“Diagnostisk nød”
Thyroidea og webreqprofiler

Esther A. Jensen
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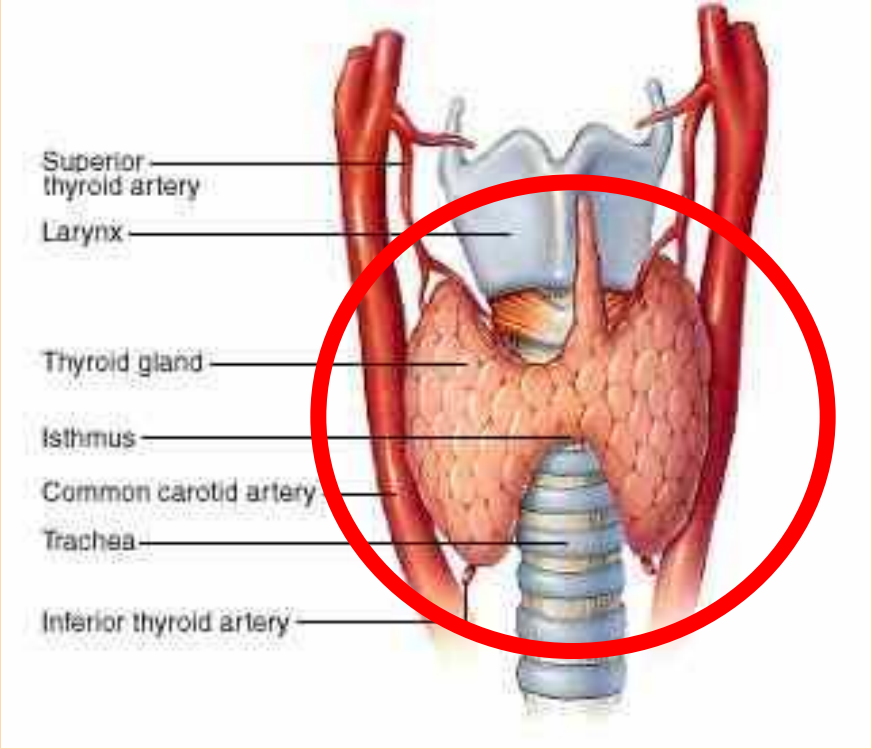
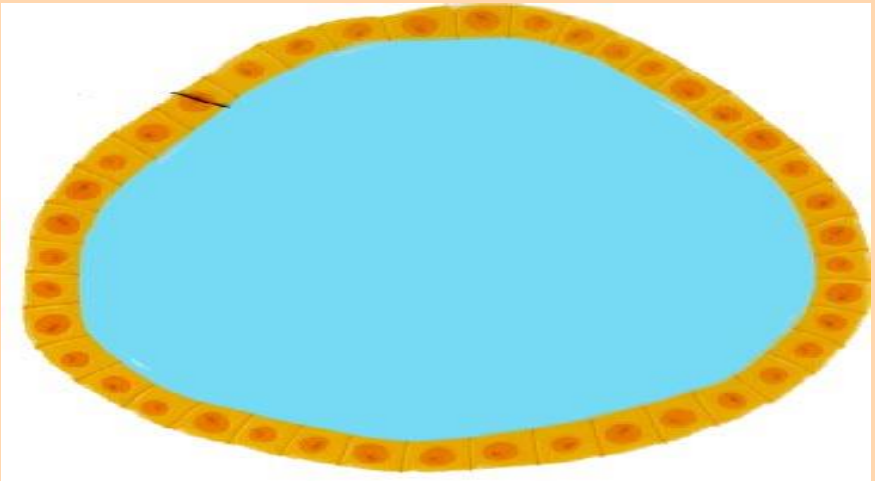
Minisymposium, CEK, 4. nov 2016

Thyroid, Anatomy





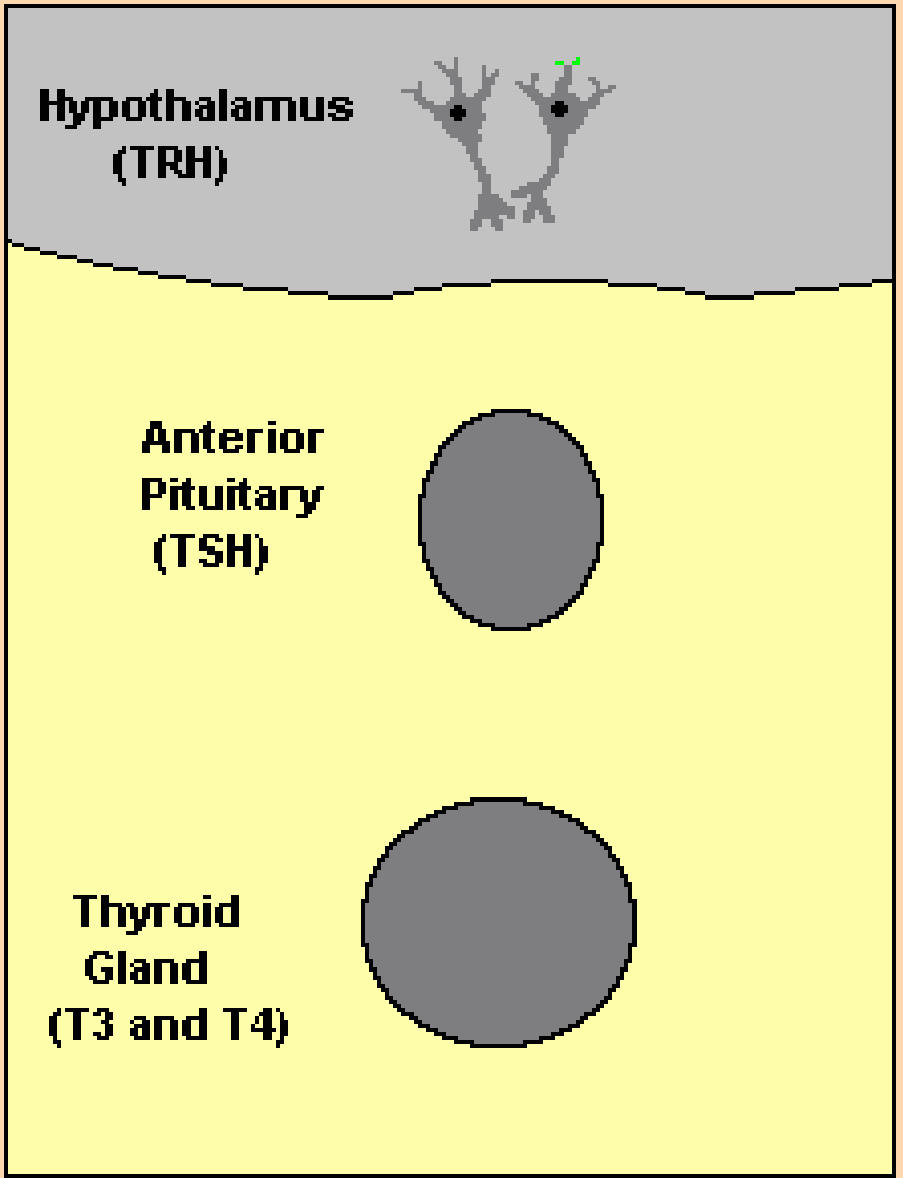
Incidence of endocrine disease
new cases per million / year (DK)

• Diabetes mellitus, type 2	1500
• **Hyperthyroidism**	**460 ♀ + 80 ♂**
• **Hypothyroidism**	**200 ♀ + 40 ♂**
• Diabetes mellitus, type 1	150
• Hyperparathyroidism	100
• Hypoparathyroidism	10
• Akromegali, Mb. Cushing	4
• Phaeochromocytomas,	< 4
• Mb Addison,	< 4
• Diabetes insipidus,	< 4
Vasopressinhypersekretion,	< 4
Panhypopituitarisme	< 4

Normal thyroid function

- Hypothalamus producerer Thyrotropin Releasing Hormone (TRH)
- Hypofyseforlappen Thyrotropin (TSH)
- Thyroidea

