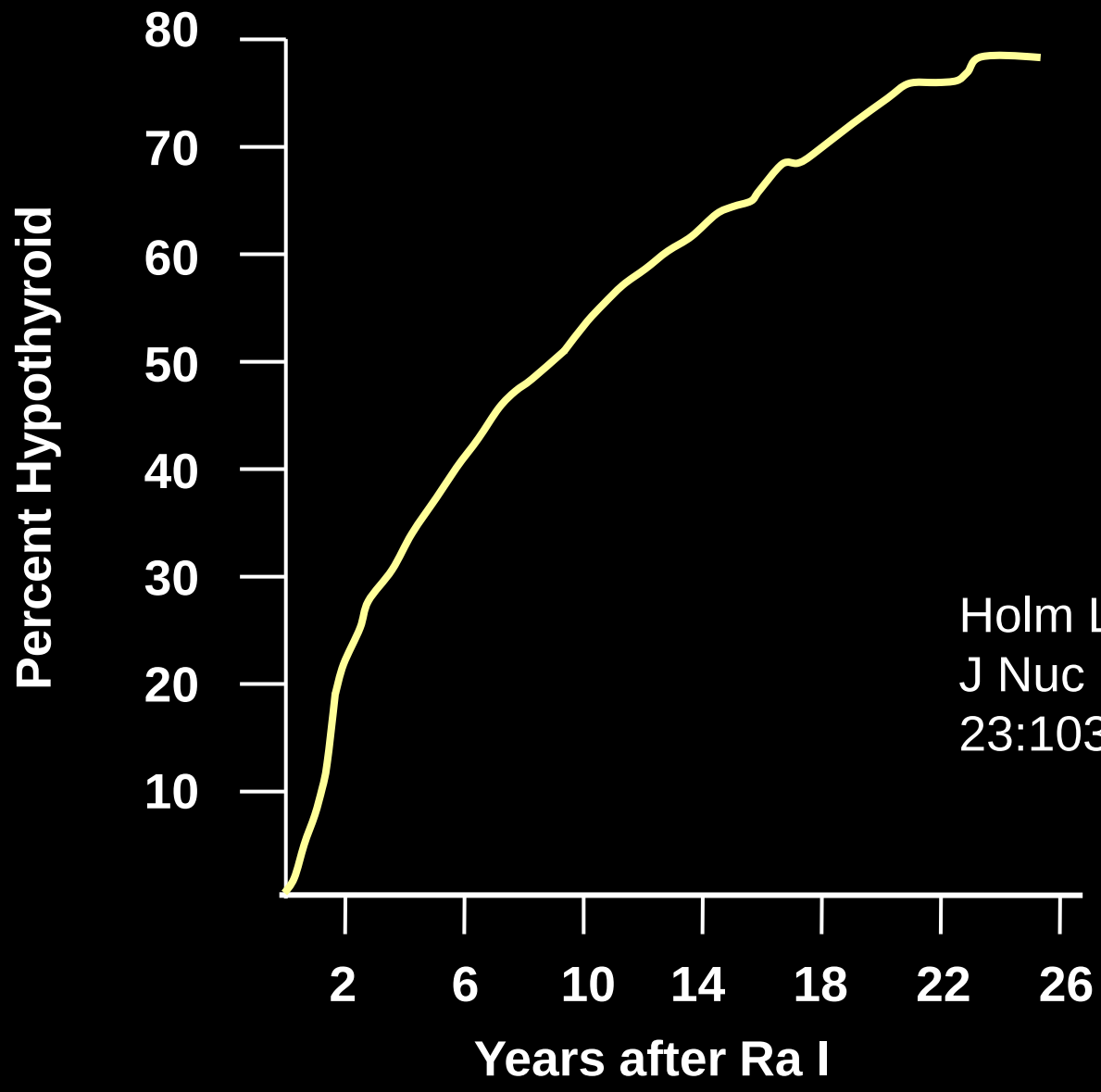
Anti-Thyroid Drugs

Major Toxicity

- Agranulocytosis (0.2 - 0.5 %)
- Pancreatitis (MMI) (0.2%)
- Toxic Hepatitis (PTU)
- Cholestatic Jaundice (MMI)
- Vasculitis (ANCA positive) (PTU)


Propylthiouracil : 100 mg q 8 h
Methimazole : 30 mg q d
Nicholas et al S.Med J 1995; 88: 973
Serum T 3 (ng / ml)
600
500
400
300
200
100
0
Normal range
Propylthiouracil
p = 0.12
Methimazole
p = 0.04
p = 0.058
p = 0.030
0
4
8
12
Weeks

^{131} Iodine Therapy - Graves' Disease

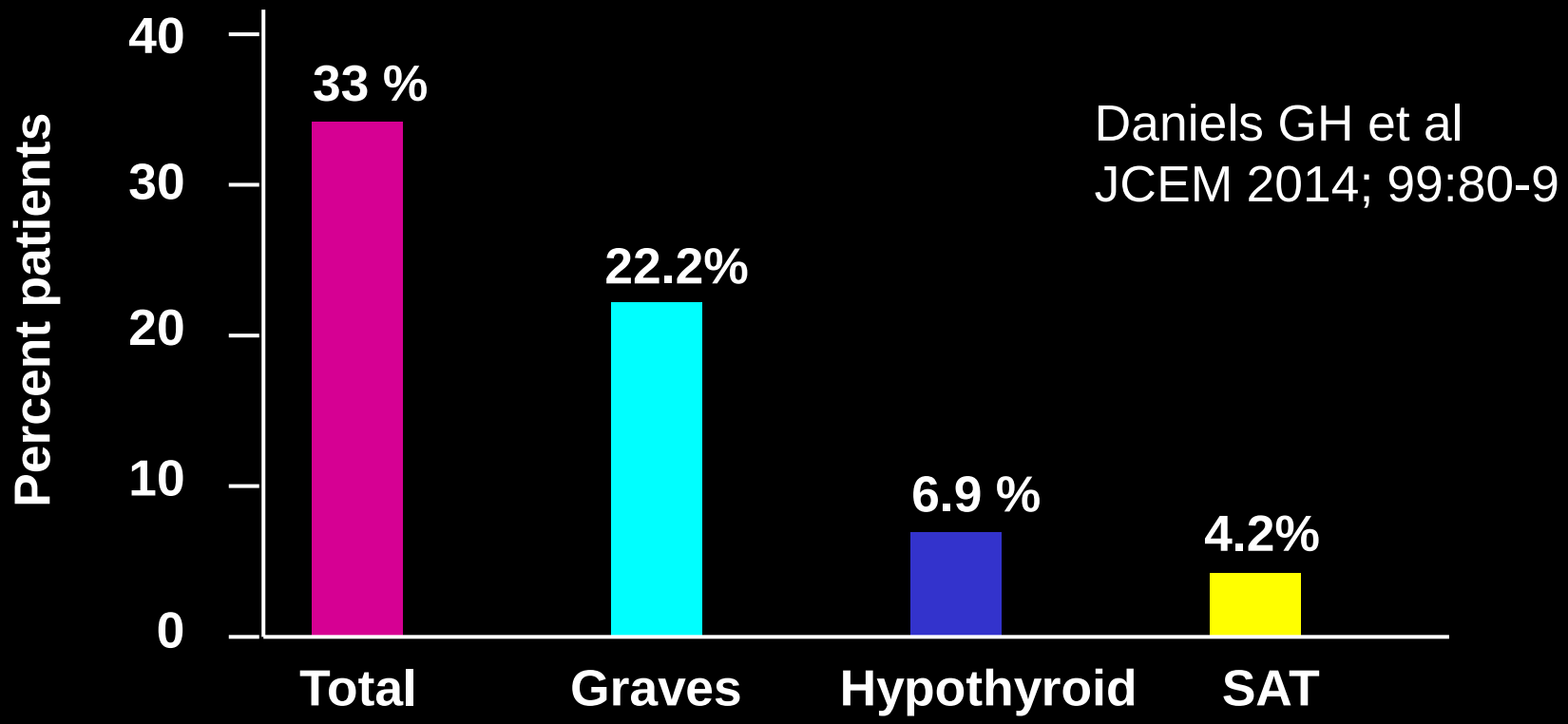


Holm L-E et al
J Nuc Med 1982;
23:103

Alemtuzumab: Reconstitution Autoimmunity

Anti-CD52 Antibody for MS

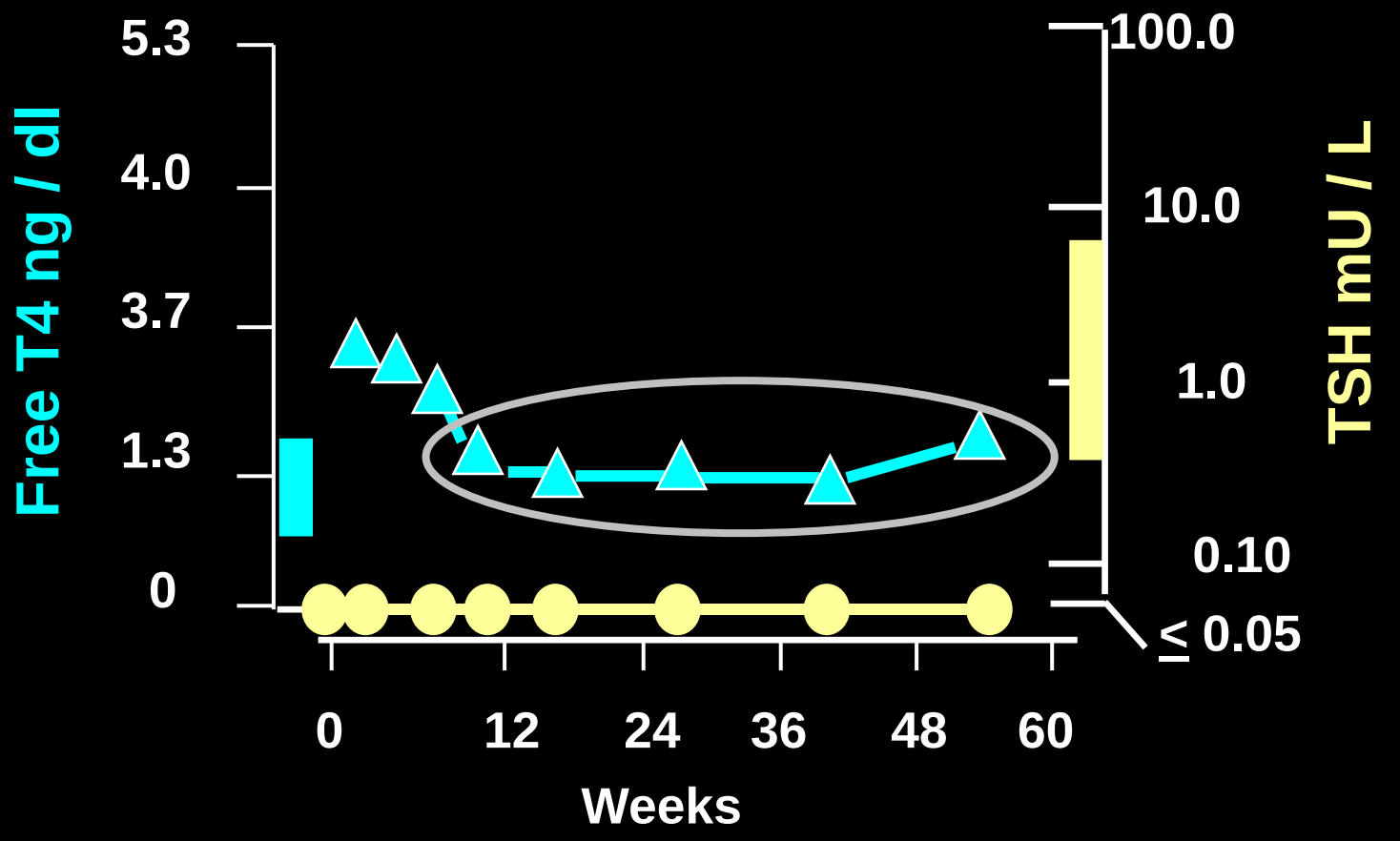
Thyroid dysfunction in 73/220 pts. (33%)



Daniels GH et al
JCEM 2014; 99:80-9

Hyperthyroidism Therapy

TSH Suppression



Interesting Patient

- High Free T4: > 7.8 ng/dL (0.9 – 1.8)
- High T3 > 650 ng/dL (60 - 181)
- Low TSH < 0.02 (0.4 – 5.0) mU/L
- High TBII 36 (< 1.75)

There is nothing wrong with this patient !!

The patient is on Biotin which (in high doses) causes all these aberrant blood test results in some drug platforms. TSI normal.

Barbesino Thyroid 2016: 26: 860

	Patient 1	Patient 2	Normal Range
TSH	< 0.01mU/L	< 0.01mU/L	0.4-5 mU/L
T4	10.7 ug/dl	25.0 ug/dl	4-11 ug/dl
FT4	1.7 ng/dl	3.5 ng/dl	0.8-1.8 ng/dl
TT3	179 ng/dl	530 ng/dl	80-180 ng/dl

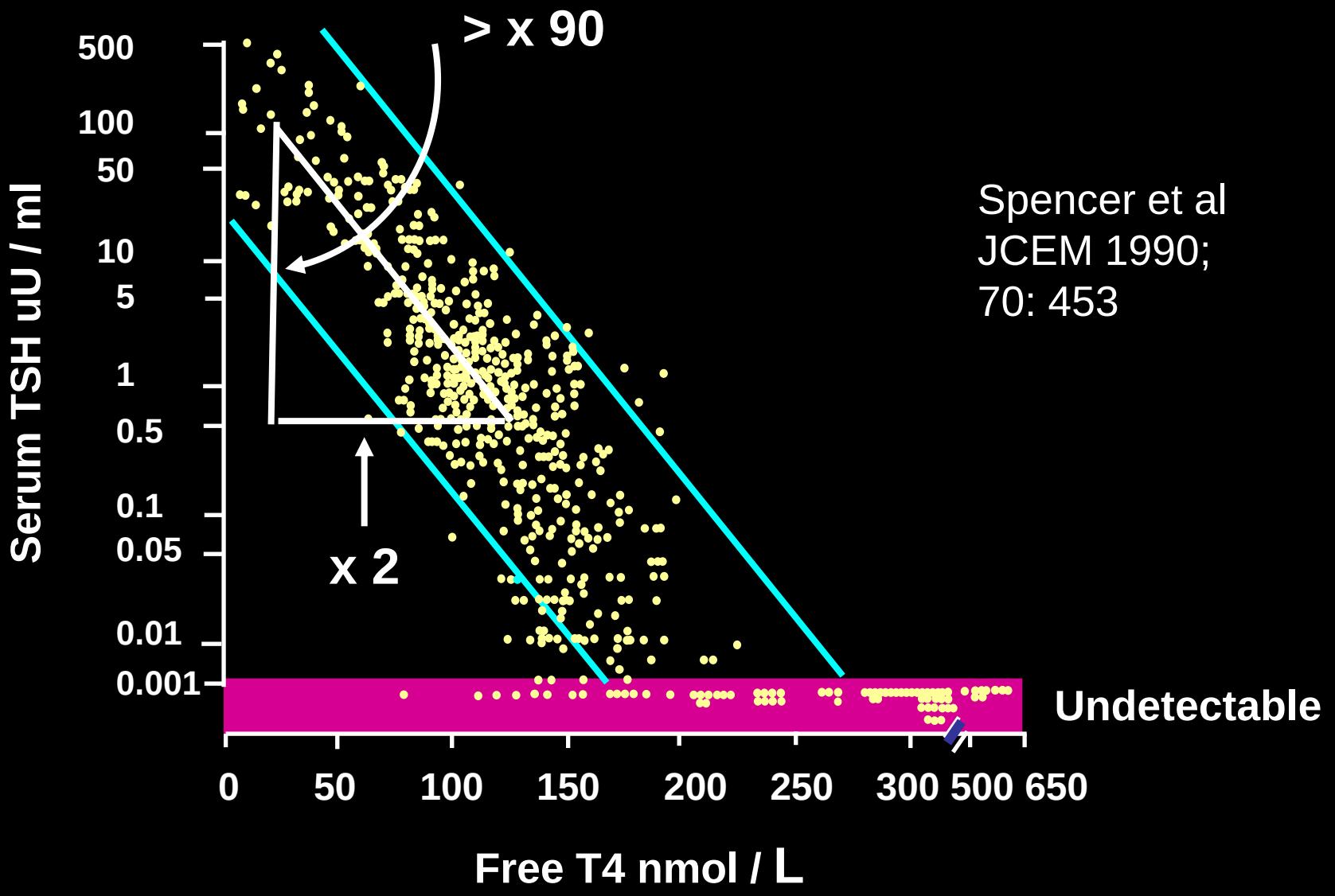
Subclinical Hyperthyroidism

- Low serum TSH
- Normal free T4
- Normal T3 or free T3

Subclinical Hyperthyroidism

- Patient may or may not be symptomatic !
- Exclude other causes of decreased serum TSH.

FT4 vs. TSH



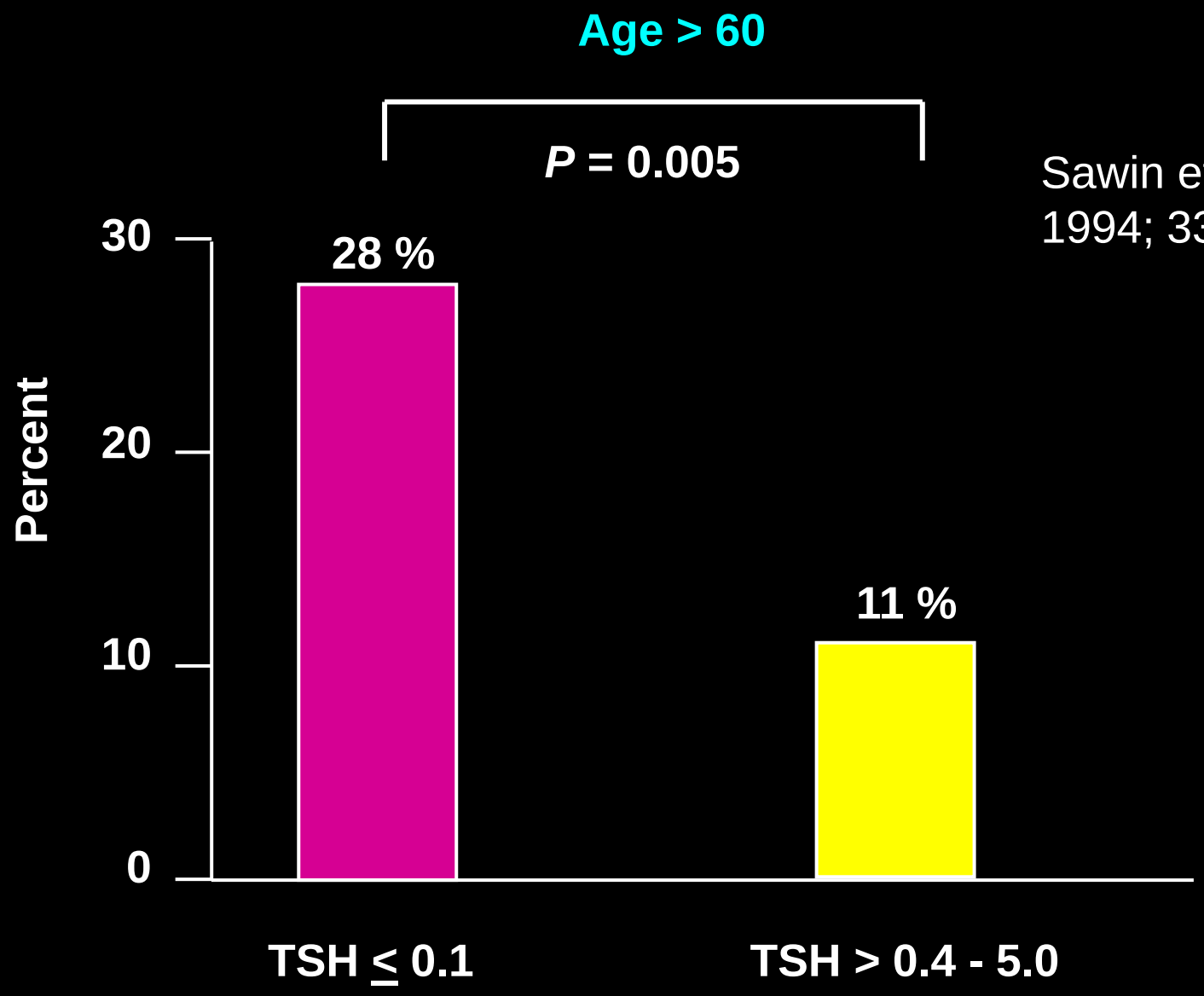
Spencer et al
JCEM 1990;
70: 453

Subclinical Hyperthyroidism

- **Uncertain effects on overall mortality.**
- **Some studies show increased cardiovascular mortality, greater with TSH < 0.1 mU/L, compared to 0.1 – 0.4**
- **Endogenous subclinical hyperthyroidism is associated with osteoporosis and possibly fractures in post-menopausal women, particularly with TSH < 0.1.**

Ross DS Thyroid 2016: 26: 1343

Atrial Fibrillation: Ten Year Prevalence



Sawin et al NEJM
1994; 331: 1249

Subclinical Hyperthyroidism

- As a general rule, the lower the serum TSH (particularly < 0.1), the older the patient, the more the concern about the heart or the bones, and the longer the duration of subclinical hyperthyroidism the more we are inclined to treat.