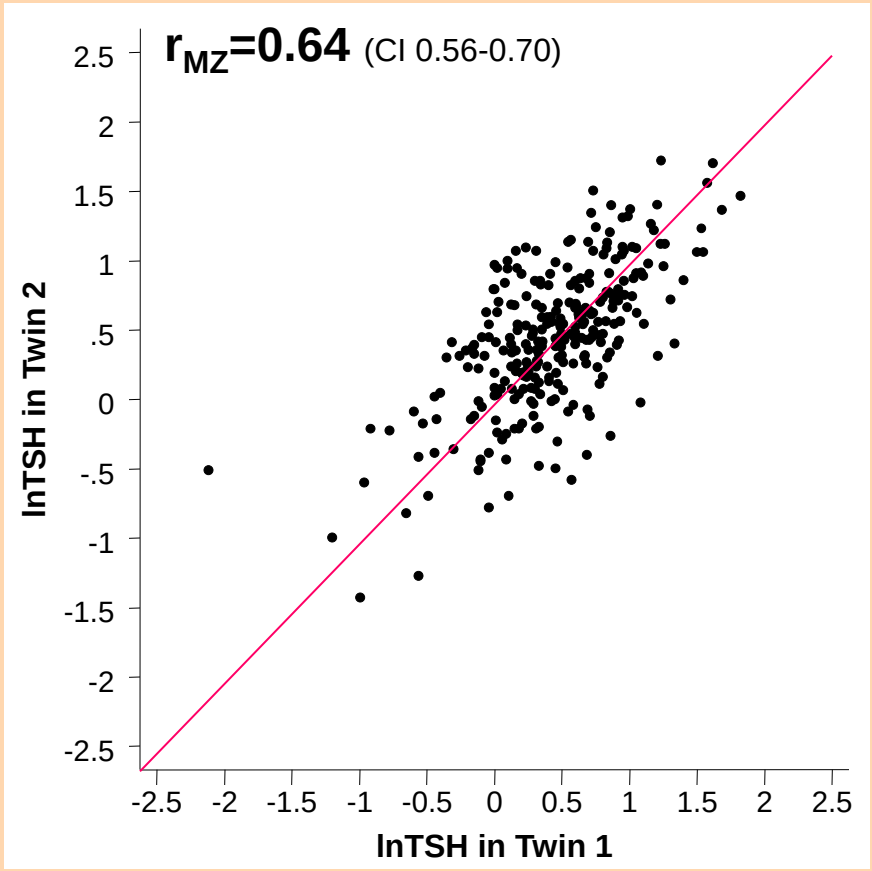
  T3 and T4 hormones



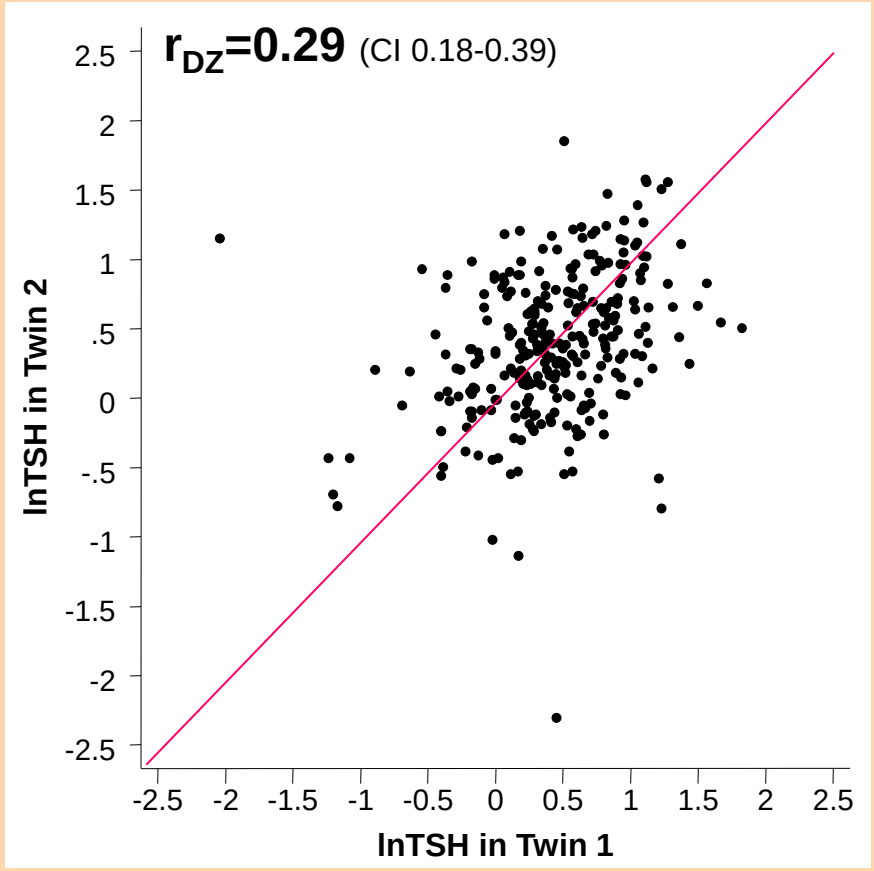
Tight genetic regulation of thyroid function (TSH)

ln TSH

MZ
n=284 pairs



DZ
n=285 pairs



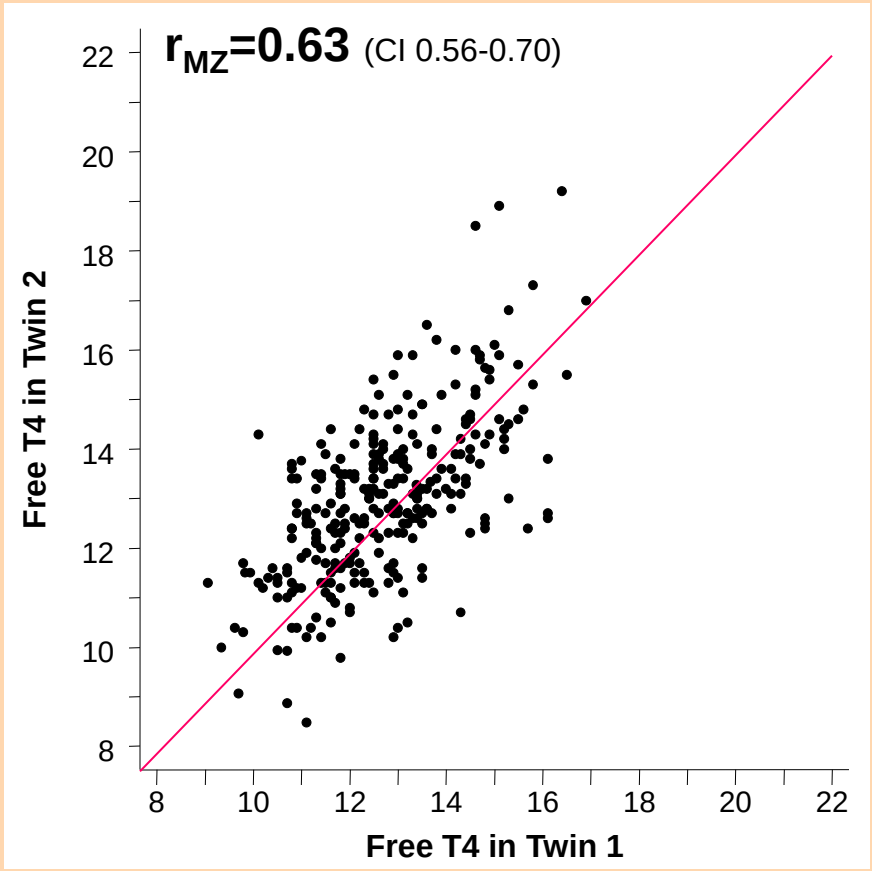
p-value<0.00005

Hansen PS et al. JCEM 2004

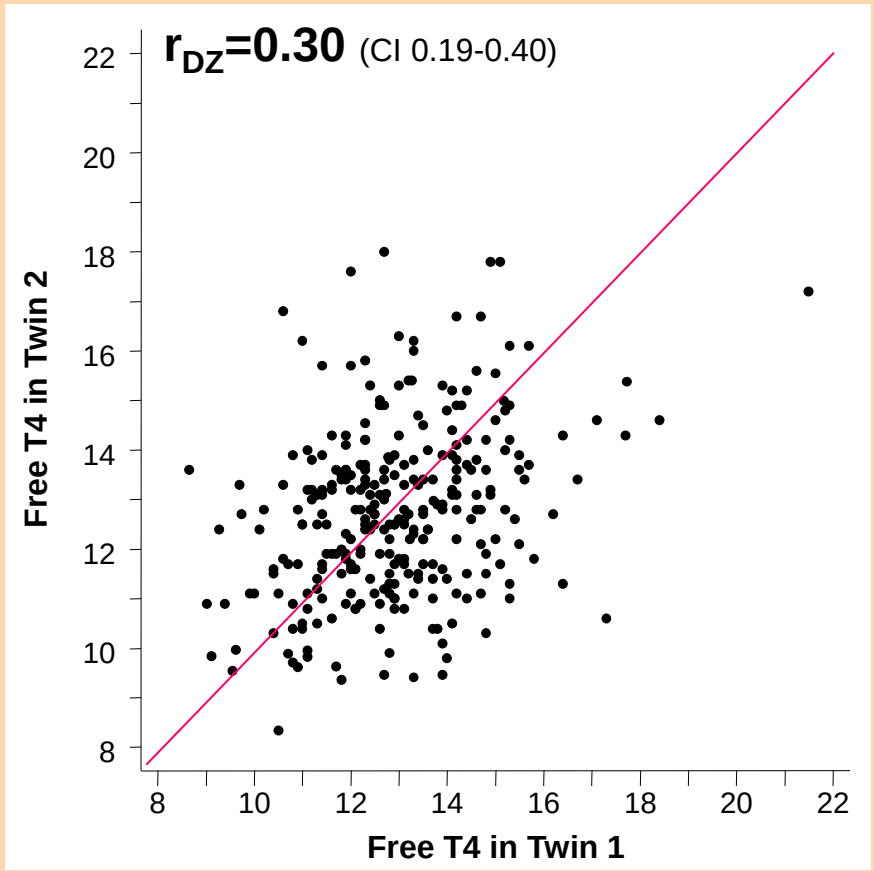
Tight genetic regulation of thyroid function (FreeT4)

Free T4

MZ
n=284 pairs



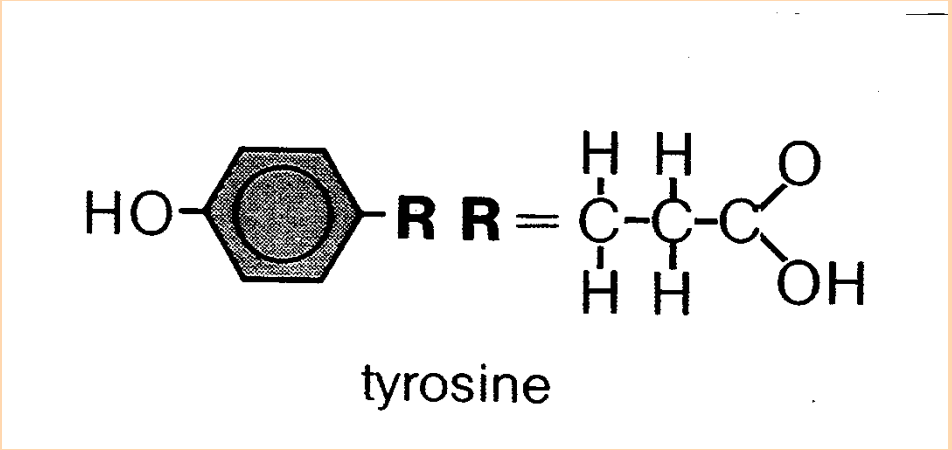
DZ
n=285 pairs



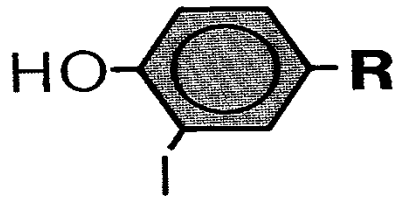
p-value<0.00005

Hansen PS et al. JCEM 2004

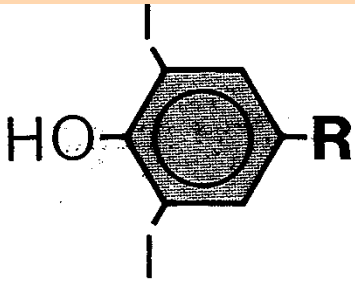
Thyronine's road to a hormone



tyrosine

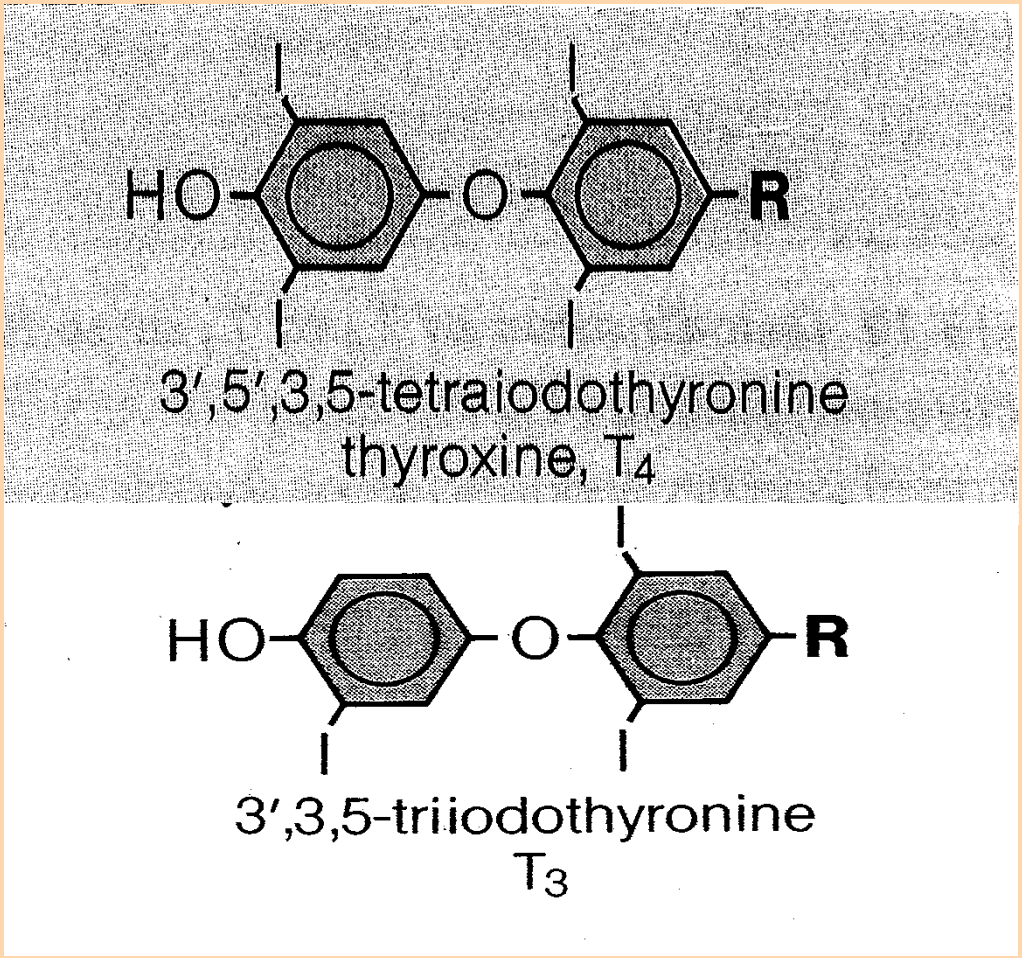


3-monoiodotyrosine
MIT



3,5-diiodotyrosine
DIT

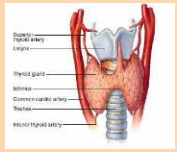
T4 and T3



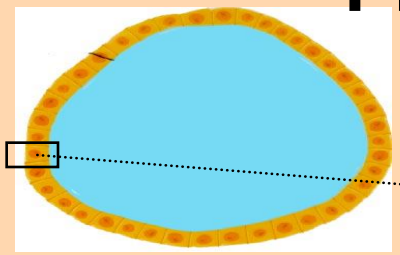