- For specific guidelines see Ross DS et al Thyroid 2016: 26: 1343.

Subclinical Hyperthyroidism

- There are no large scale randomized, placebo- controlled intervention trials.

Hyperthyroidism - 0 or near nil RaI U

- Factitious hyperthyroidism
- Painful subacute thyroiditis
- Painless subacute thyroiditis
- Amiodarone destructive thyroiditis
- Excess iodine
- Struma ovarii
- Metastatic follicular carcinoma

Covid- 19 Related Painful Subacute Thyroiditis

- **Painful Subacute thyroiditis may be an under-recognized manifestation of Covid-19 infections.**
- **Generally occurs 16 – 36 days after resolution of coronavirus infection, but in others simultaneous.**
- **The 4 cases described here had mild cases of Covid-19. Many others reported.**

Brancatella A et al. J Clin Endocrinol Metab. 2020 Oct 1;105

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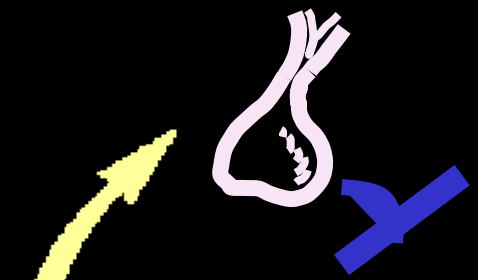
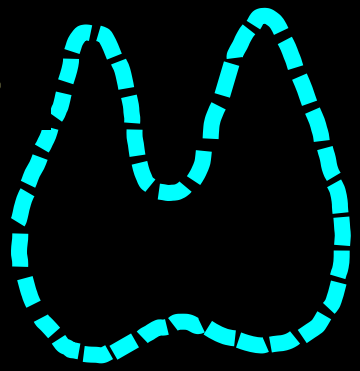
Destructive Thyroiditis



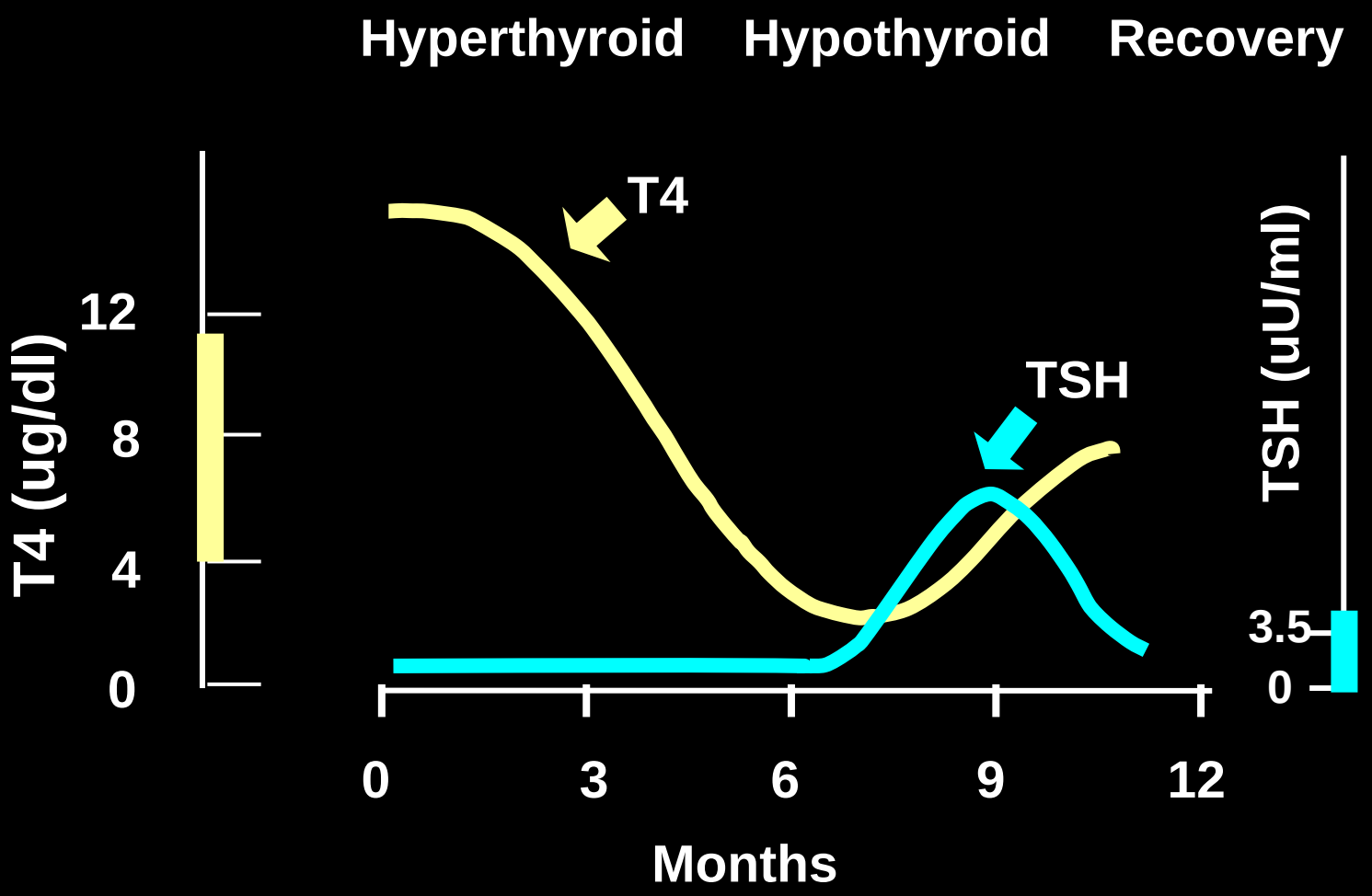
TSH

T3 and T4



RaI uptake = 0

Destructive Thyroiditis : Subacute Thyroiditis



Destructive Thyroiditis

^{123}I Scan

24 hr RaI uptake 0.04 %

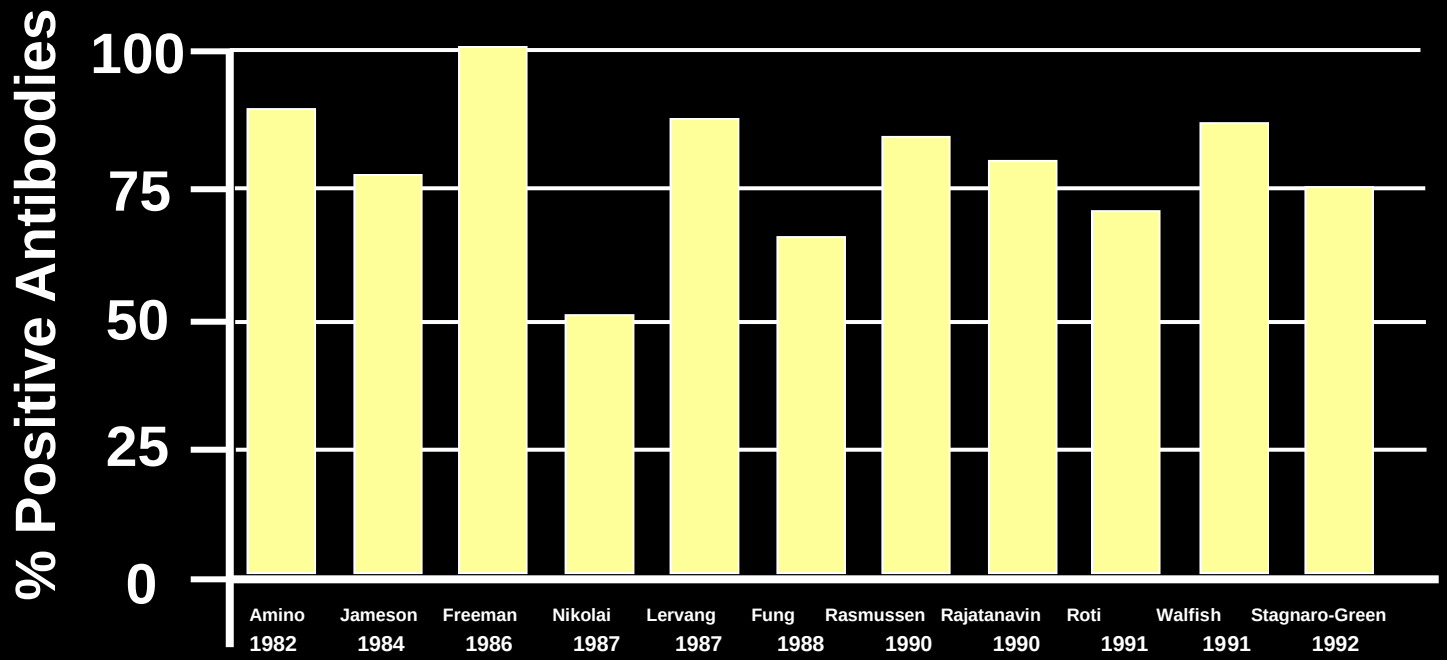
Prevalence of Post-Partum Thyroiditis

Name	Year	Country	FU	Number	Preg Screen	PPT
Amino	1982	Japan	6	507	N	**5.5 %**
Jansson	1984	Sweden	5	460	N	**6.5 %**
Freeman	1986	USA	3	212	N	**1.9 %**
Nikolai	1987	USA	3	238	N	**6.7 %**
Lervang	1987	Denmark	12	591	N	**3.9 %**
Fung	1988	UK	12	901	Y	**16.7 %**
Rasmussen	1990	Denmark	12	736	N	**3.3 %**
Rajatanavin	1990	Thailand	12	812	N	**1.1 %**
Roti	1991	Italy	12	372	N	**4.8 %**
Walfish	1992	Canada	12	1376	N	**6.0 %**
Stagnaro-Green	1992	USA	6	545	Y	**8.8 %**

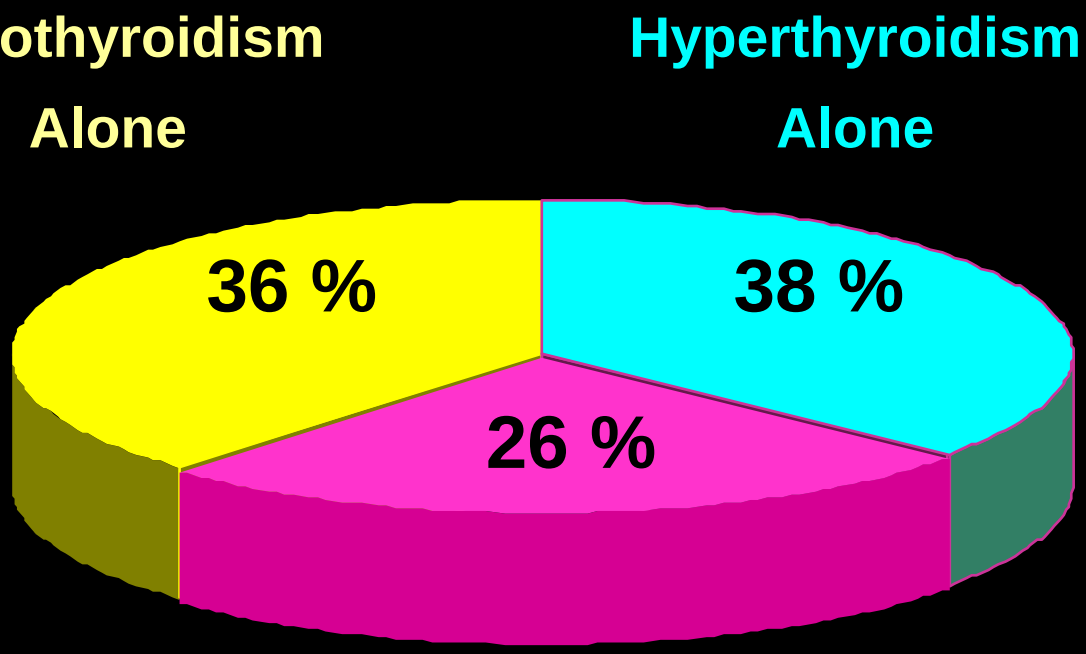
Post-Partum Thyroiditis: Antibodies

Stagnaro-Green A. Thyroid Today 16: 1 : 1993

Prospective Studies



Post-Partum Thyroiditis: Clinical



Stagnaro-Green
Thyroid Today
16; 1 : 1993

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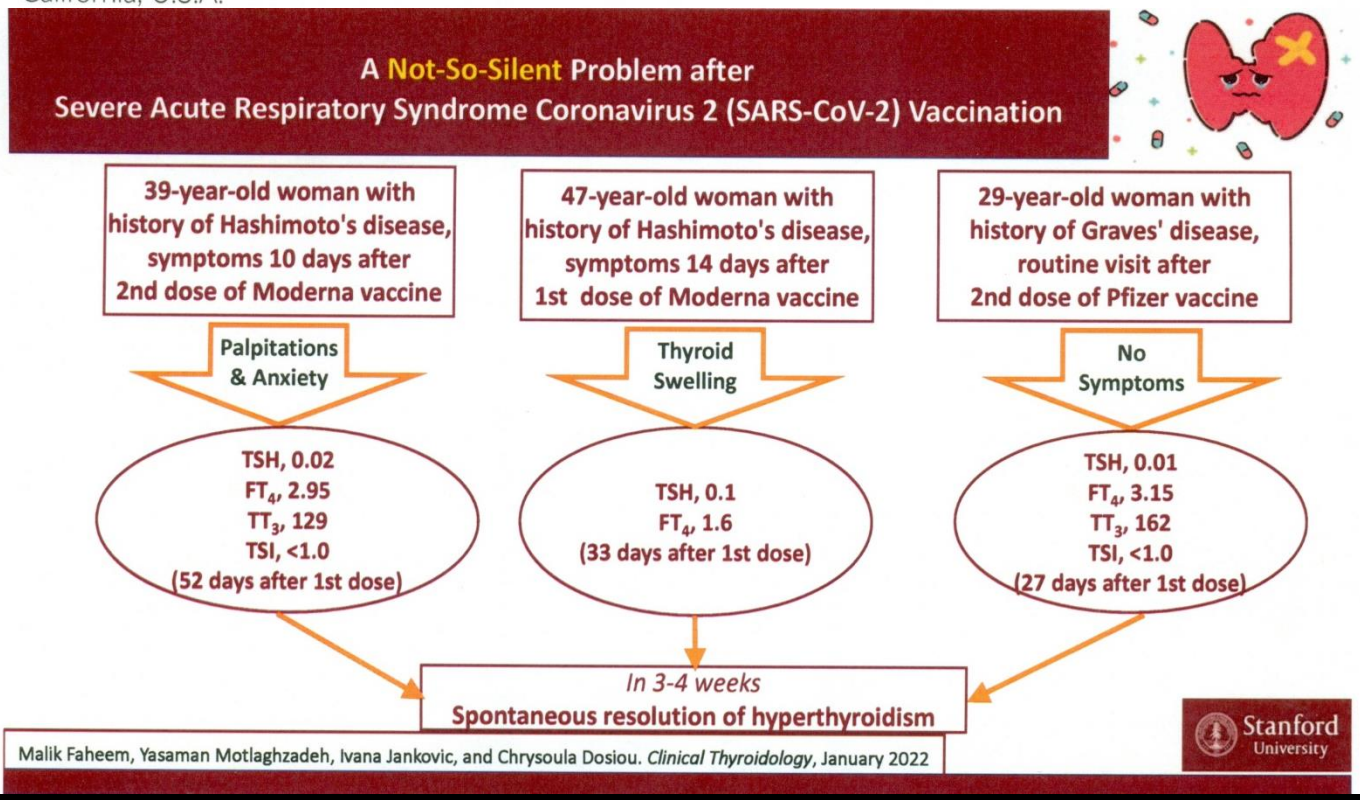
CASE REPORT

Clin Thyroidol 2022: 34: 38

A Not-So-Silent Problem After SARS-CoV-2 Vaccination

Malik Faheem, Yasaman Motlaghzadeh, Ivana Jankovic, and Chrysoula Dosiou

Division of Endocrinology, Gerontology and Metabolism, Stanford University School of Medicine, Stanford, California, U.S.A.



Graves' also reported after SARS-CoV-2 Vaccination

Immune Checkpoint Inhibitors

CTLA 4	PD-1	PDL-1
Ipilimumab	Pembrolizumab	Avelumab
Tremelimumab	Nivolumab	Atezolizumab
	Pidizumab	Durvalumab

Combinations

Ipilimumab + Nivolumab

Ipilimumab + Pembrolizumab

Tremelimumab + Durvalumab

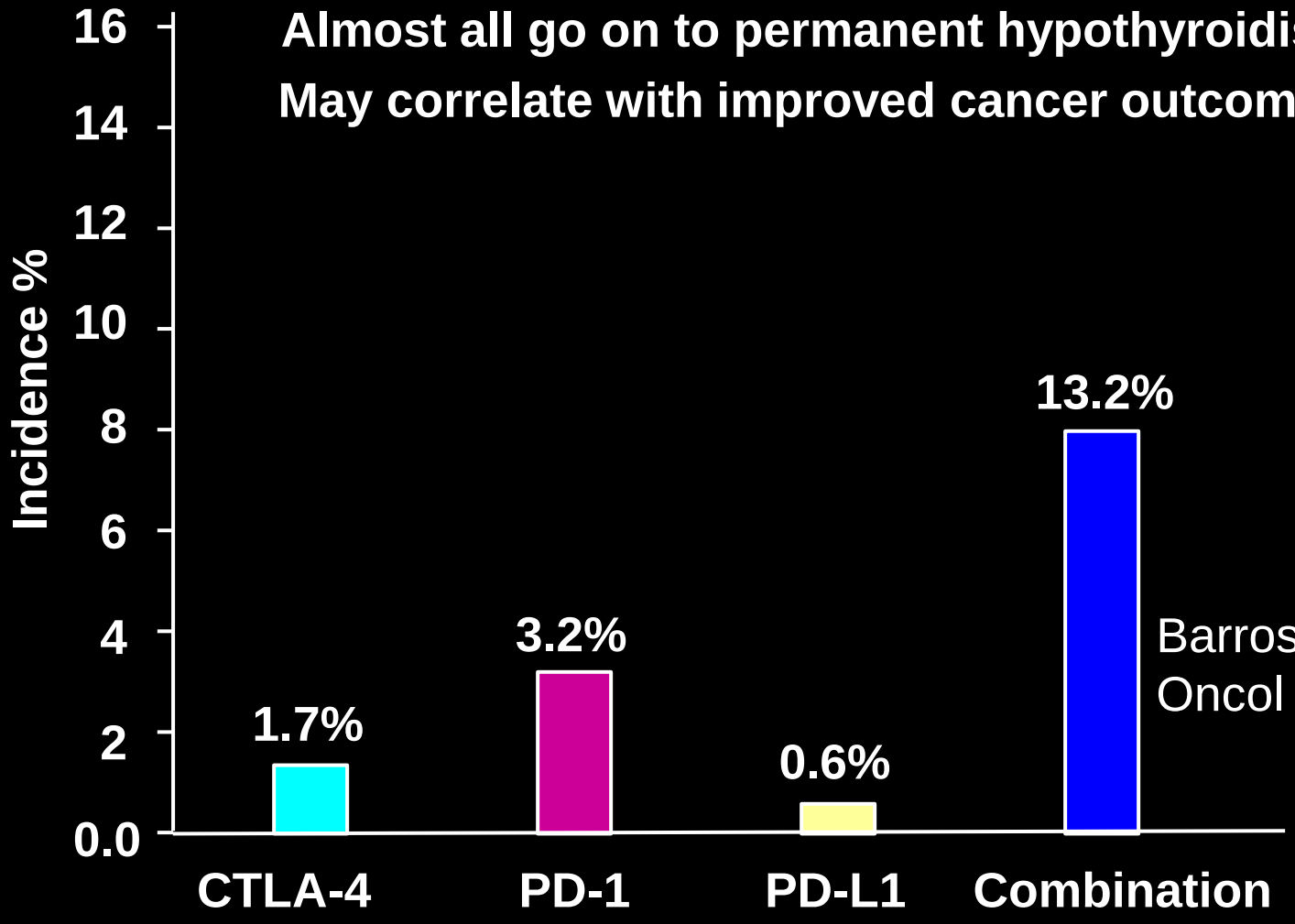
Gonzalez-Rodriguez et al.Oncologist 2016: 21: 804

Check-Point Inhibitor Hyperthyroidism

Almost all destructive thyroiditis, presumed autoimmune

Almost all go on to permanent hypothyroidism.

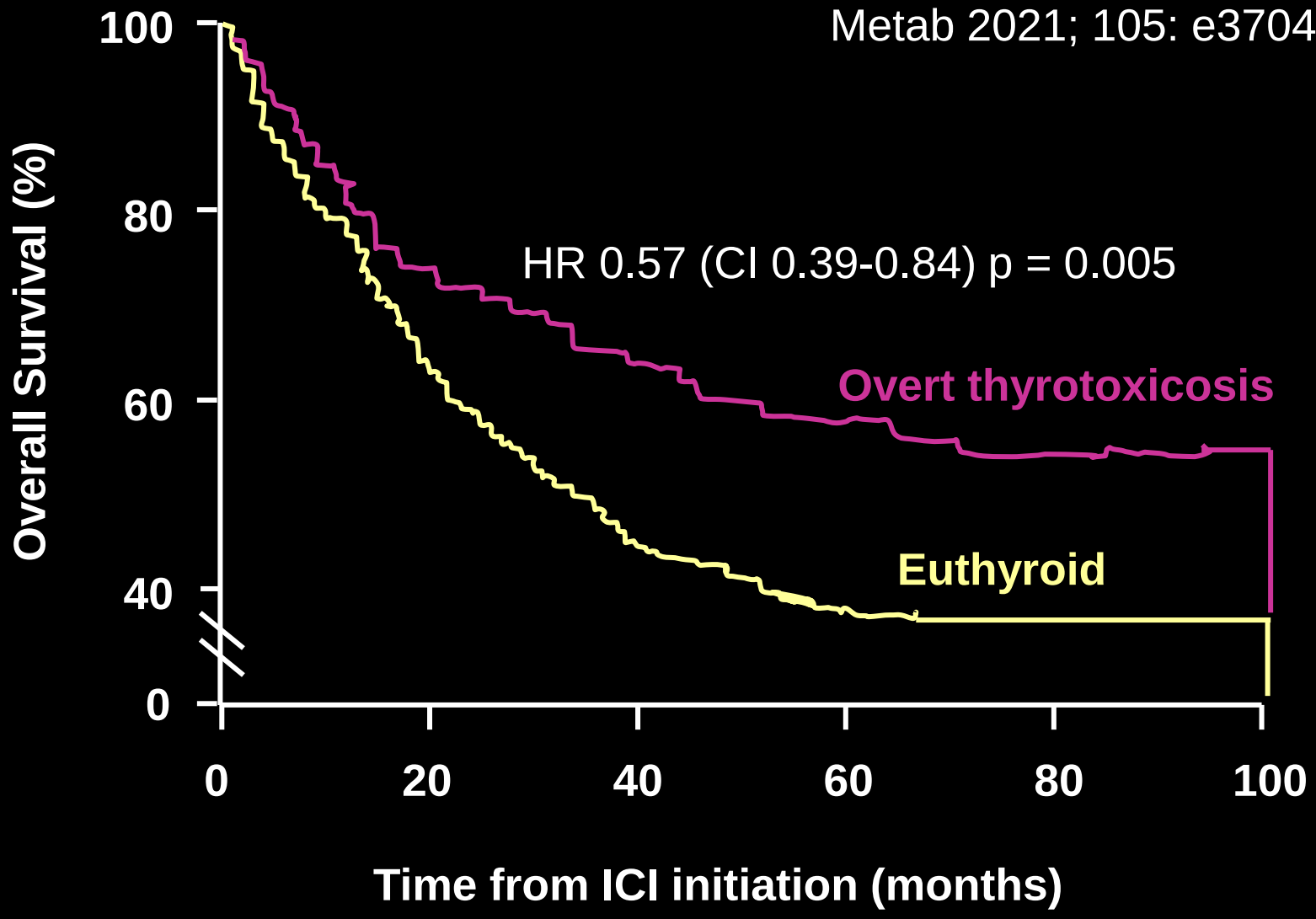
May correlate with improved cancer outcomes.



Barroso-Sousa JAMA Oncol 2018: 4: 173-182

Check-Point Inhibitor Thyrotoxicosis

Muir CA et al. J Clin Endocrinol Metab 2021; 105: e3704



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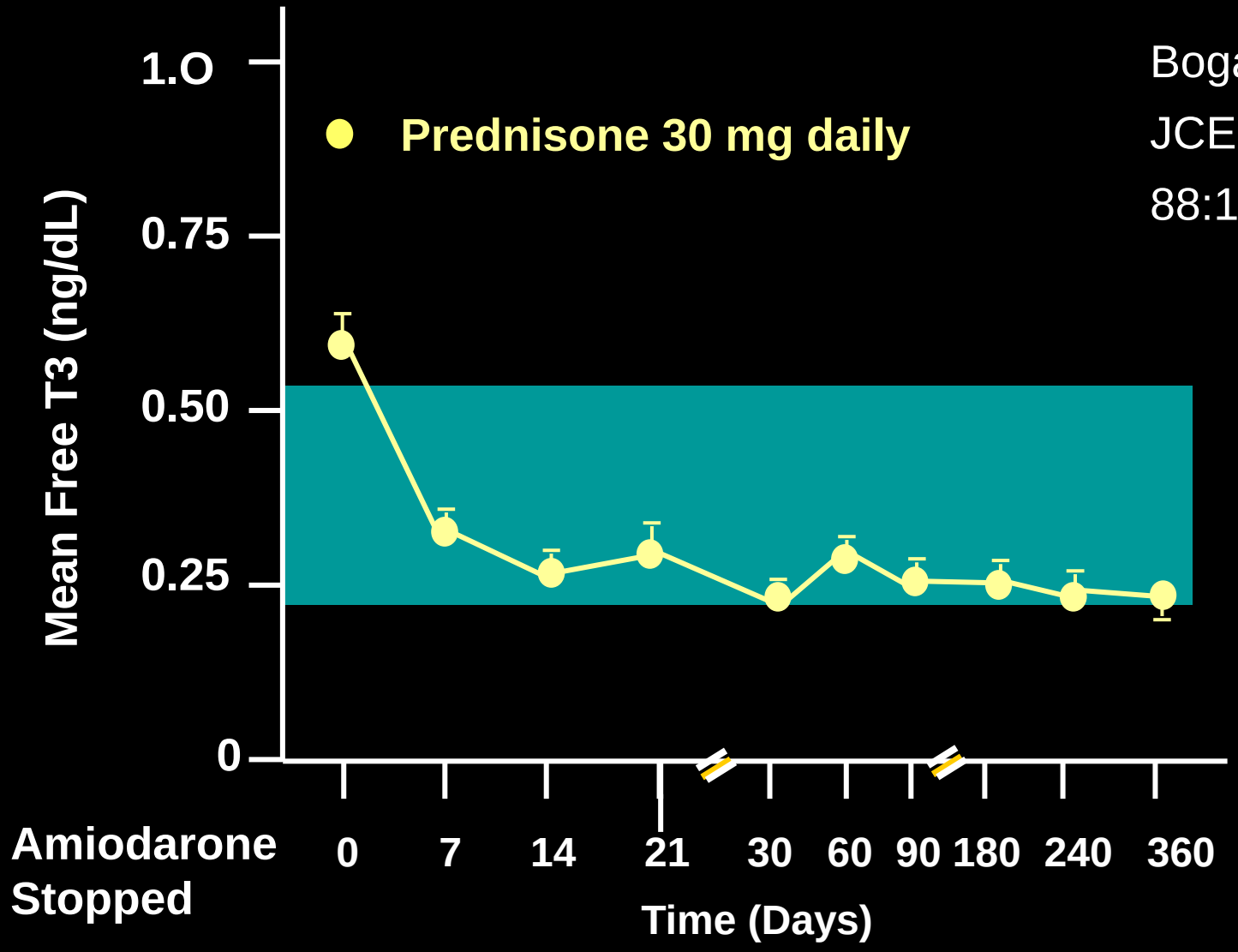
Amiodarone Induced Thyrotoxicosis

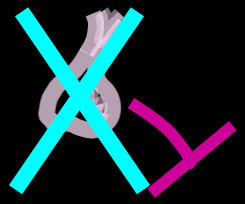
	Type 1 (10%)		Type 2 (90%)
	MNG	Graves	SAT
US	Nodules	No nodules	No nodules
TRAb	Neg	Positive	Negative
Ra I U	Nil	Nil	Nil
Flow	Nl or hi	Nl or hi	Low
Response to prednisone	None	None	Dramatic

Amiodarone Induced Thyrotoxicosis Type 2



Bogazzi et al
JCEM 2003;
88:1999

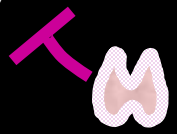
Secondary Hypothyroidism



↓ TSH

↓ T 4

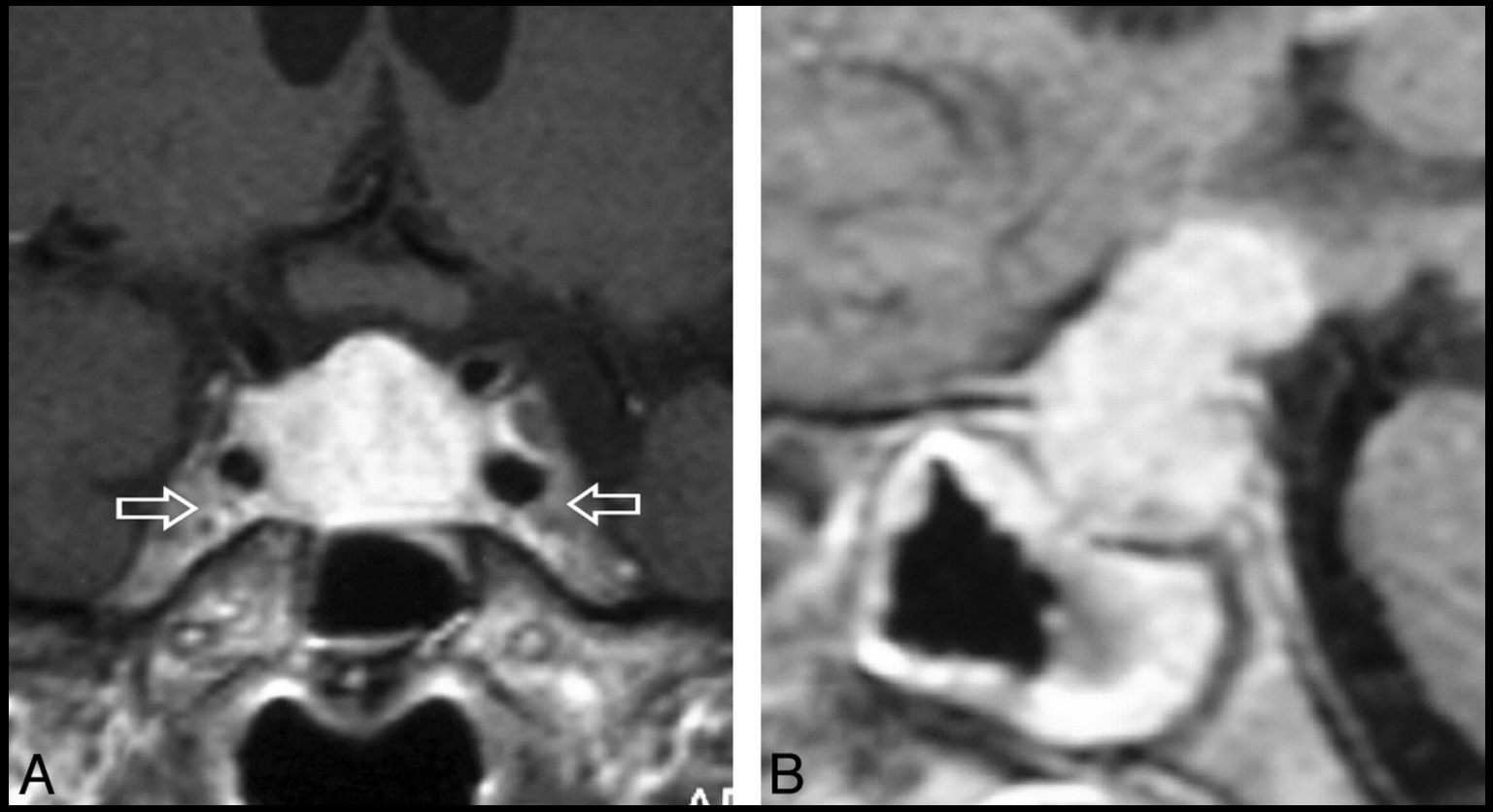
↓ T 3



Ipilimumab

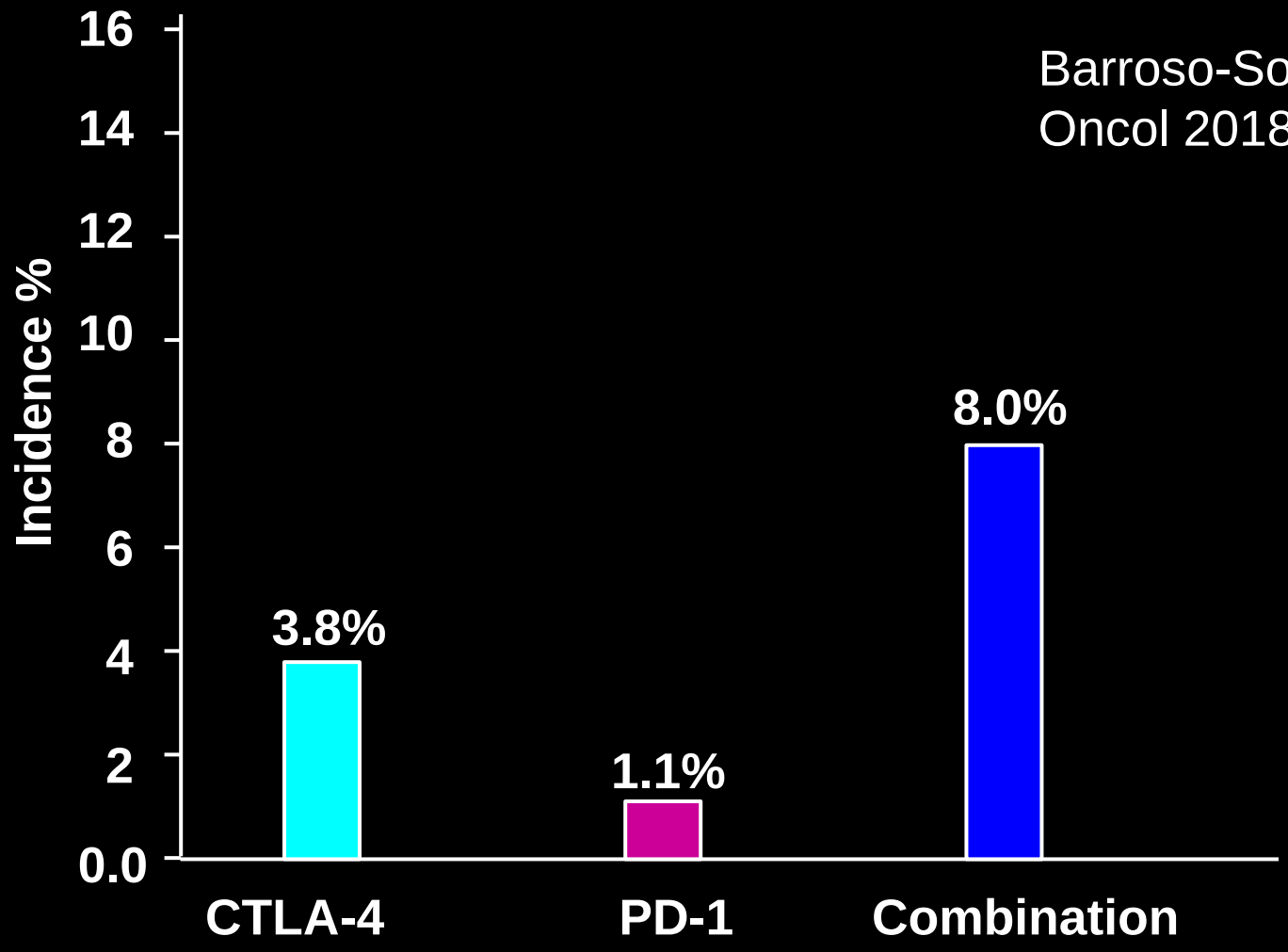
A 75 year old woman with Stage IV metastatic melanoma was treated with ipilimumab an antibody against cytoxic T-lymphocyte-associated antigen 4 (CTLA-4). Two weeks following her third infusion she presented with bifrontal headaches. Her serum sodium was 114. Her serum TSH was 0.2 with a nil free T4. Her plasma cortisol was 2 ug/dl with an ACTH of 2 pg/ml (both very low). She was diagnosed with pan-hypopituitarism and improved with glucocorticoid and levothyroxine therapy.