$T_{½}$~7 days

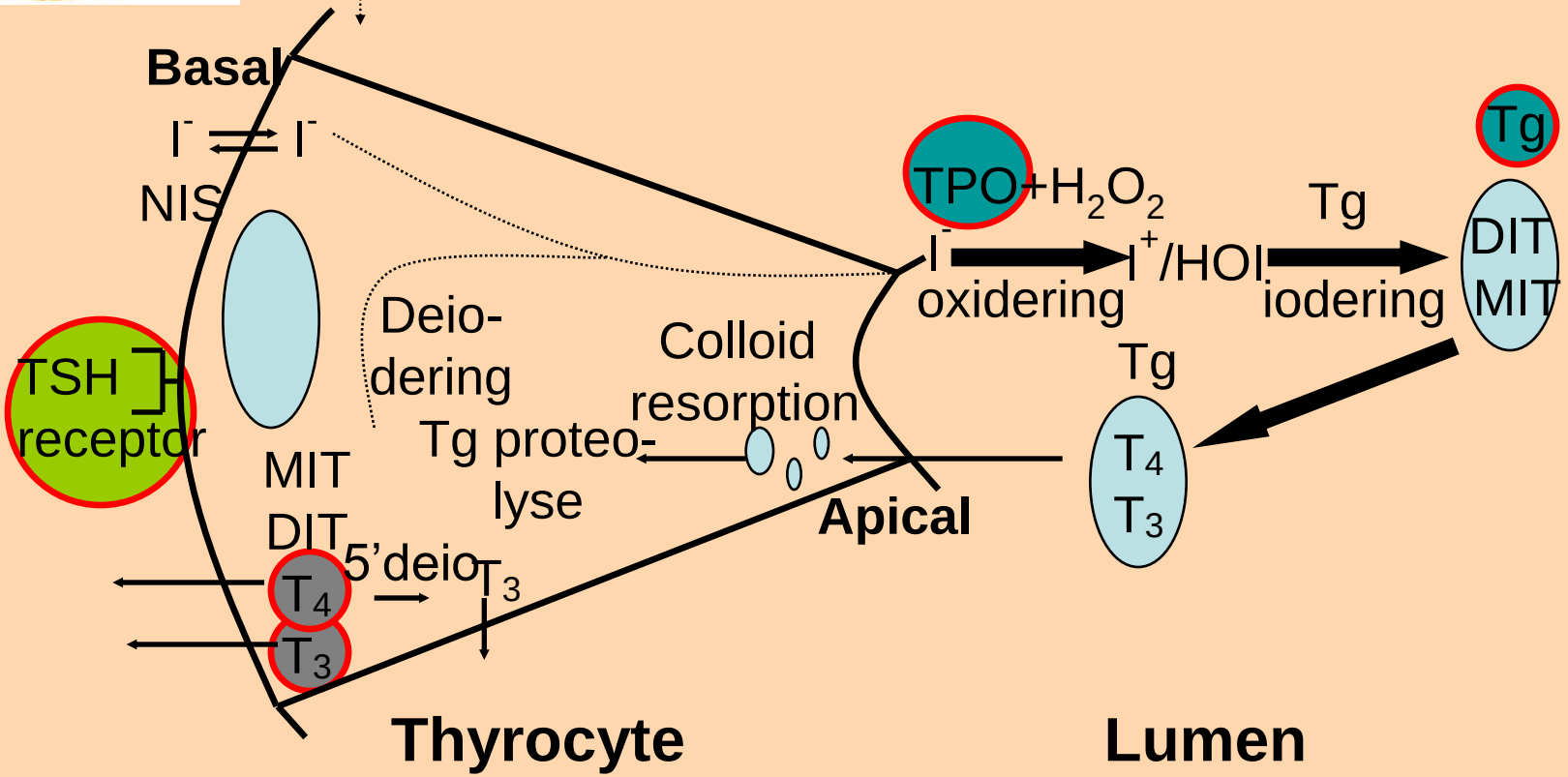
$T_{½}$~ 1 day

NB! Routine laboratory methods do not measure reverse T3

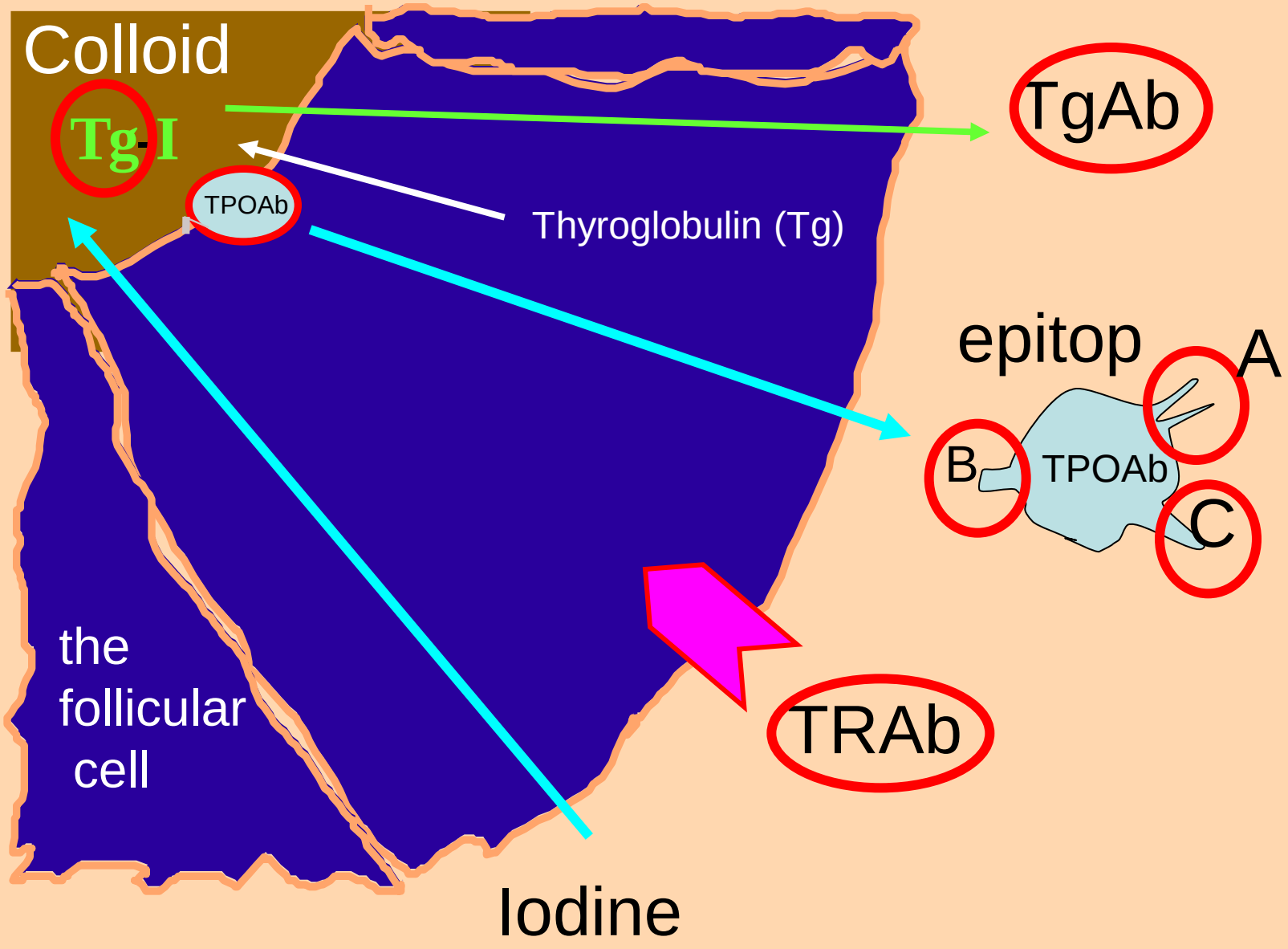


Thyroidea hormon syntese

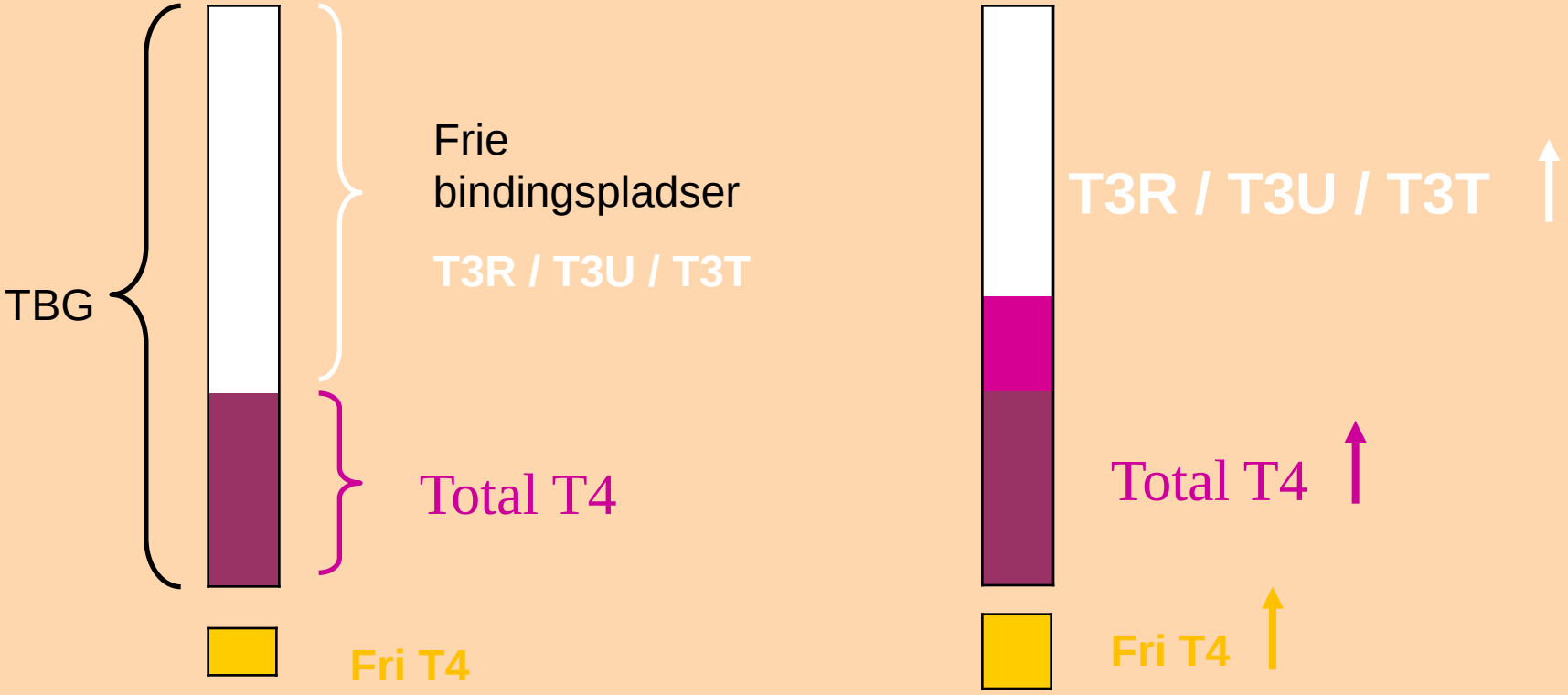




Thyroidea autoantistoffer



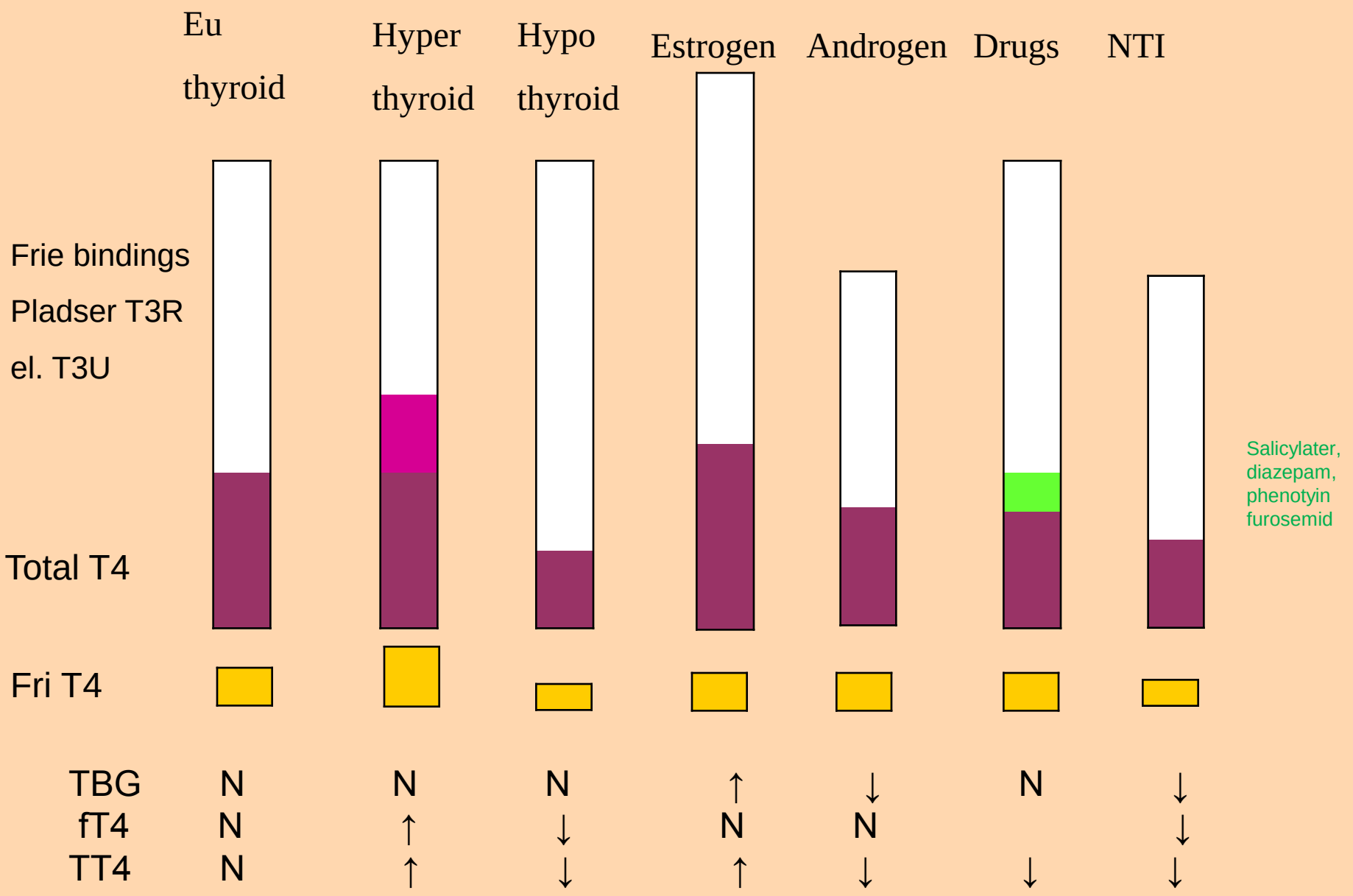
TBG, TT4, fT4, T3R



Euthyroid

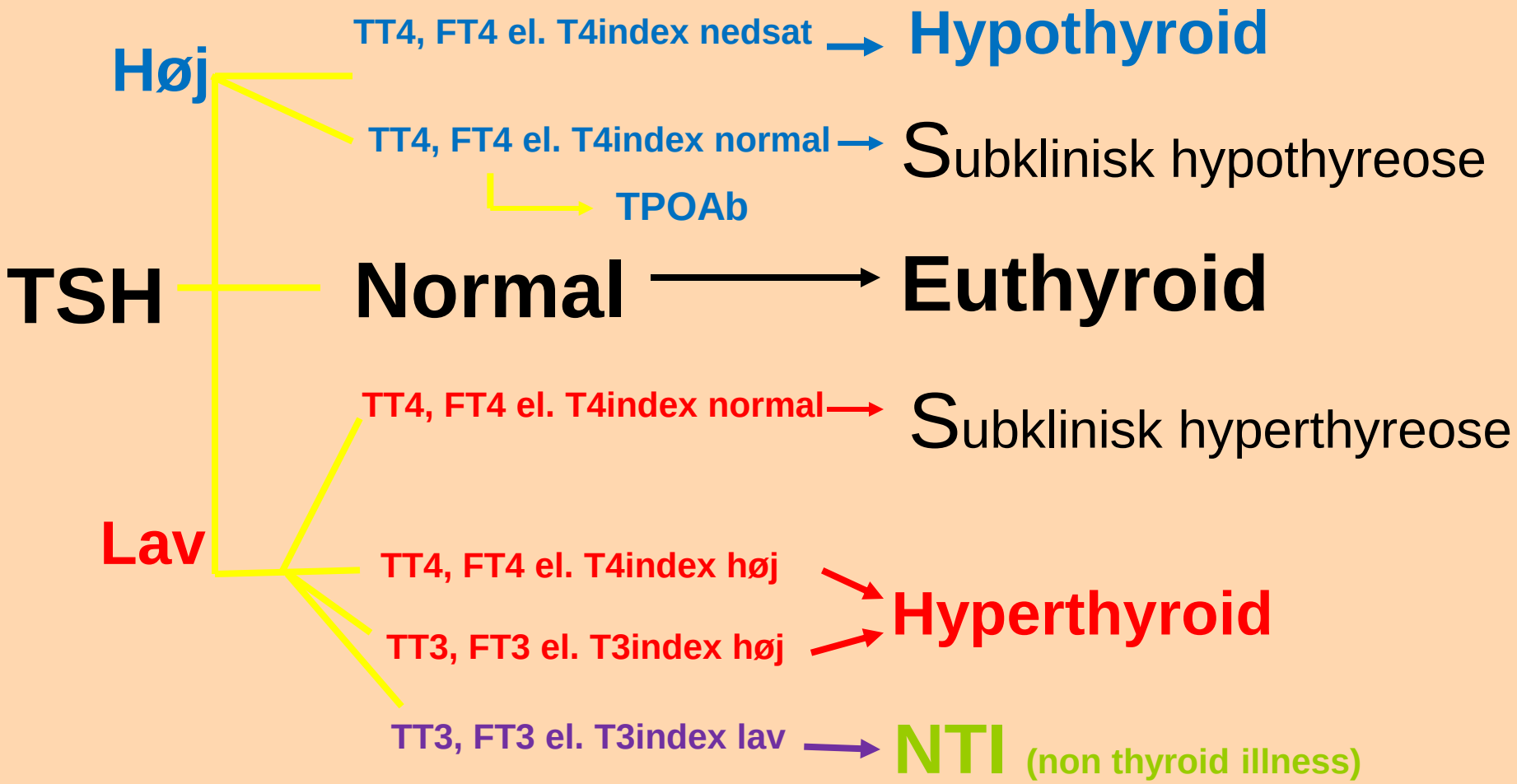
Hyperthyroid

TBG, TT4, fT4, T3R