Ipilimumab Hypophysitis



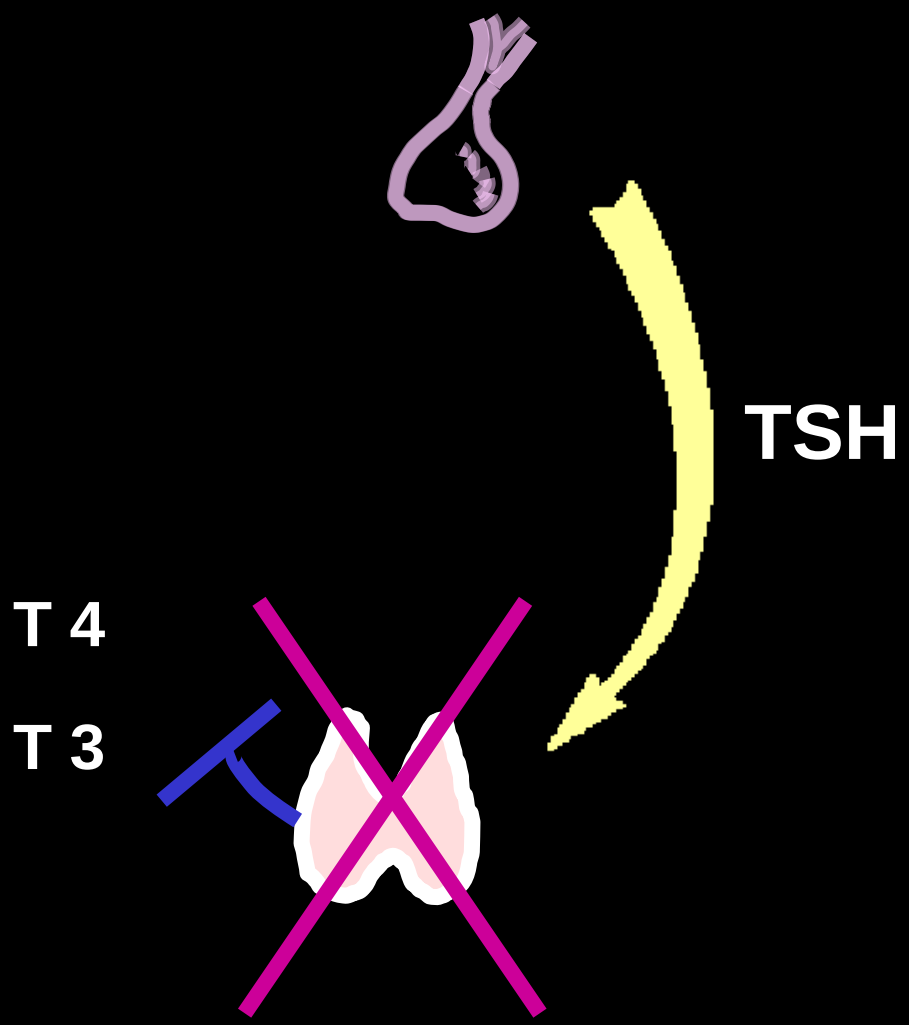
Gutenberg et al. Am J Neuroradiology 2009, 30: 1766

Hypophysitis



Barroso-Sousa JAMA Oncol 2018: 4: 173-182

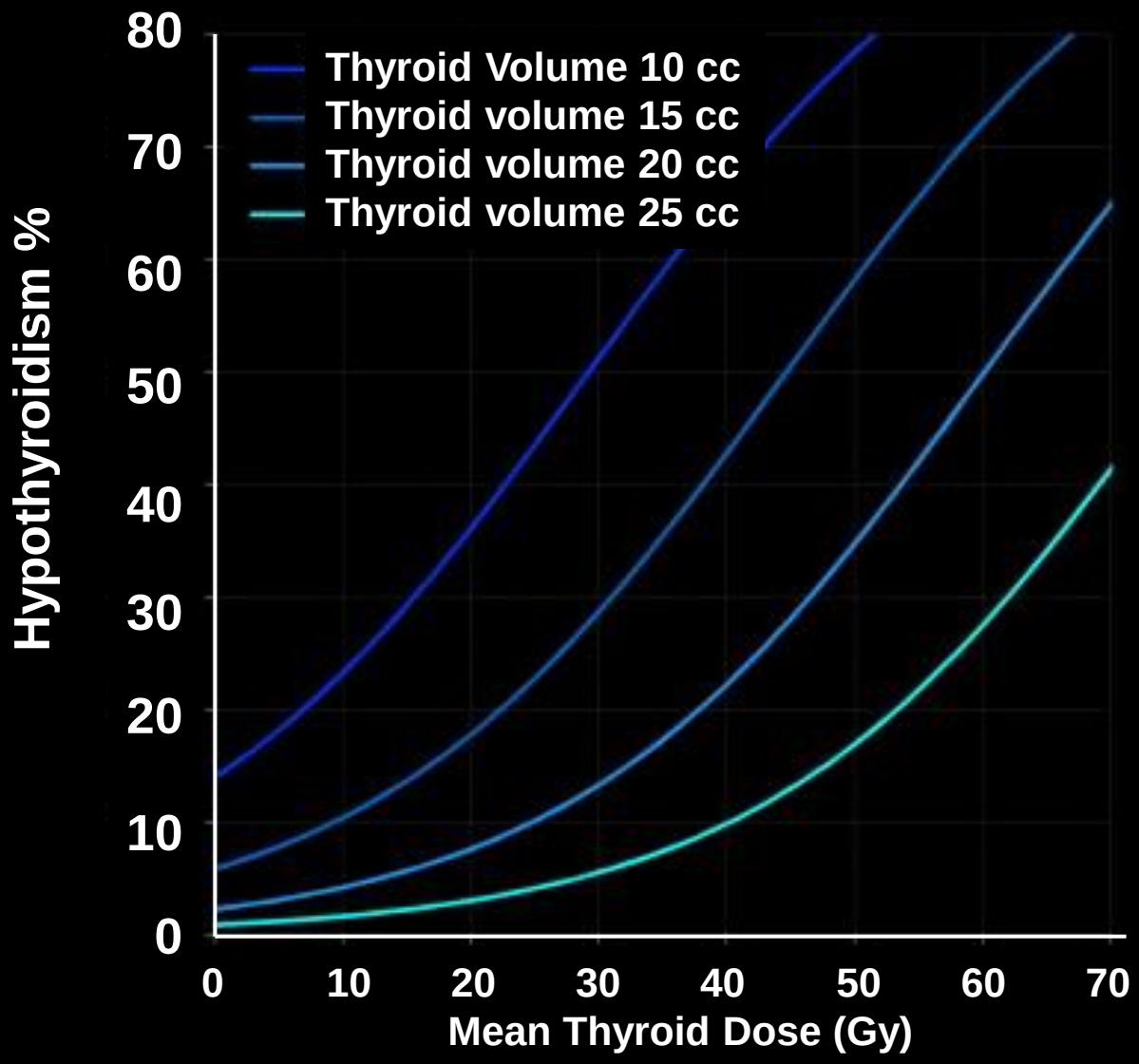
Primary Hypothyroidism



Atrophic Primary Hypothyroidism

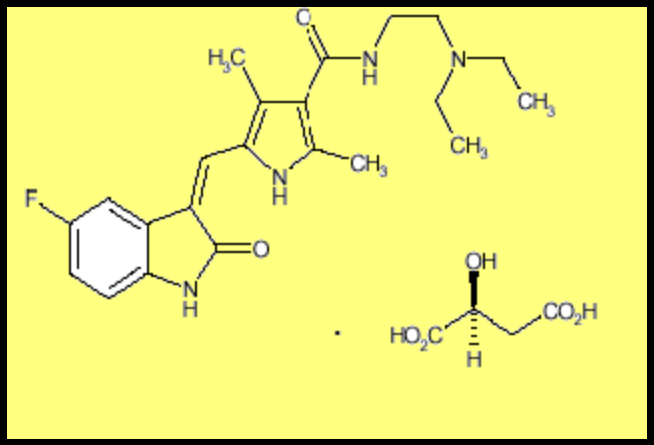
- Radioactive Iodine
- Surgery
- External Radiation
- Drugs
- Atrophic thyroiditis
- TSH Receptor Antibodies
- Mutant TSH receptor
- Congenital Hypothyroidism

External Radiation: Hypothyroidism



Boomsma MJ et al
Int J Rad Oncol Bio Phys
2012; 84: e 351

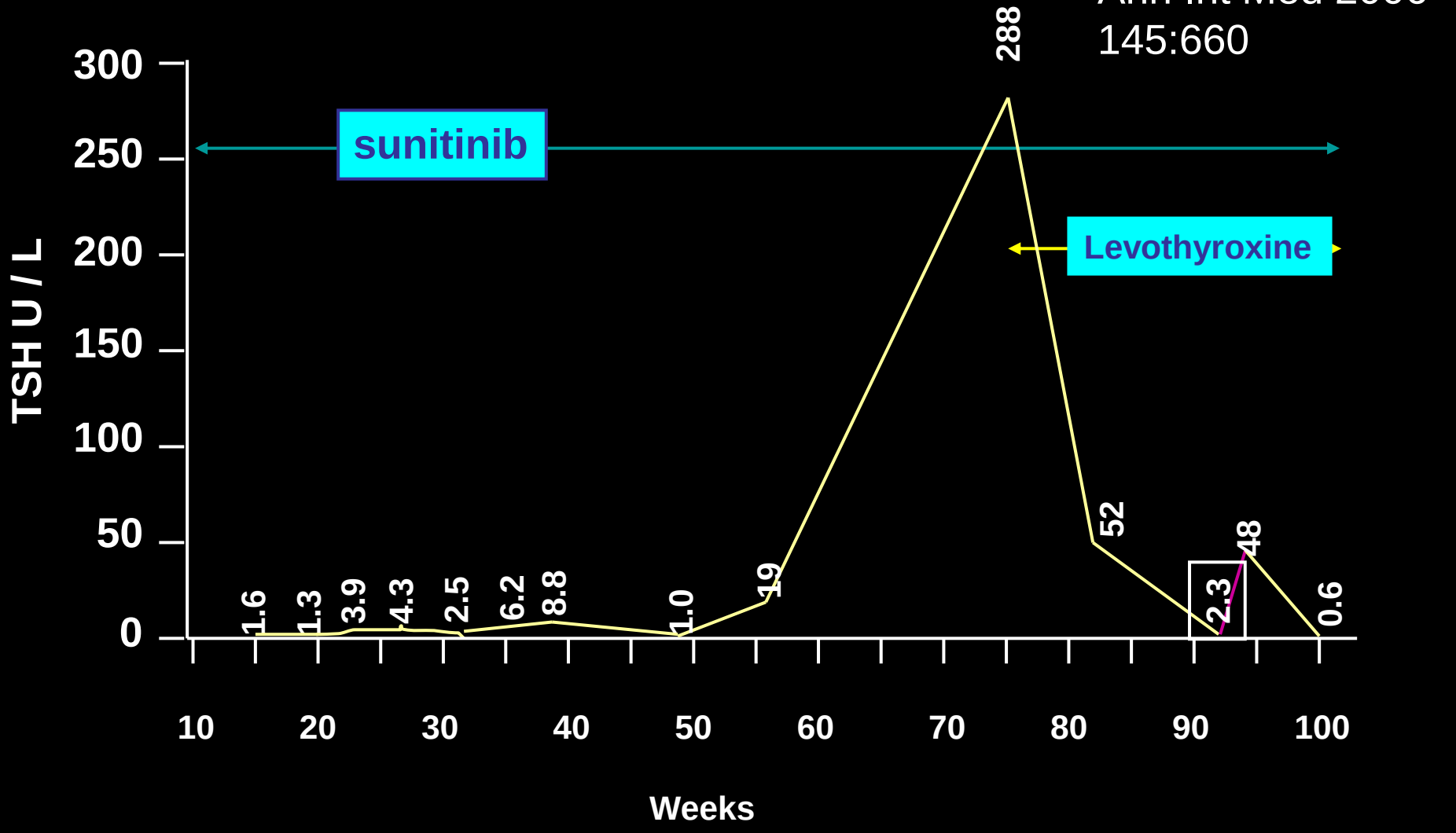
Sunitinib



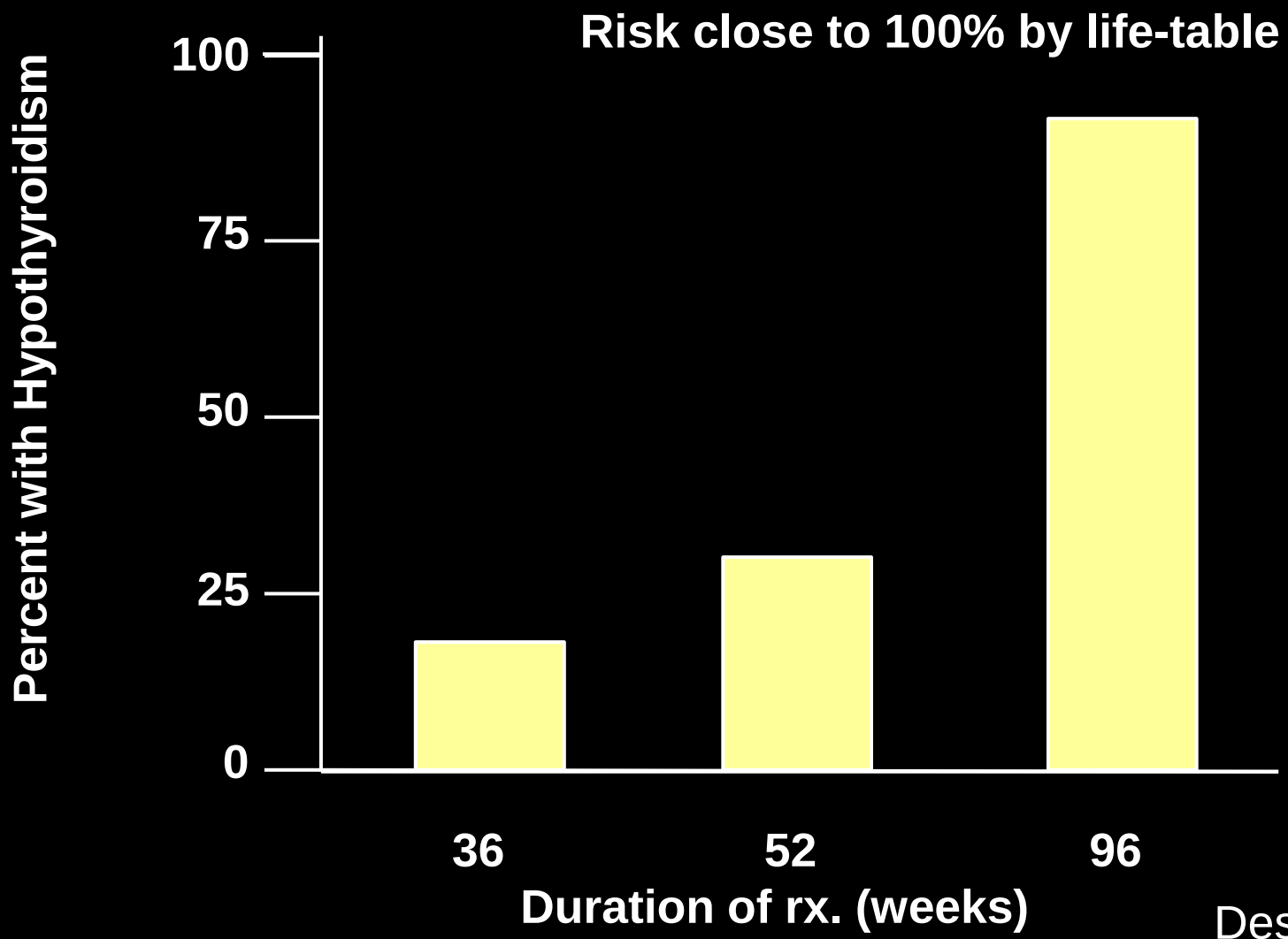
Tyrosine kinase inhibitor licensed for therapy of renal cell carcinoma and GIST tumors.

Sunitinib Hypothyroidism

Desai et al.
Ann Int Med 2006
145:660



Sunitinib Hypothyroidism

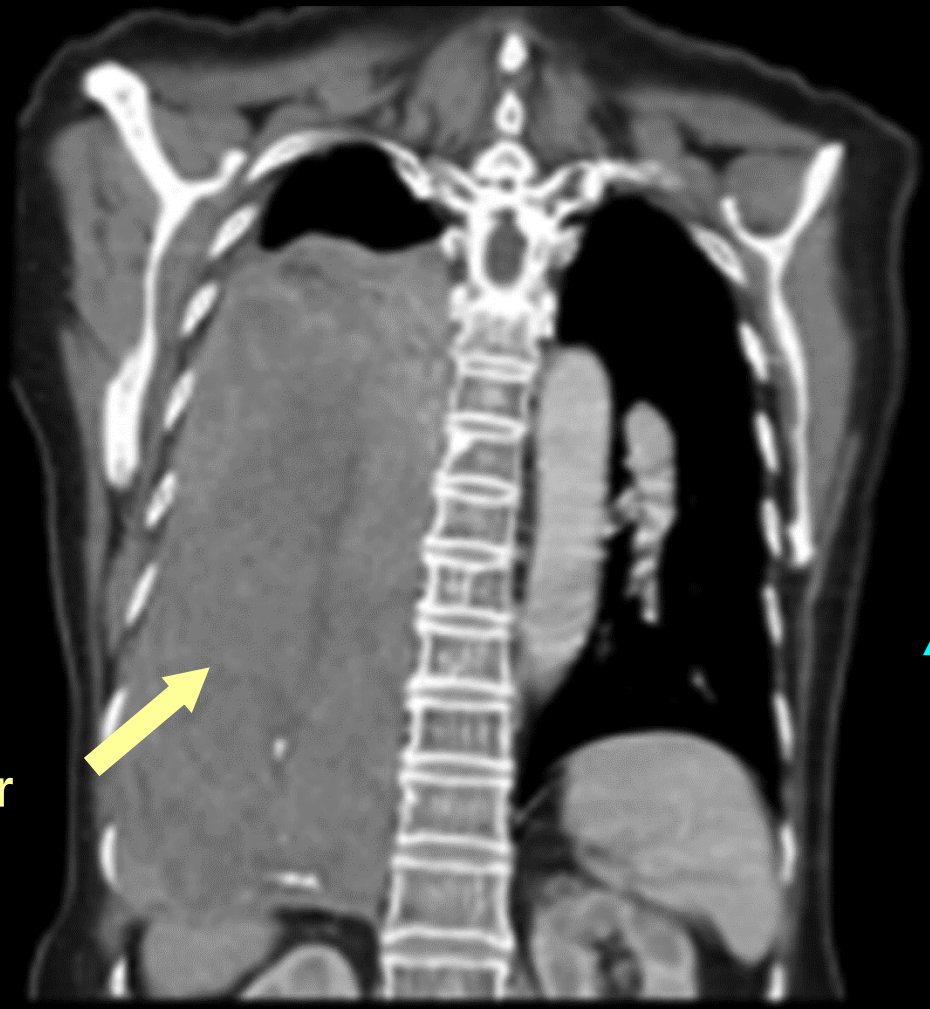


Desai et al.
Ann Int Med 2006

Goitrous Primary Hypothyroidism

- Hashimoto's Thyroiditis
- Painful Subacute Thyroiditis
- Silent Subacute Thyroiditis
- Drugs
- Transient Post RaI
- Biosynthetic Defects
- Iodine Deficiency
- Consumptive
- Congenital (Ectopic)

Consumptive Hypothyroidism



Intrathoracic Fibrous Tumor

↑ Type 3 Deiodinase

Aw et al. JCEM 2014: 99: 3965

Goitrous Primary Hypothyroidism

- **Hashimoto's Thyroiditis**
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Dr. Hakaru Hashimoto

Archiv fur Klinische Chirurigie
1912; 97: 219

Hashimoto's Thyroiditis

Premature Gray Hair

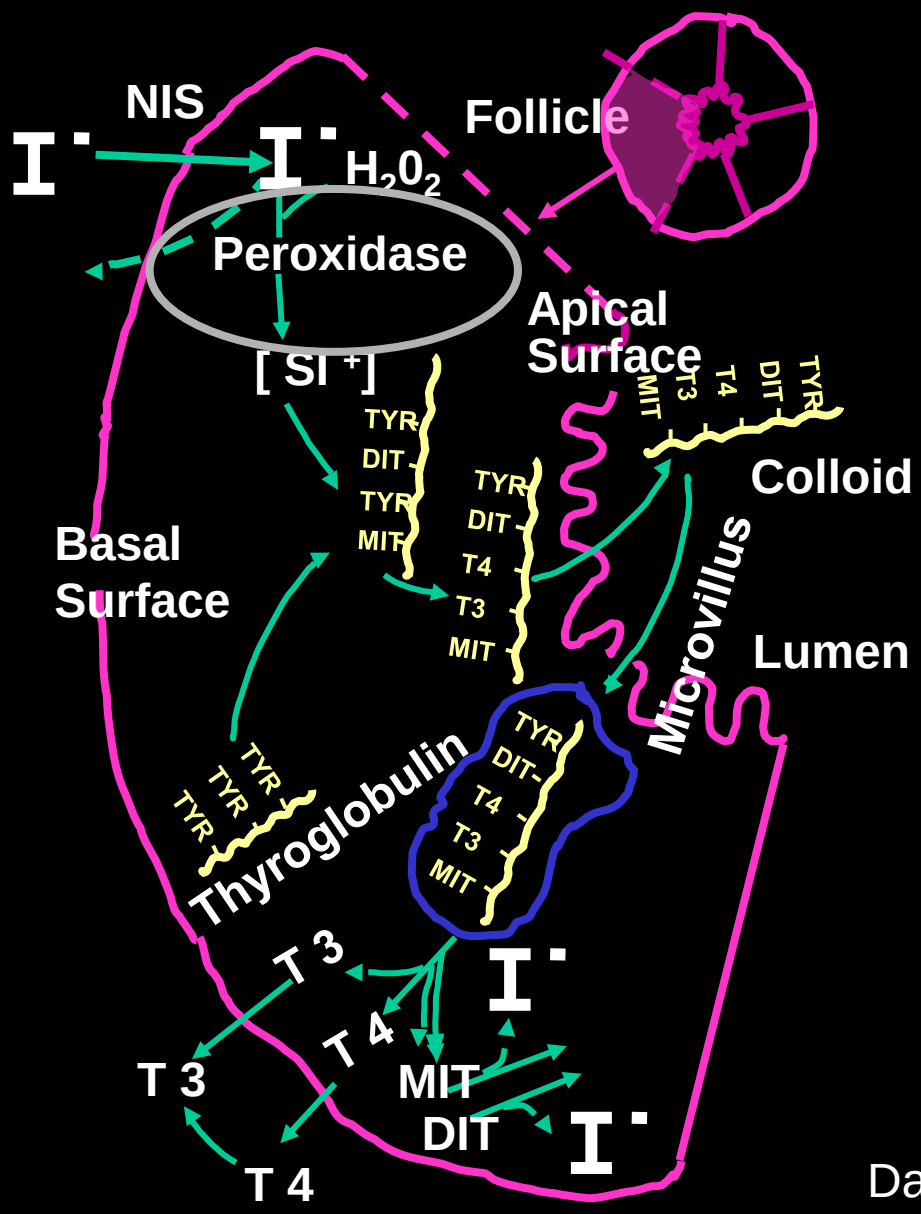
Hall et al. Color Atlas of Endocrinology 1979

Vitiligo

Lancet 2002; 360: 1639

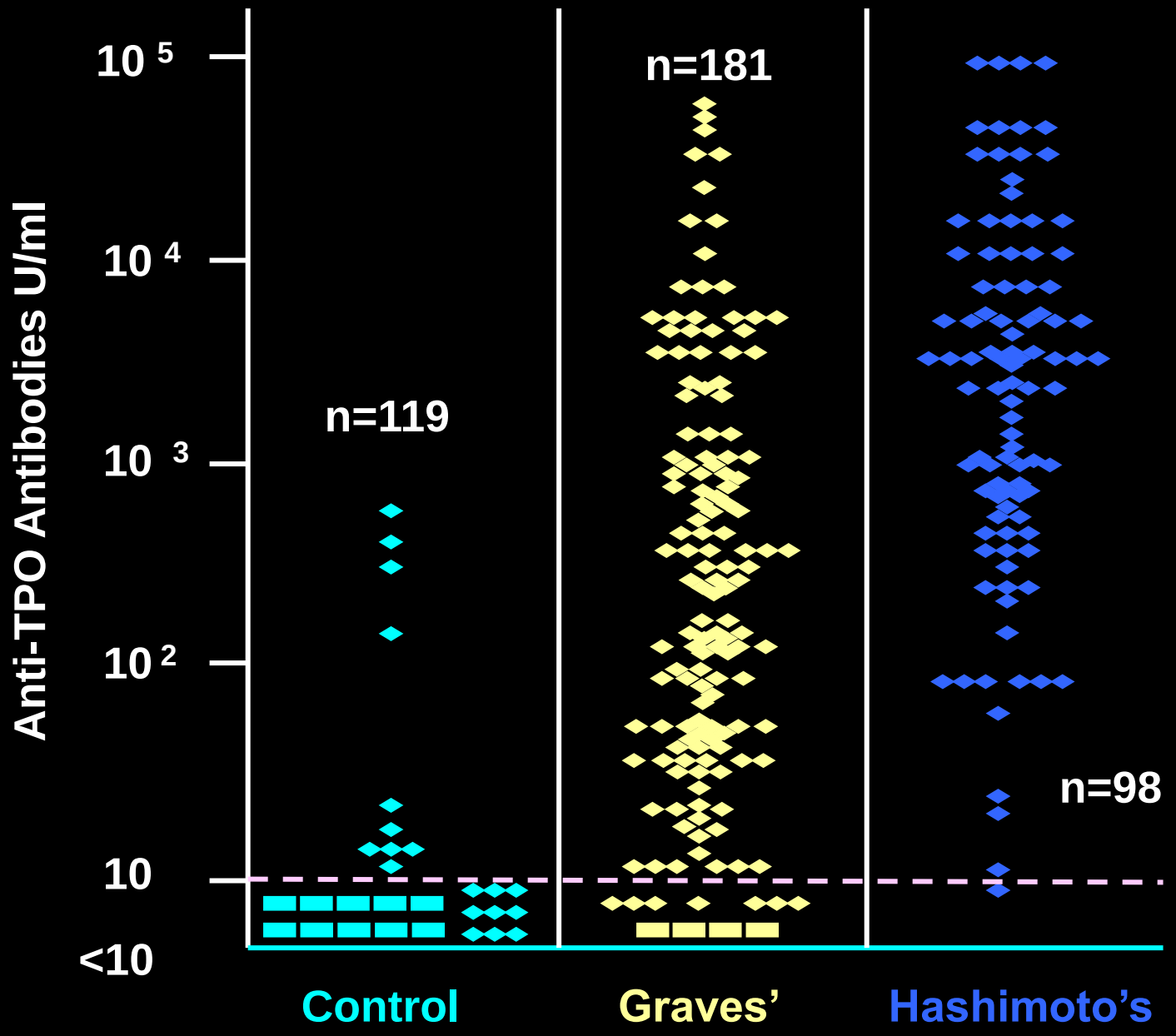
Vitiligo

NEJM 2004; 26: 2698



Daniels & Maloof 1976

Anti-TPO Antibodies



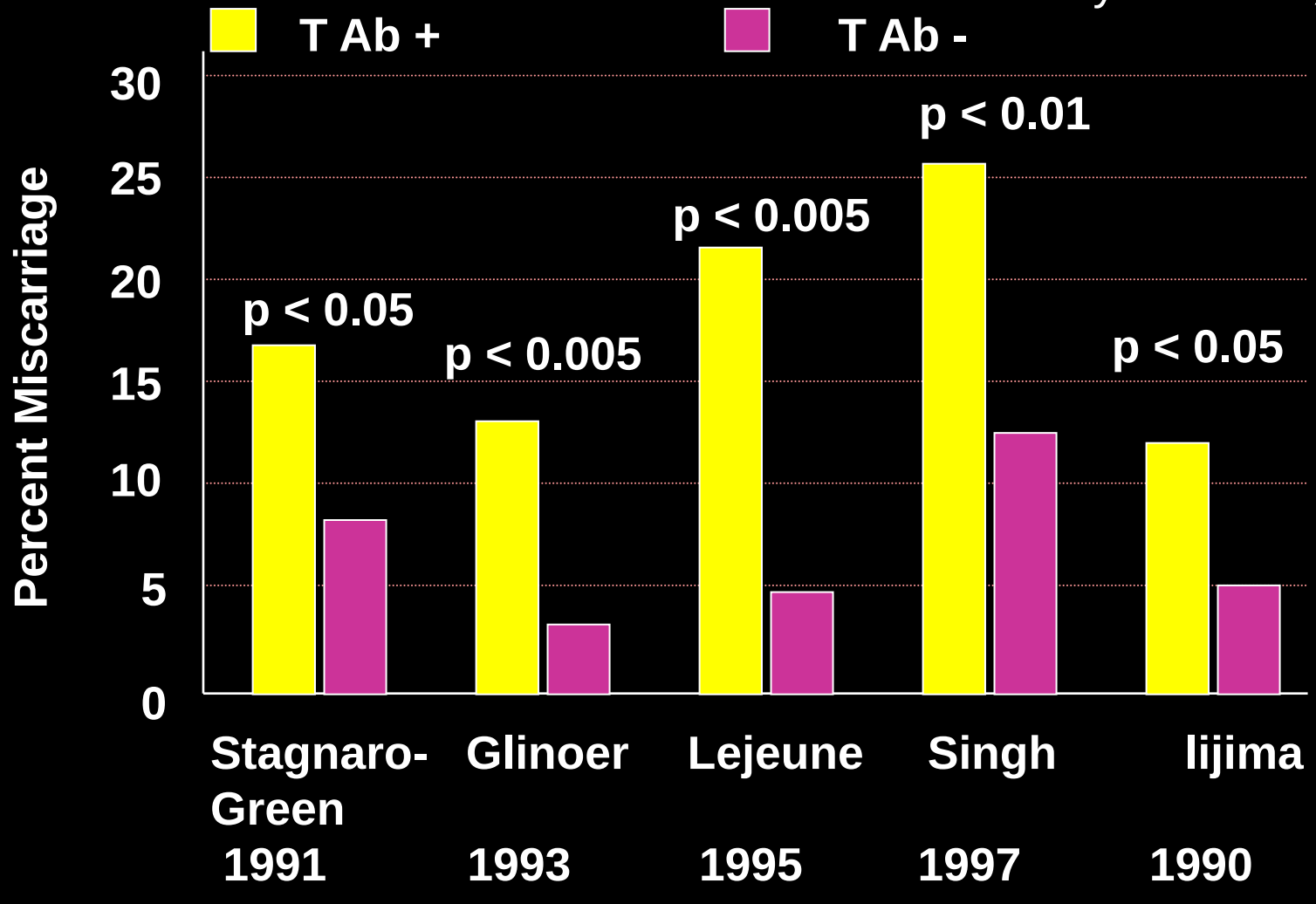
Mariotti et al
JCEM 1990;
71 : 661

Is it worthwhile diagnosing Hashimoto's

thyroiditis in euthyroid individuals ?

Thyroid Antibodies: Miscarriages

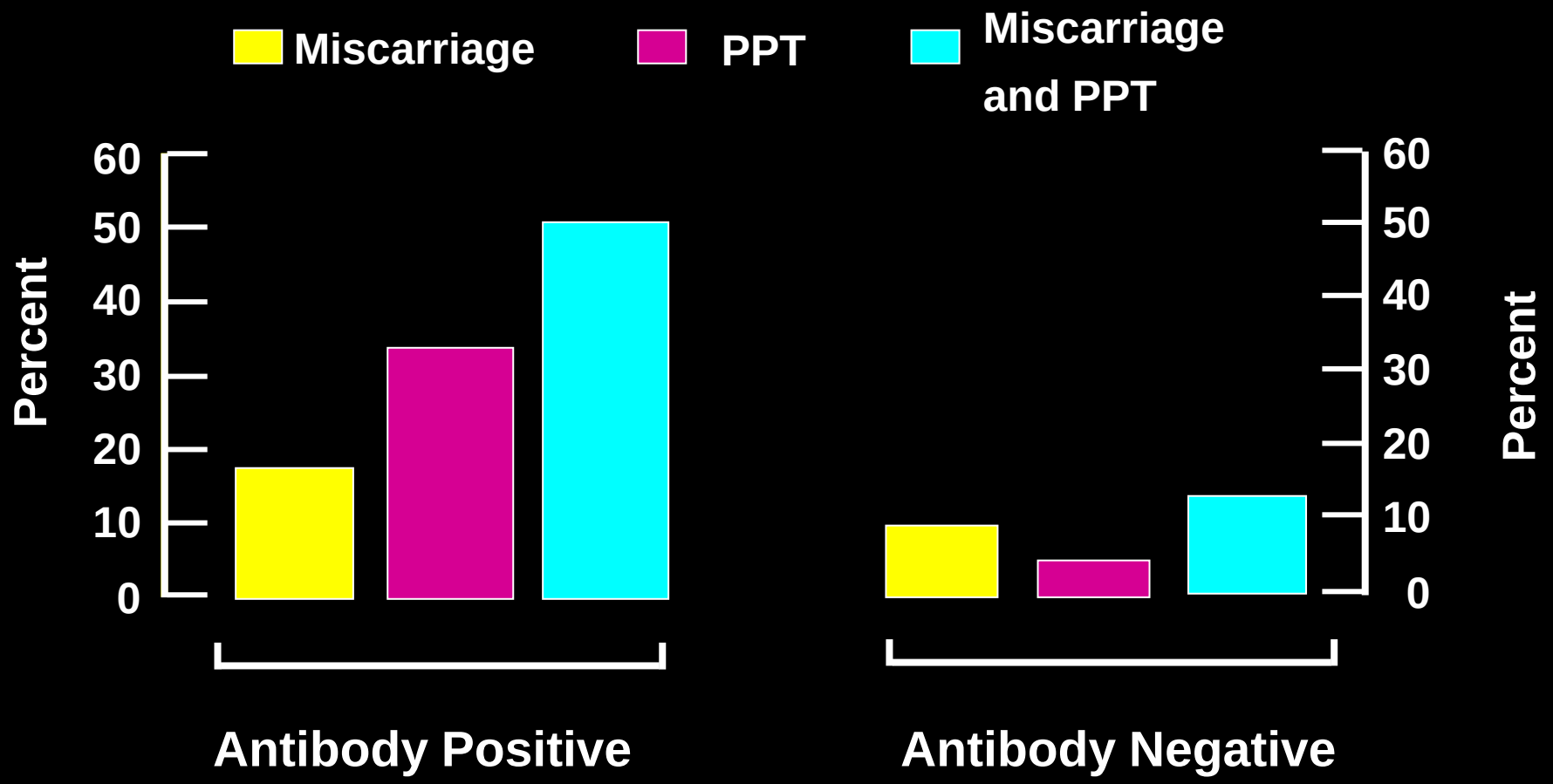
Abramson and Stagnaro Green Thyroid 2001; 11: 57