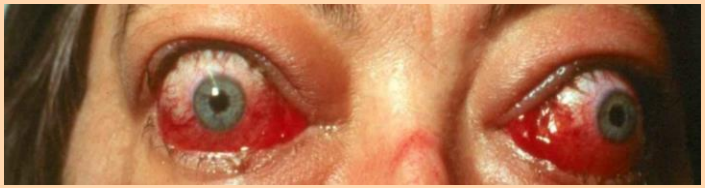


Biokemisk thyroidea diagnostik

algoritme RegionHovedstaden



45 year old woman seen in General Practice

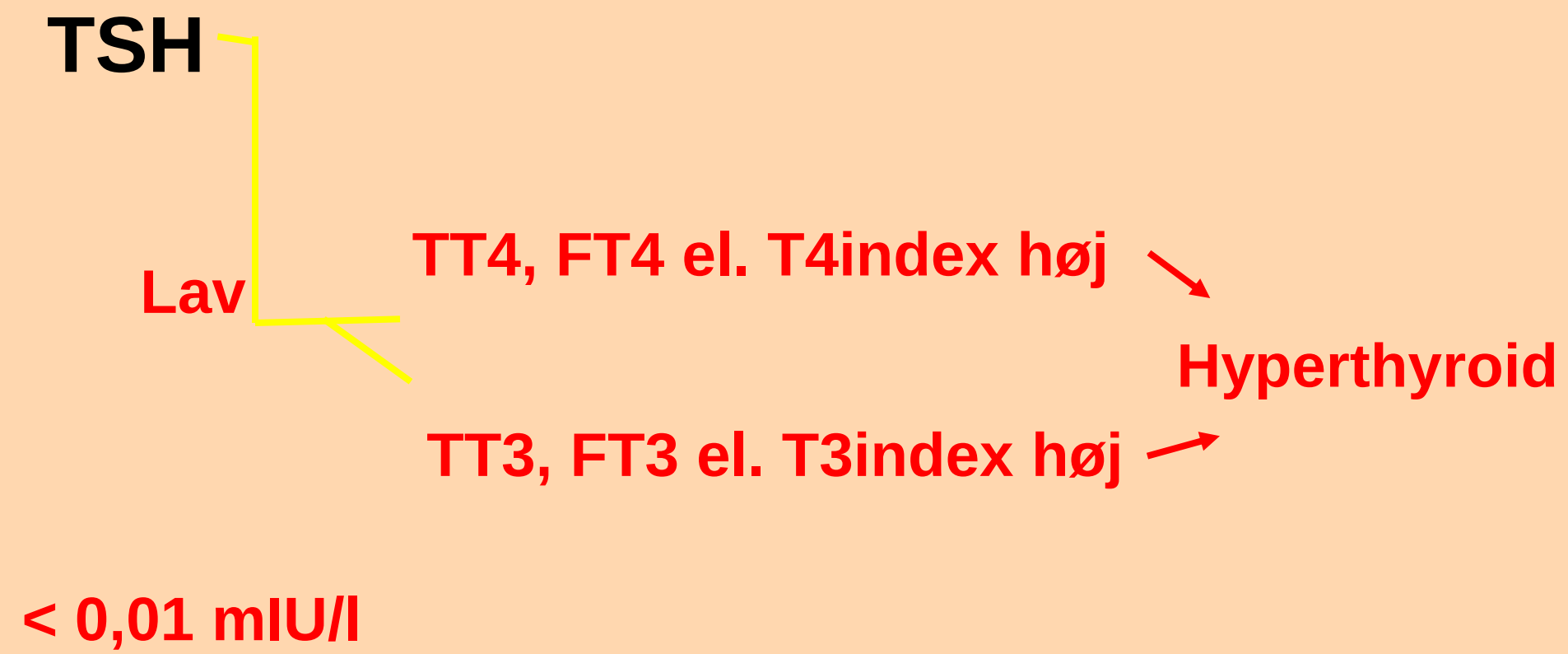


- Tired
- No medication except estrogen
- Nervous, irritable
- Concentration problems
- Weight loss 5 kg in 3 months
- Sinus tachcardia (120 hbm)
- Sweating
- Considerable eye symptoms

Is thyroid function testing recommended?