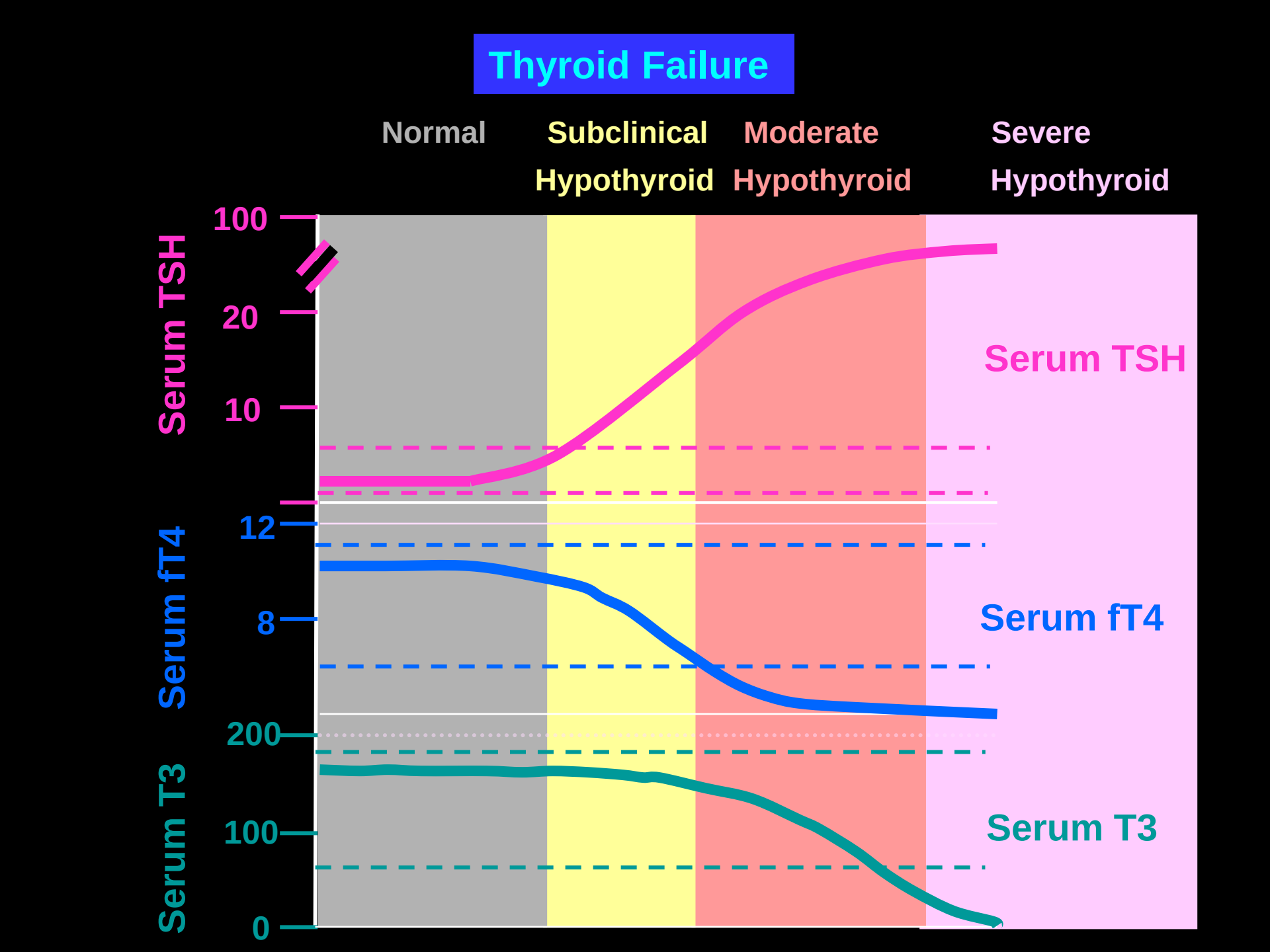


Thyroid Antibodies

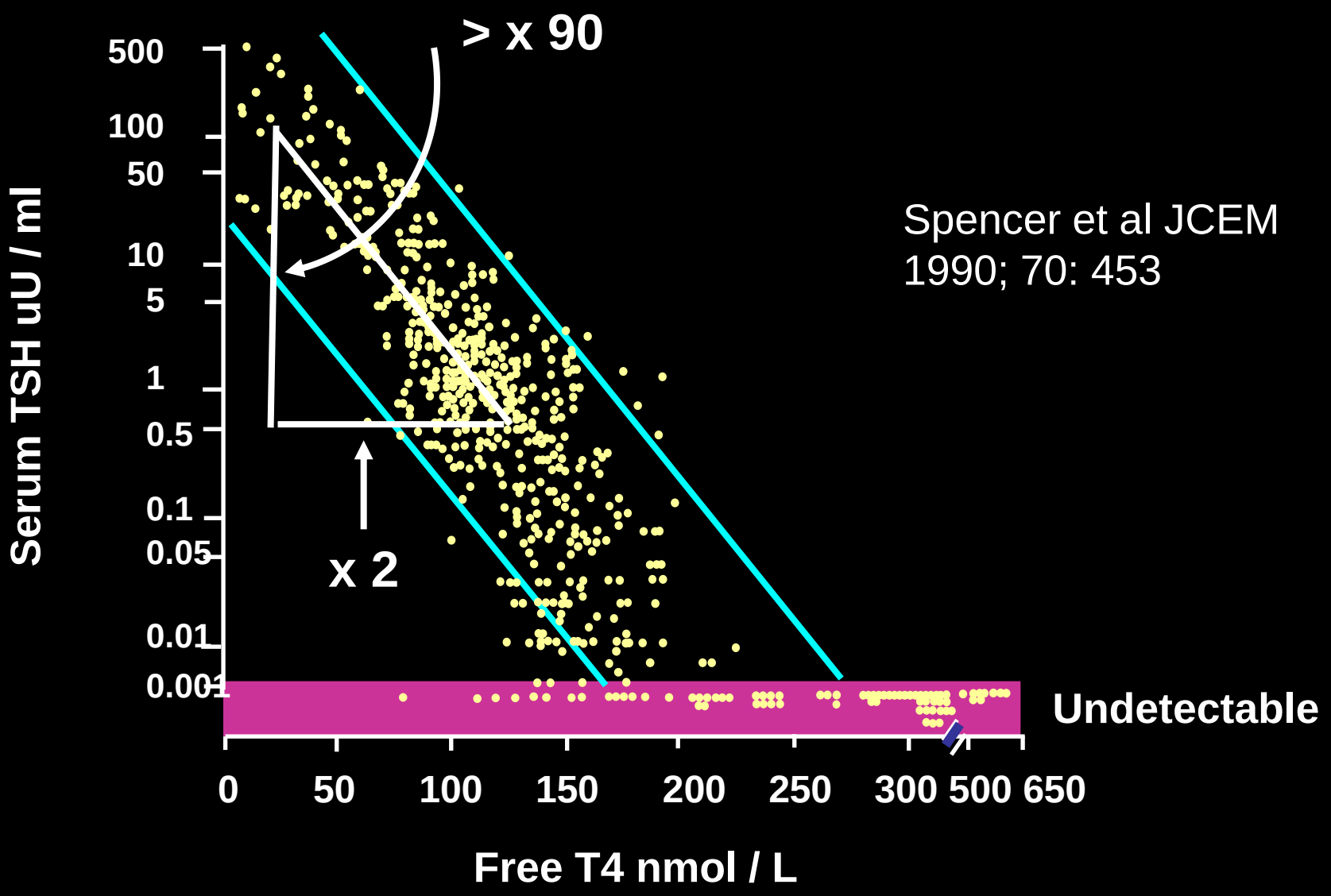
Stagnaro-Green A.

Thyroid Today 16: 1 : 1993




Thyroid Failure
Normal
Subclinical Hypothyroid
Moderate Hypothyroid
Severe Hypothyroid
Serum TSH
100
20
10
Serum fT4
12
8
Serum T3
200
100
0
Serum TSH
Serum fT4
Serum T3

Free T4 vs. TSH



Spencer et al JCEM
1990; 70: 453

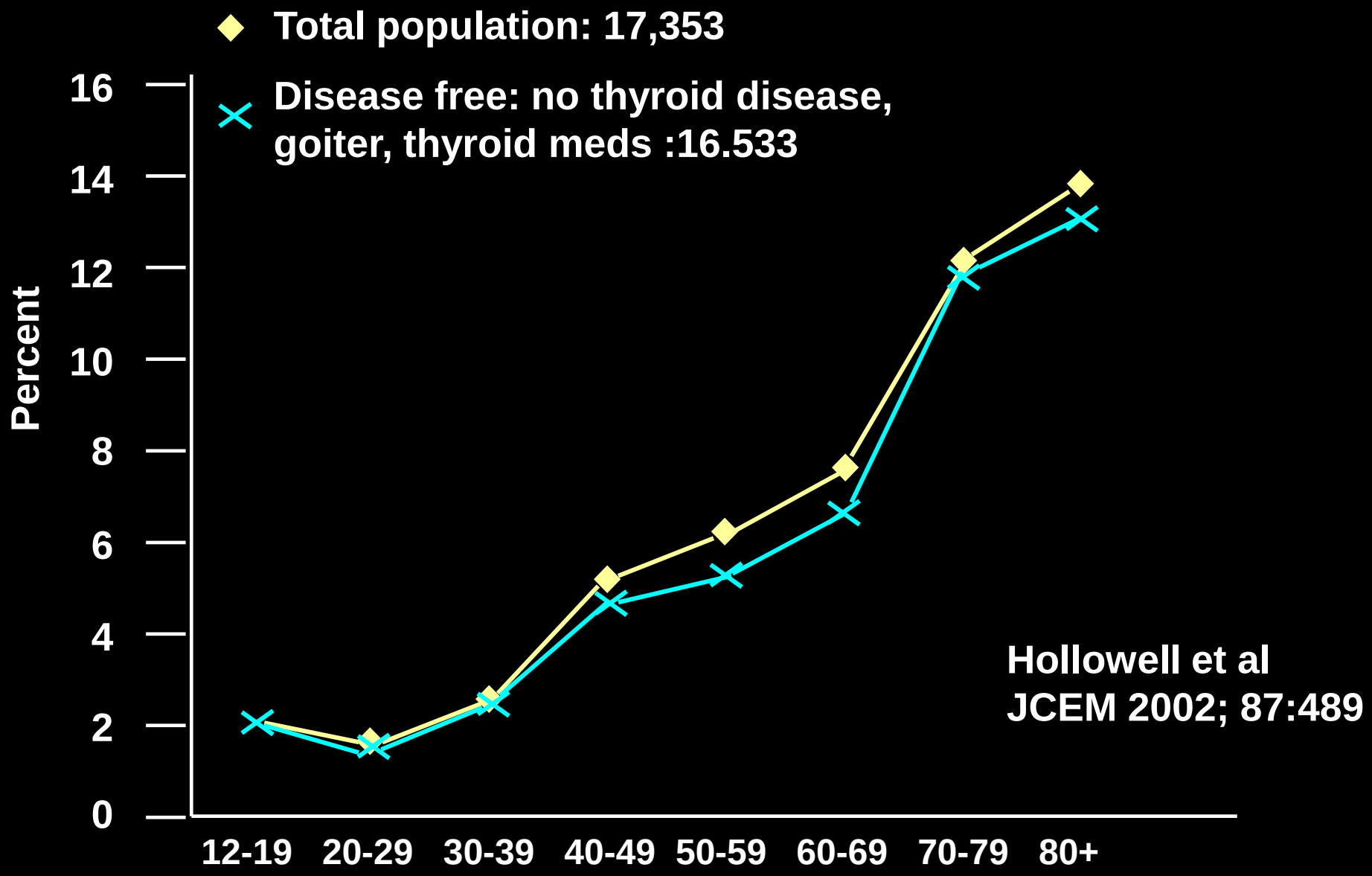
Subclinical Hypothyroidism

- Normal T4
- Normal Free T4
- Elevated TSH

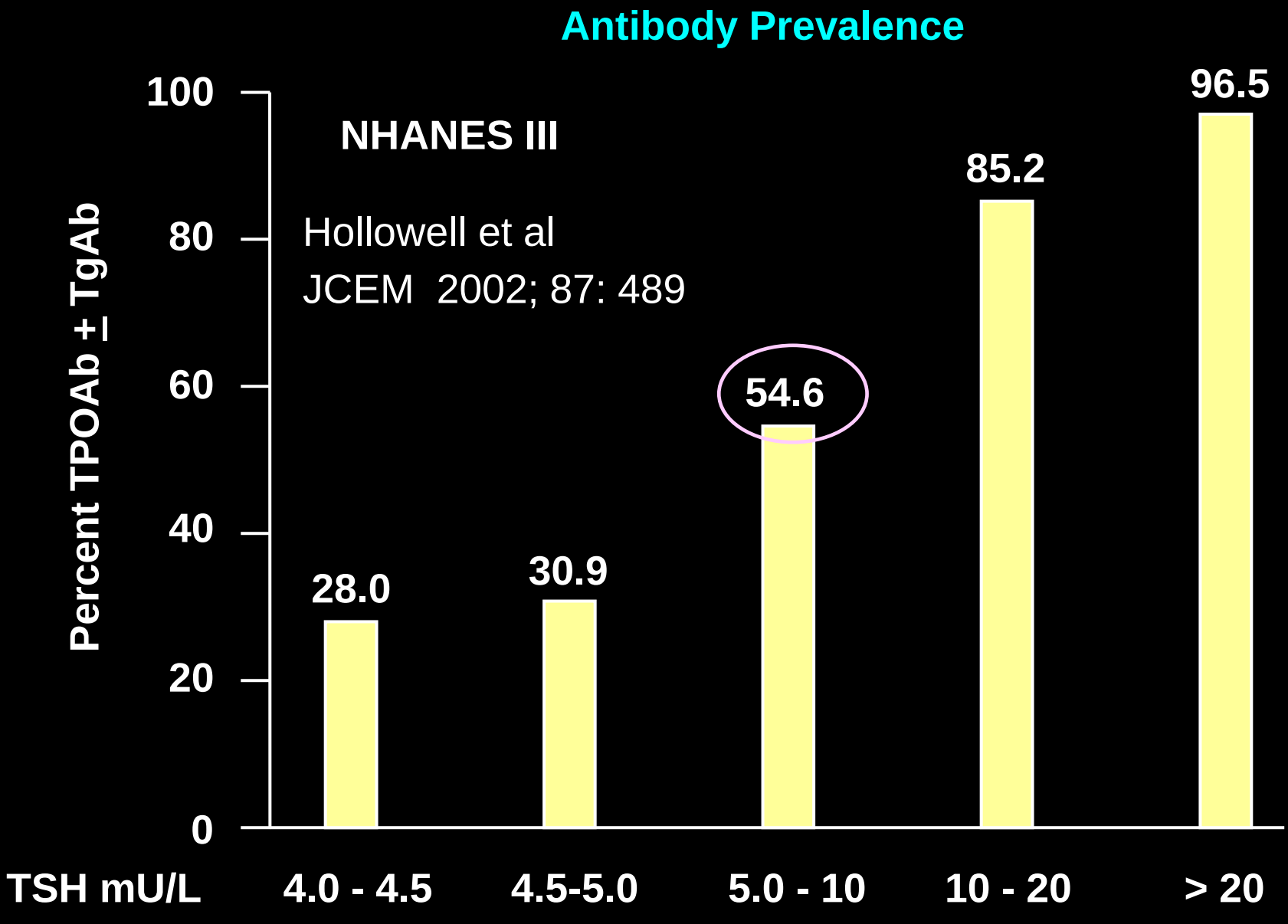
Subclinical Hypothyroidism

- Exclude other causes of elevated TSH
- Patient may be symptomatic or asymptomatic !!

NHANES TSH > 4.5 mU/L



Subclinical Hypothyroidism



Community Practice

422,242 pts in Tel Aviv

5 year FU

3 % TSH > 5.5 - ≤ 10

n = 12,600

0.7 % TSH > 10 (overt)

n = 2,950

Treatment started in 75% of those with abnormal TSH.

25% had only a single TSH determination !

Meyerovitch et al Arch Int Med 2007;167: 1533

5 Year untreated TSH > 10

Repeat TSH :	> 10	5.5 - ≤ 10	Normal
	35 %	36.5 %	27.7 %

5 Year untreated TSH 5.5 - ≤ 10

Repeat TSH :	> 10	5.5 - ≤ 10	Normal
	2.9 %	35 %	62.1%

Overall 2.9 % of those not treated, progressed from subclinical hypothyroidism to “overt” over 5 years

Meyerovitch et al Arch Int Med 2007;167: 1533

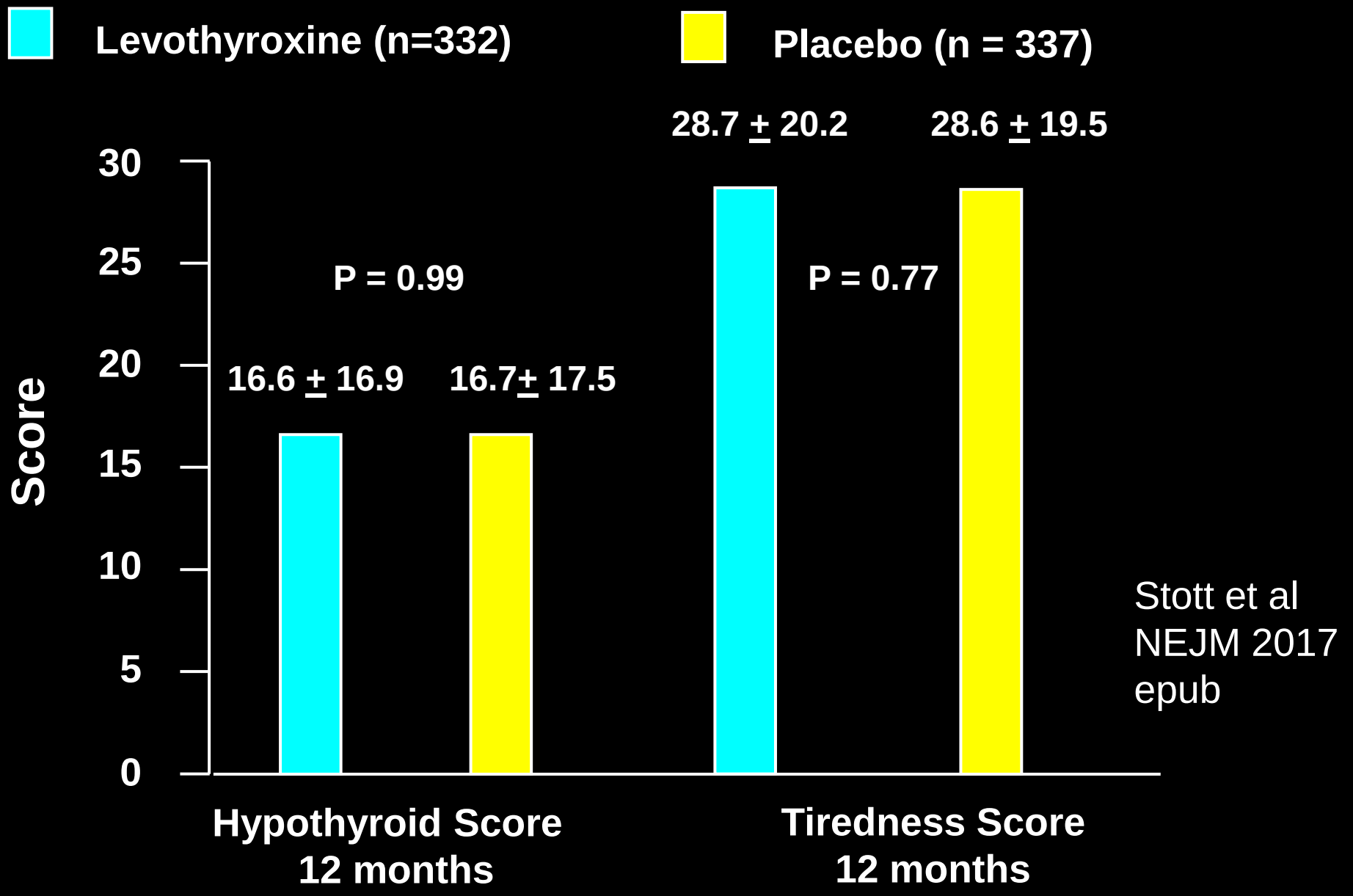
Stott DJ et al. Thyroid hormone therapy for older adults with subclinical hypothyroidism. **New Engl. J Medicine 2017: 376: 2534**

Persistent TSH 4.6 – 19.99 mIU/L (mean 6.4 ± 2.01 mIU/L)

Stott et al.

- Mean age 74.4 years
- Randomized placebo-controlled trial. Goal of therapy to to normalize TSH.
- Major endpoints Hypothyroid Symptom Score or Tiredness Score.
- Of note at baseline 27 % had nil hypothyroid symptoms and 8.7% had nil tiredness score.

Subclinical Hypothyroidism Elderly



Stott et al
NEJM 2017
epub

Moon et al. Subclinical hypothyroidism and the risk of cardiovascular disease and all-cause mortality: A meta-analysis of prospective cohort studies. Thyroid 2018: 28: 1101.

Subclinical Hypothyroidism: Meta-analysis

- **35 articles.**
- **555,530 participants.**
- **Subclinical hypothyroid: n = 21,176**
- **“High TSH with normal fT4” - not further stratified.**

Moon et al. Thyroid 2018: 28: 1101.

Subclinical Hypothyroidism Age < 65

- **Increased cardiovascular mortality: RR 1.54 (CI 1.21-1.96)**
- **Increased all cause mortality : RR 1.28 (CI 1.1 – 1.48)**

Moon et al. Thyroid 2018: 28: 1101.