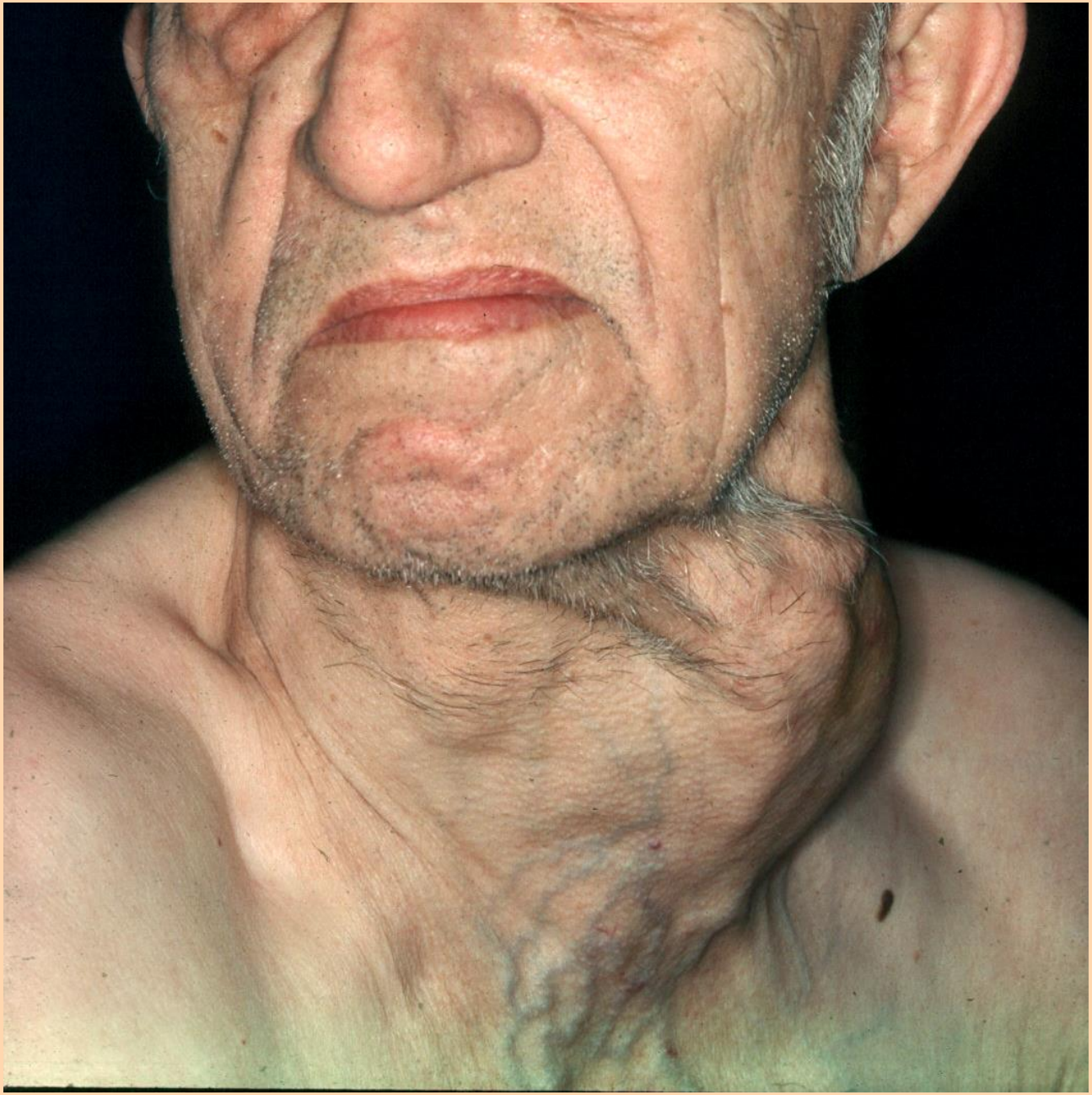
Biokemisk thyroidea diagnostik

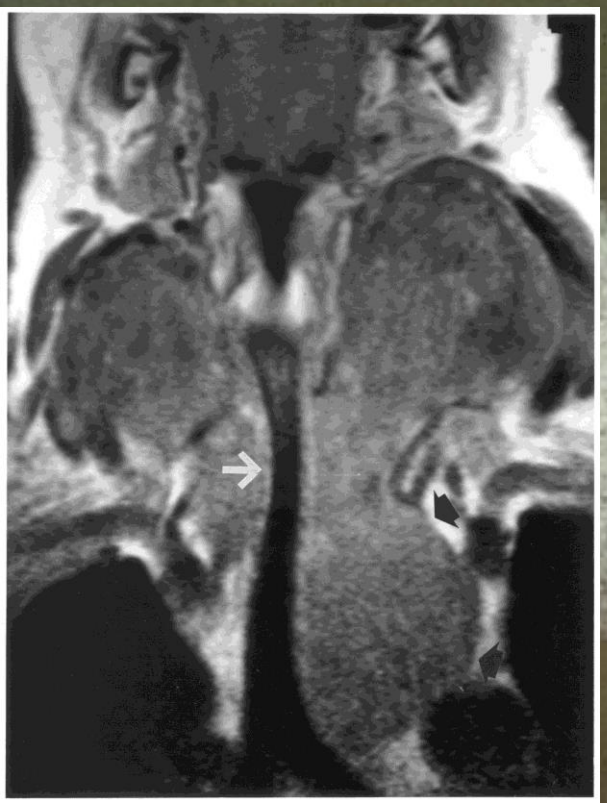
algoritme RegionHovedstaden

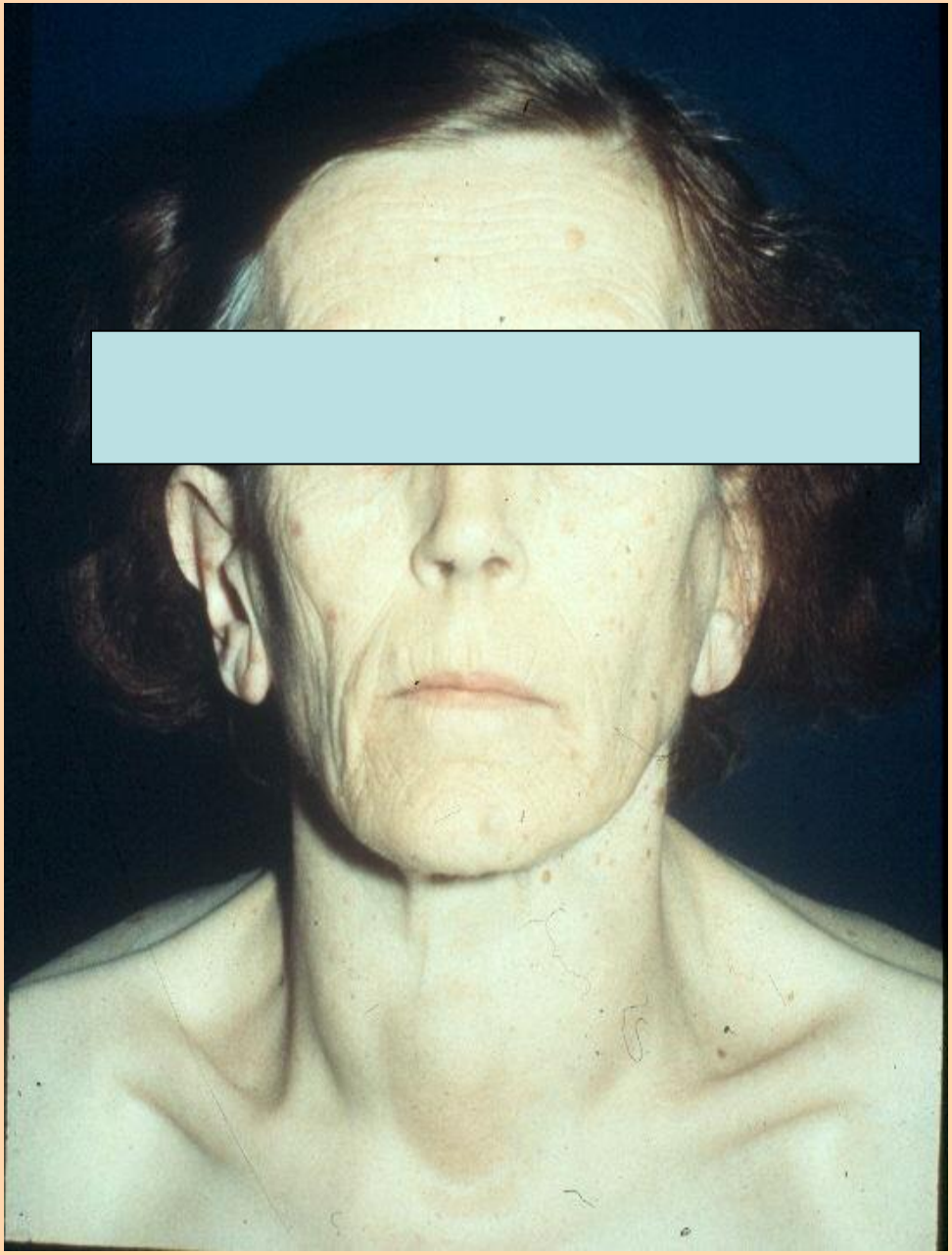


Scintigraphic investigation diffuse toxic

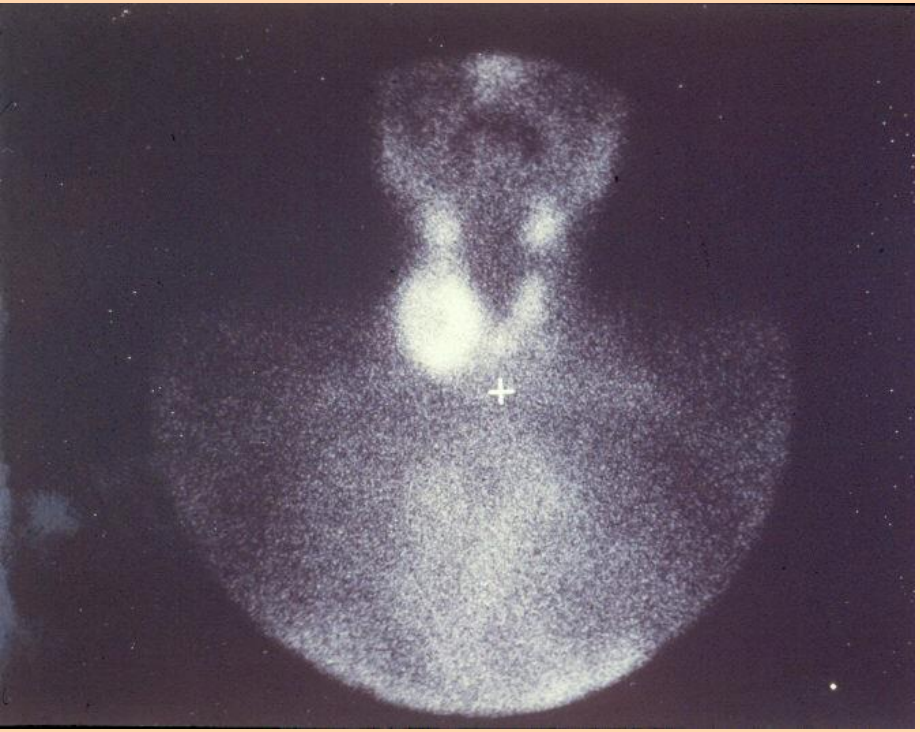
Odense University Hospital, Denmark





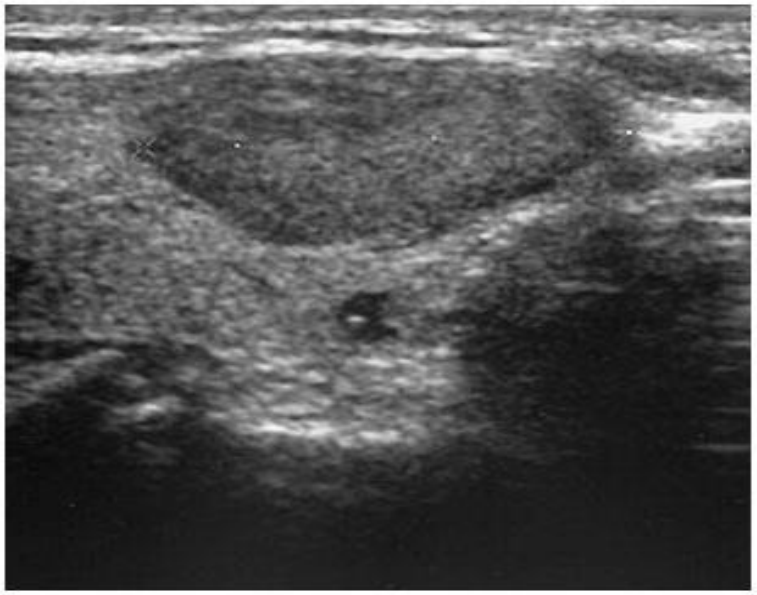


Adenom scientigrafi



OUH

Knude i højre thyreoidealap Ultralyd



Åse Krogh, RH

Hypertyreose

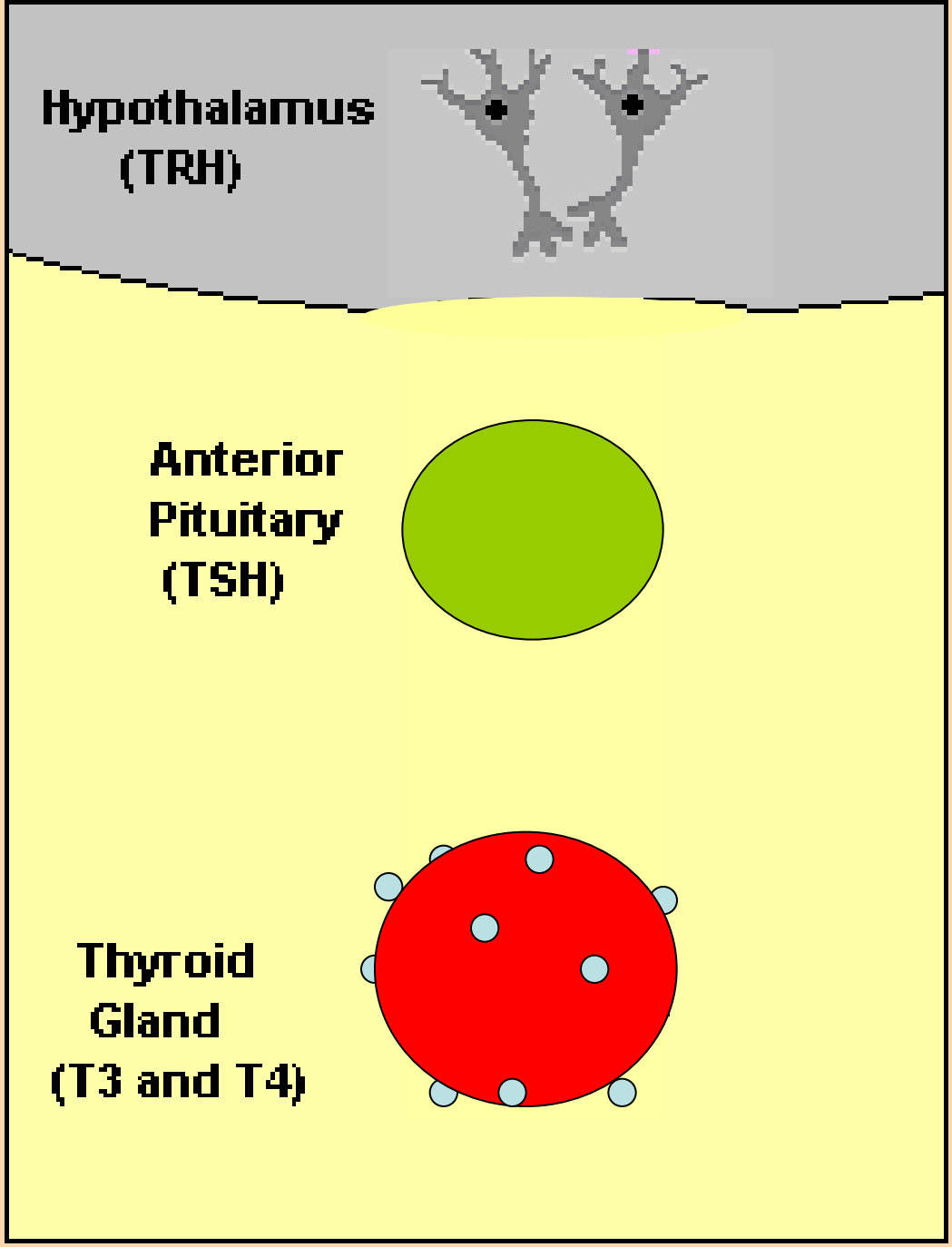
- 40% Diffus toksisk struma (Graves sygdom)
- 45% Multinodøs toksisk struma
- 10 % Toksisk adenom
- Thyreoiditis

Husk, etiologien til thyrotoxicose kan være øget sekretion, destruktion af kirtel eller indtagelse af thyroideahormon (Thyrotoxicosis factitia)