Subclinical Hypothyroidism Age ≥ 65

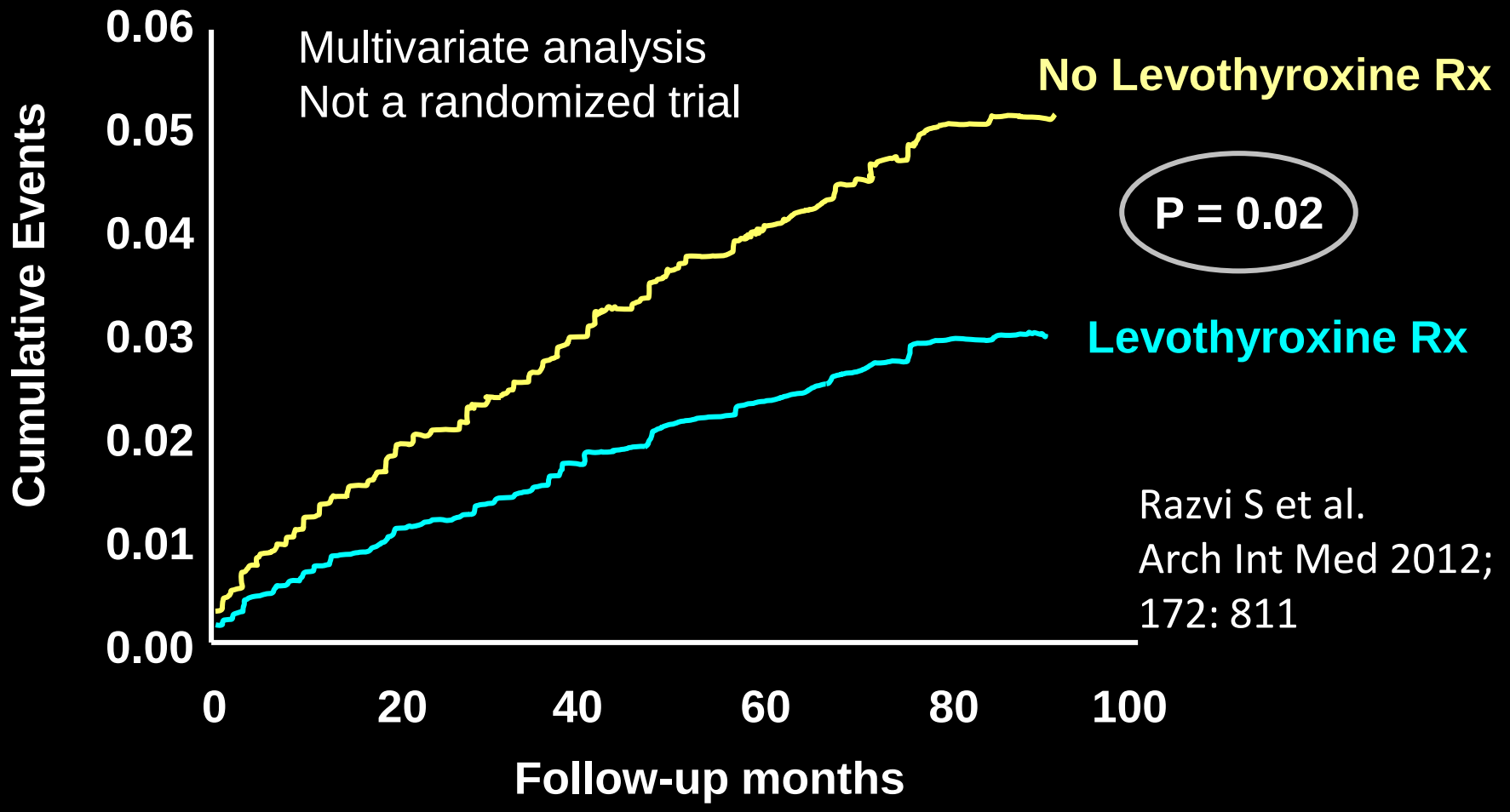
- **No significant association with CVD and all cause mortality.**
- **Low CVD risk: no association with mortality.**
- **High CVD risk: increased all cause mortality RR 1.41 (1.08-1.85) but no increased CVD mortality: RR 1.5 (0.89-2.54)**
- **Note studies from the USA did not show increased mortality but most had low CVD risk.**

Moon et al. Thyroid 2018: 28: 1101.

Fatal and non-fatal ischemic heart disease events

Subclinical Hypothyroidism: ages 40 – 70 (n = 3093)

TSH 5 – 10 mU/L



Subclinical Hypothyroidism : Mortality Conclusions

- Ultimately requires an adequately powered, randomized, placebo-controlled therapeutic trial !

- This is particularly difficult when some (many) patients normalize their TSH over the course of the study.

What to do when TSH elevated

Patient on thyroid hormone:

generally increase dose.

What to do when TSH elevated

Patient not on thyroid hormone:

Repeat measurement.

Use common sense !

My TSH is 6. I feel terrible. Nothing is right. I'm cold, tired, hungry, constipated and depressed. Please treat me with thyroid hormone!

Subclinical Hypothyroidism

My TSH is 6. I feel fine !
Do I really have to be treated with thyroid hormone for the rest of my life ?

Subclinical Hypothyroidism

To treat or not to treat ?

Subclinical Hypothyroidism

	Treat ?	Observe ?
Symptoms	Yes	No
Age	Younger (> 7)	Older
TSH mU/L	> 10	5 - 10
+ Thyroid Ab	Yes	No
Post-RaI	Yes	No
Goiter	Yes	No
Heart Disease	No	Yes
Pregnancy	Yes	No

Subclinical Hypothyroidism

- With TSH 4.7 - 10 mU/L : most are asymptomatic.
- No good evidence for L-T4 symptomatic benefit in this range.
- No good evidence for L-T4 cholesterol lowering in this range.
- There may be symptomatic and cholesterol benefit with TSH > 10.
- On the other hand, in the absence of overtreatment, there is no compelling evidence for harm with levothyroxine treatment.
- If you decide to treat, particularly in the elderly, stop if no benefit !

Elevated serum TSH

- **Age 20-29 97.5 centile for TSH: 3.45 mU/L**
- **Age 80 + 97.5 centile for TSH: 7.5 mU/L**
- **Older patients: 70% with TSH > 4.5 mU/L are within their age-specific reference range.**

Surks and Hollowell JCEM 2007: 92: 4575

Levothyroxine

- 7 day half life
- Single daily dose
- Absorption : 80 %
- We primarily use generic

Thyroid Hormone Adjustment

- Worsening hypothyroidism
- Increased clearance
- Decreased absorption
- Pregnancy
- Age
- Poor compliance

Increased Clearance

- Phenytoin
- Carbamazepine
- Rifampin
- Phenobarbital
- Imatinib
- Other Tyrosine Kinase Inhibitors

Thyroid Hormone Adjustment

- Worsening hypothyroidism
- Increased clearance
- Decreased absorption
- Pregnancy
- Age
- Poor compliance

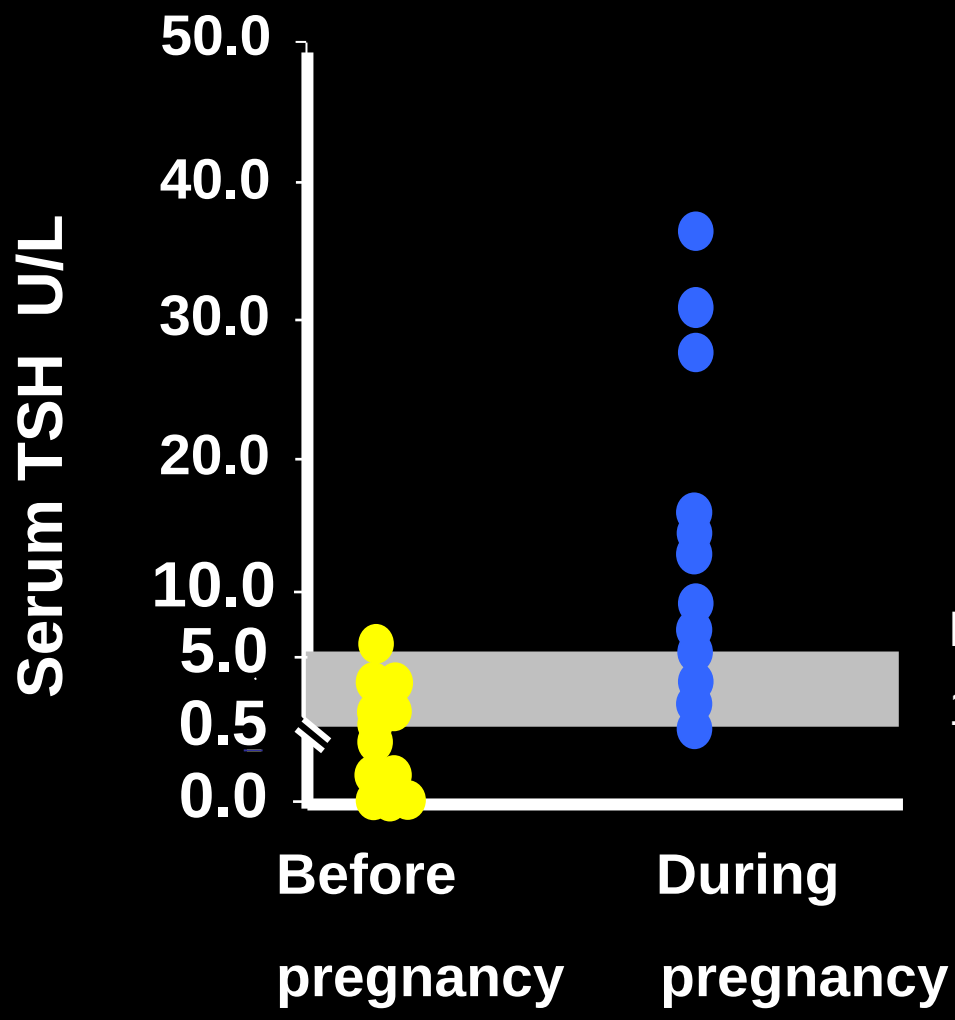
Decreased Absorption

- Iron
- Aluminum hydroxide
- Calcium
- Lanthanum
- Cholestyramine and other resins
- Sucralfate
- Raloxifene
- Ciprofloxacin
- GI disorders - cryptic sprue
- Decreased stomach acid
- Food - including espresso
- “Insoluble Pills”

Increased Levothyroxine Requirement

- Estrogen
- ? Sertraline

Thyroid Hormone Therapy



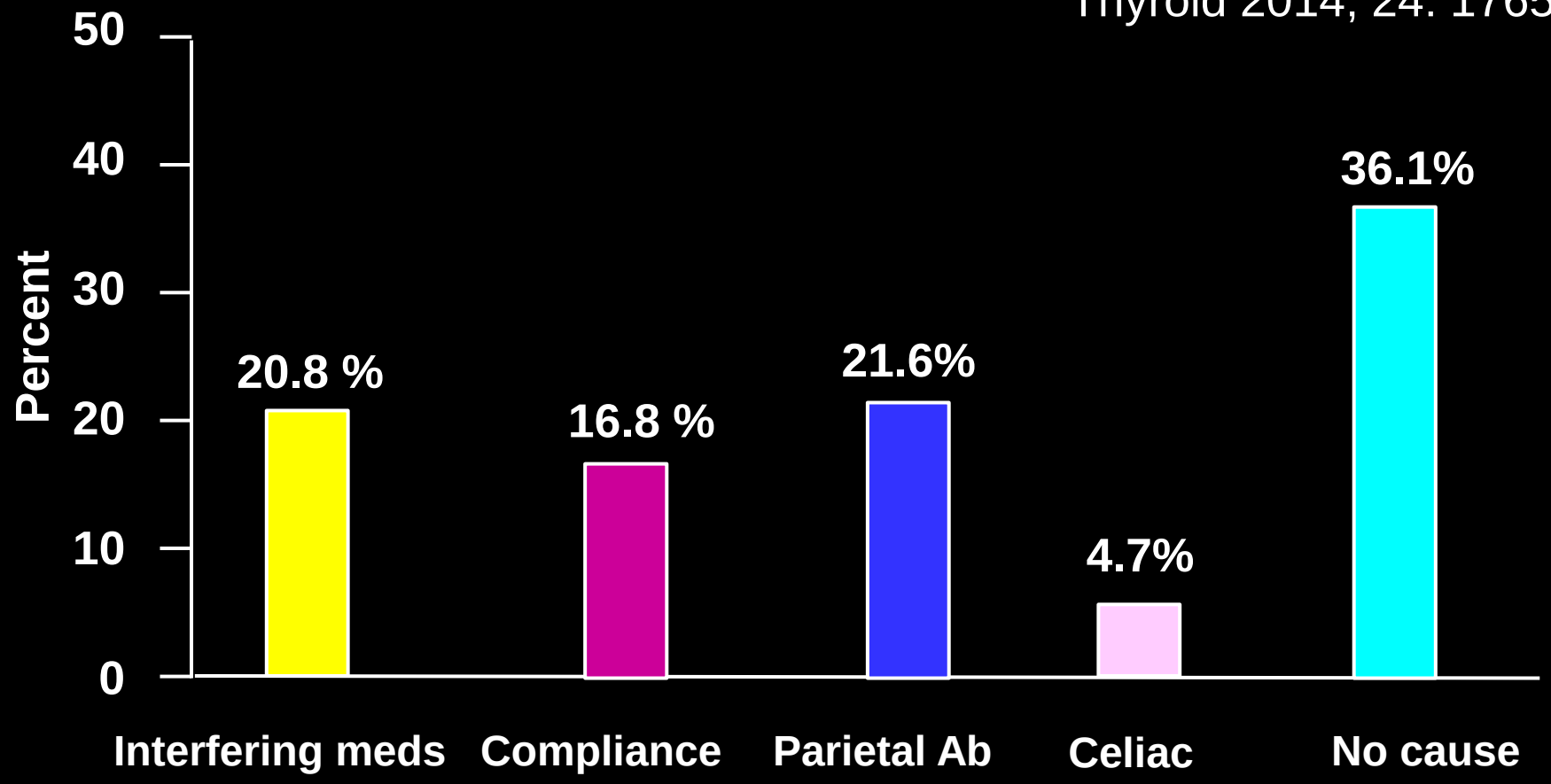
Mandel et al NEJM 1990; 323: 91

High L-T4 Requirement in a Community Setting

T4 dose > 225 mcg

N = 125

Robertson HMA et al
Thyroid 2014; 24: 1765



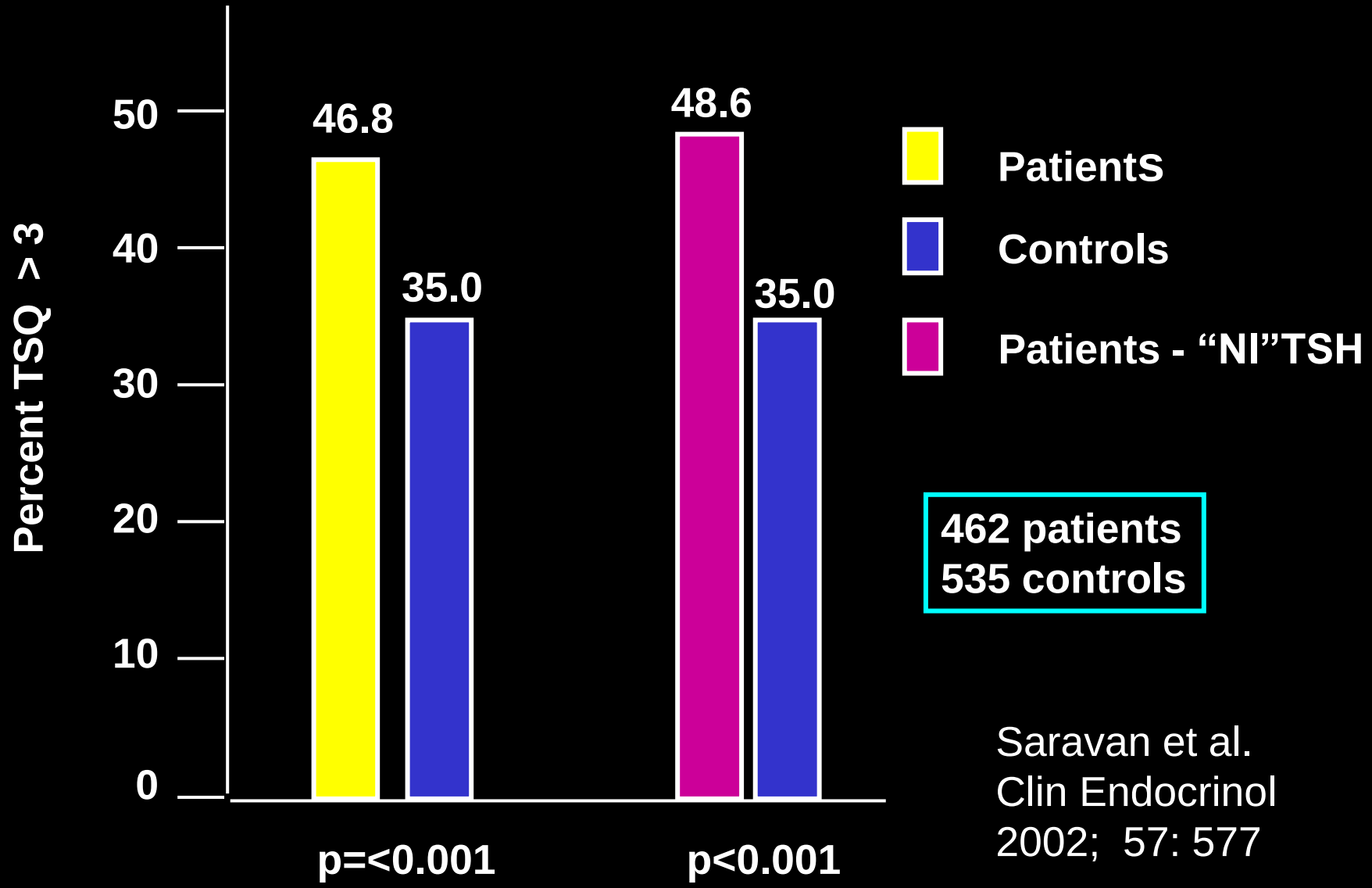
Fable

Once upon a time there was a symptomatic hypothyroid patient with an elevated serum TSH. Thyroid hormone therapy was begun. The TSH normalized, the symptoms disappeared and the patient lived happily ever after !

88 – 90 % feel well on levothyroxine therapy.

Levothyroxine Therapy

Thyroid Symptom Questionnaire

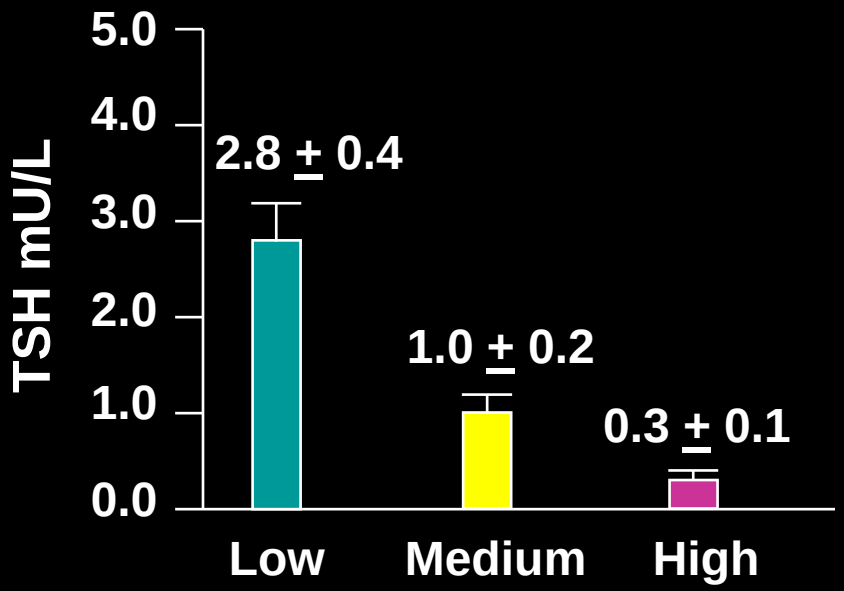


Saravan et al.
Clin Endocrinol
2002; 57: 577

Possible Explanations

- Failure to titrate TSH to “low normal”
- T 3 supplementation required
- Co-morbid disorders including depression
- Having an illness (“Labeling”)
- Coincidence (“squeaky wheel gets tested”)
- Hashimoto’s thyroiditis

Levothyroxine Dose Titration



No Difference

- Weight
- Zulewski score
- Visual Analog Scale
- SF-36 Questionnaire
- GHQ-28
- Thyroid Symptom Q
- Treatment Satisfaction

Walsh et al. JCEM 2006; 91:2624-30

Possible Explanations

- Failure to titrate TSH to “low normal”
- T 3 supplementation required
- Co-morbid disorders including depression
- Having an illness (“Labeling”)
- Coincidence (“squeaky wheel gets tested”)
- Hashimoto’s thyroiditis

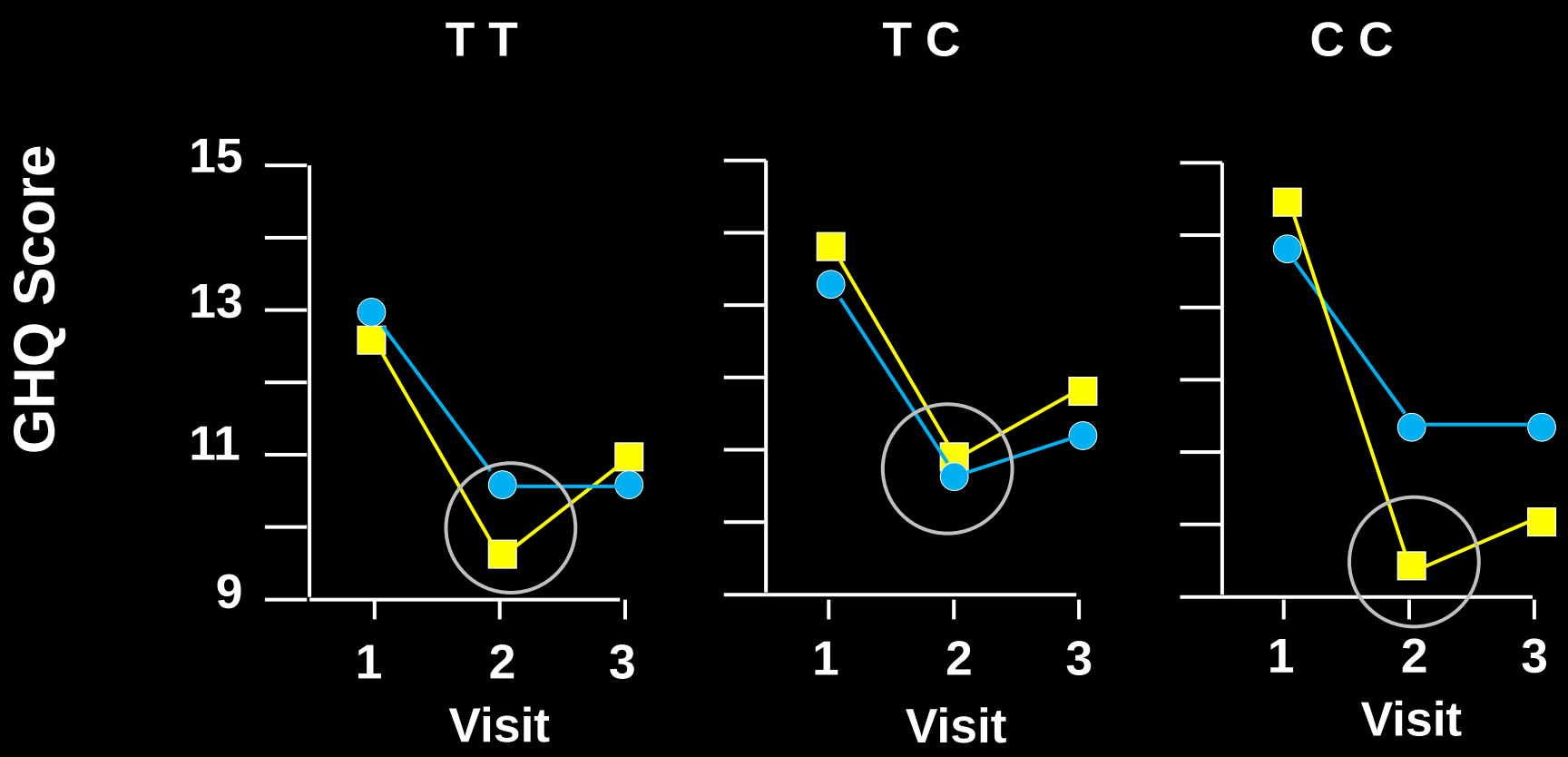
Panicker V. et al. **Common variations in the DIO2 gene predicts baseline psychological well-being and response to combination thyroxine plus triiodothyronine therapy in hypothyroid patients.** **J Clin Endocrinol Metab 2009; 94: 1623**

General Health Questionnaire

Deiodinase Genotype

Panicker et al JCEM
2009 ; 94: 1623

P = 0.03



Satisfaction

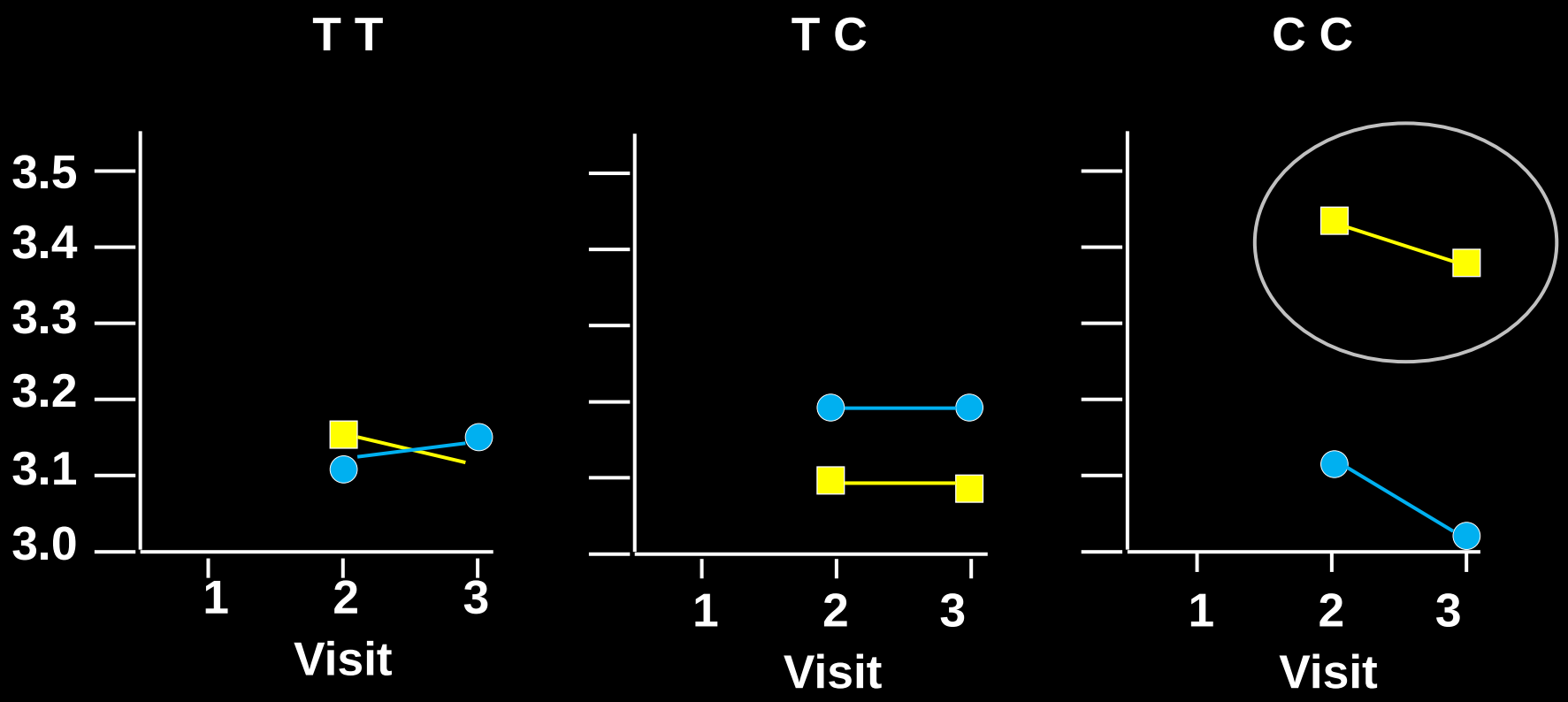
Deiodinase Genotype

Panicker et al JCEM
2009 ; 94: 1623

T4 + T3

T4

P = 0.02



T 4 + T 3 vs. T4 Therapy

- **Overall, most trials do not show benefit of T4 + T3 compared to T3 by the tested metrics, but some do.**
- **In some trials T4 + T3 preferred despite no benefit by metrics.**
- **In some trials patients with Thr92Ala-DIO2 polymorphism or a mono-carboxylate transporter (MCT) 10 polymorphism or both feel better with T4 + T3. Other trials do not show this**
- **Some patients feel better for a while and then benefit disappears.**

Jonklass J et al. Thyroid 2021; 31: 156.

Concerns about T3 Trials

- None have specifically analyzed patients who do not feel well on levothyroxine.
- Although T3 is generally lower in the L-T4 treated group, there are no studies targeting those with lower T3 and no evidence that those with lower T3 respond better.

If Beneficial : Possible Explanations

- Missing thyroidal T3 component.
- Intracellular T3 cannot be predicted based on circulating T3.
- In some cells higher circulating T4 leads to down regulation of T3 production.
- We cannot extrapolate from rodents, but no dose of levothyroxine completely normalizes T3 in all cells in hypothyroid animals.
- If beneficial we cannot be certain that we are giving T3 physiologically. T3 in high doses has pharmacologic anti-depressant properties.

T4 + T3 Conclusions

- There may be some patients who (are genetically pre-disposed to) feel better on the combination therapy. Whether this is due to a physiological role of T3 or a pharmacological property of T3 in some individuals is uncertain.
- There is a strong placebo effect.
- Even if we agree that T3 is necessary, we do not know the ideal way to prescribe T3.

What I do when patients don't feel well on T4

- Realize that many patients don't feel well (with or without T4)
- Look for other concomitant disorders: these include iron deficiency and anemia in pre-menopausal women, sleep disturbances including sleep apnea, and depression.
- Titrate TSH to lower normal range (despite the controlled studies)
- Consider adding T3 (liothyronine) 5 mcg in the a.m. and 5 mcg in early afternoon. Initially I don't adjust the levothyroxine dose (unless TSH very low at the time) but ask patients to call in two months. If feeling better I check TFTs and continue the medication. If no difference I stop the medication.

Euthyroid patients with Hashimoto's thyroiditis do

not feel as well as the general population !

Guldvog I et al. Thyroidectomy versus medical management for euthyroid patients with Hashimoto Disease and persisting symptoms. **Ann Int Med 2019; 170: 453**

Hashimoto's Disease: Surgery vs. Medical Rx.

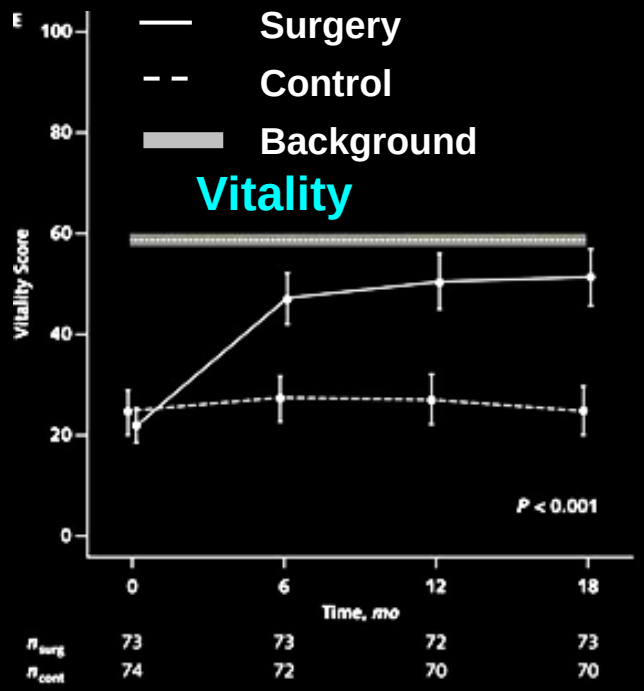
- 150 patients (age 18 – 79)
- On levothyroxine for hypothyroidism
- TPO Ab > 1000 IU/ml
- Symptoms "severe enough" to warrant surgery (NOS)
- At the "end of road", with "high motivation for surgery."
- Total thyroidectomy vs. medical management
- Short Form - 36 Health Survey at 18 months and TPO titer

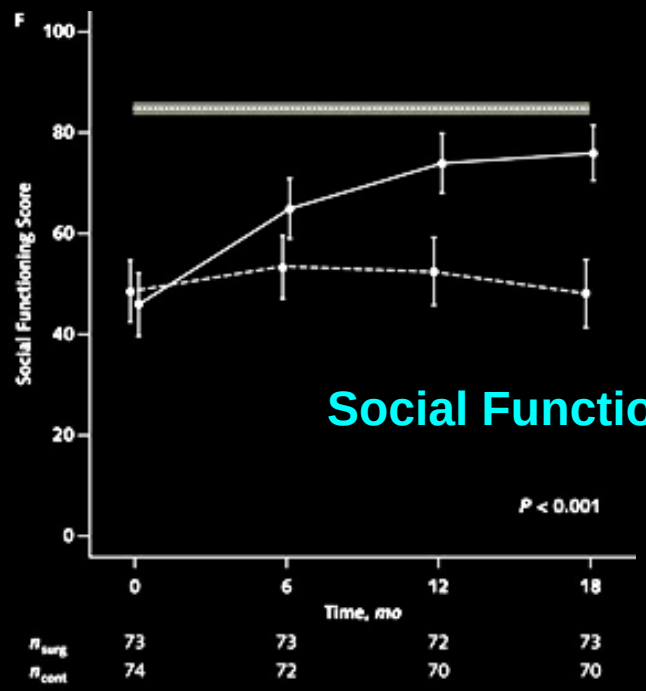
Gudlvog I et al. Ann Int Med 2019; 170: 453

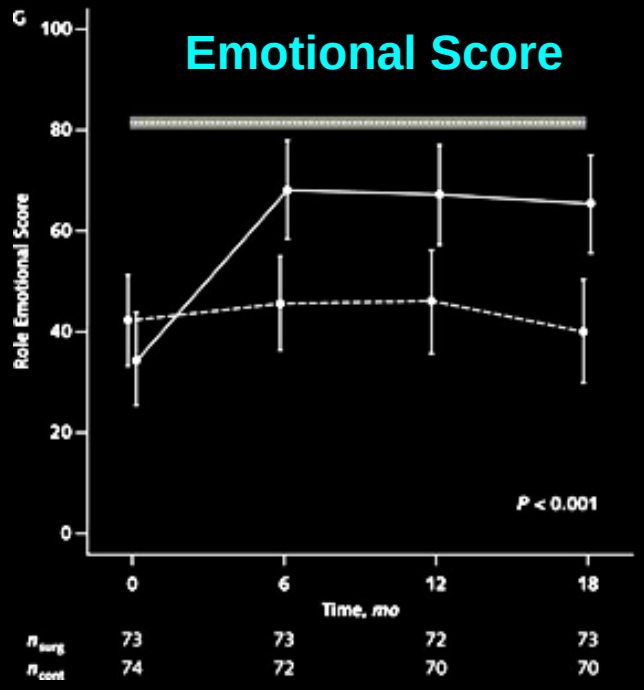
Hashimoto's Disease: Surgery vs. Medical Rx.

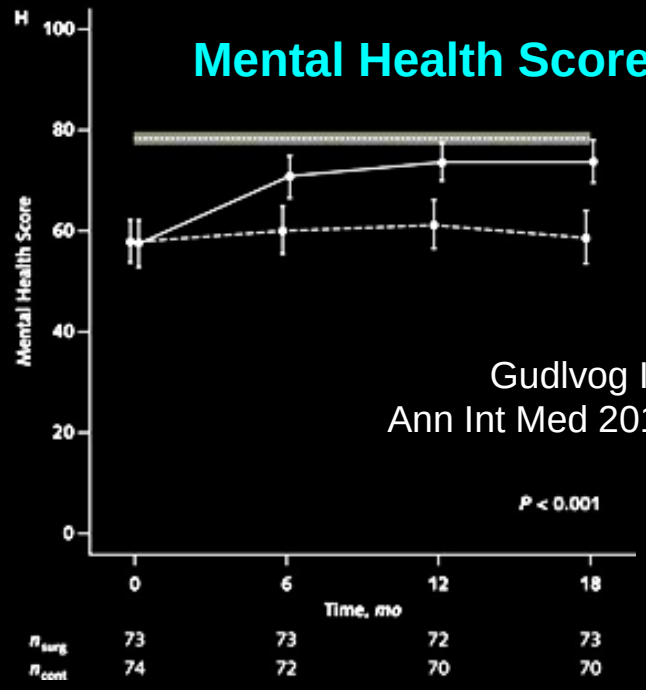
- **Surgical group improved SF – 36**
- **Fatigue score decreased**
- **Chronic fatigue decreased from 82 % to 35 %**
- **TPO Antibodies decreased from 2232 to 152**
- **3 surgical infections (4.1%); 3 longstanding hypocalcemia (4.1%) 4 unilateral RLN palsy (5.5%)**
- **Note: this is with a group of expert surgeons.**

Gudlvog I et al. Ann Int Med 2019; 170: 453









Gudlvog I et al.
Ann Int Med 2019; 170: 453

Hashimoto's Disease: Surgery vs. Medical Rx.

- **Caveat: before considering this approach it is imperative to realize that total thyroidectomy for patients with Hashimoto's thyroiditis is much more difficult than a conventional total thyroidectomy due to surrounding inflammation. (**McManus C. Surg Res 2012; 178: 529)

Summary Points

- Hyperthyroidism is not just Graves' disease
- Many drugs cause thyroid dysfunction (e.g. amiodarone, alemtuzumab, sunitinib, immune check point inhibitors and others).
- Hypothyroidisim is primarily Hashimoto's thyroiditis but think of other etiologies.
- For inappropriate TSH elevation in patients on thyroid hormone, consider increased metabolism, decreased absorption, pregnancy or poor compliance
- Possible but limited role for T3 supplementation.

Hyperthyroidism

and Hypothyroidism