Hypertyreose, ætiologi

- Diffus toksisk struma autoimmun
- Multinodøs toksisk struma ukendt
- Toksisk adenom ukendt
- Thyreoiditis autoimmun

Thyreotropin
Receptor
Anti
body



What is TRAb?

Stimulating TRAb

Anvendelse af TRAb

Anbefalinger fra National Academy of Clinical Biochemistry (NACB):

1) Diagnostisk

- Graves' sygdom eller Multinodøs toksisk struma?
- Graves' sygdom eller subakut /post partum thyreoiditis
-*[Etiologi ved hypothyroidism]*

2) Monitorering af behandling ved Graves' sygdom

3) 'Screening' i graviditet

- TRAb passerer placenta. Kan forårsage fetal eller neonatal dysfunktion.

Kontrol hyperthyreose

web-req RegionHovedstaden

AHH	**TSH, FT4, FT3**
BBH/FB	**TSH, TT4, TT3**
Gentofte	**TSH, FT4, TT3**
Herlev	**TSH, TT4 eller FT4, TT3**
NOH	**TSH, T4indeks (TT4 x TUP)**
	T3indeks (TT3 x TUP)

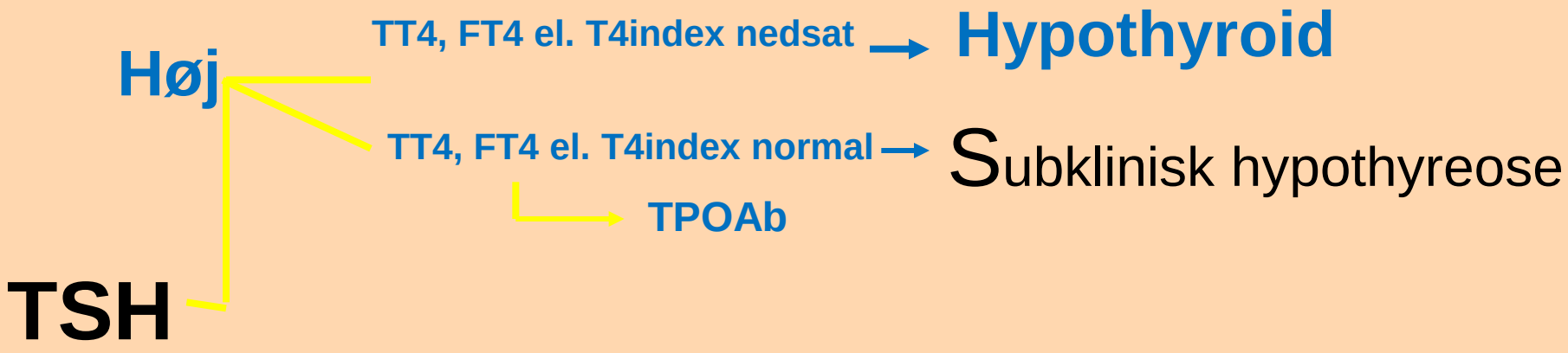
70 year old woman seen in General Practice

- Tired
- Trouble concentrating
- Cold intolerance
- Thin hair
- Dry skin
- Weight increase
- Constipation
- Loss of appetite
- Sinus bradycardia

Is a serum TSH determination warranted?

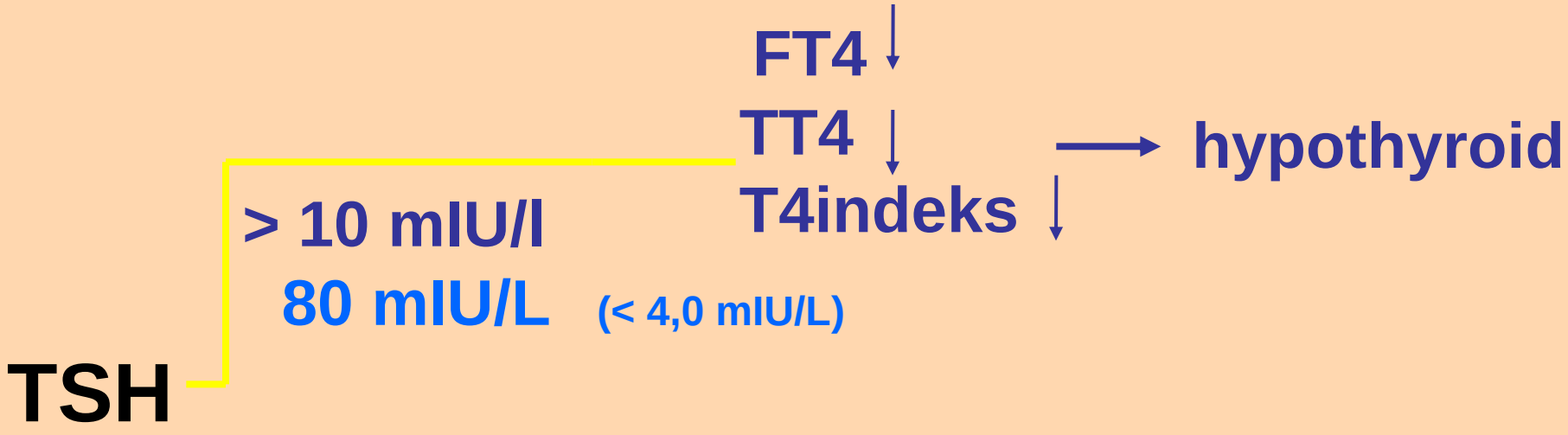
Biokemisk thyroidea diagnostik

RegionHovedstaden



Biokemisk thyroidea diagnostik

RegionHovedstaden



FT4: 5 pmol/L (10-22 pmol/L)

TT4: 35 nmol/L (67-134 nmol/L)

T3R: 0,30 (0,58-1,44)

Er behandling indiceret?

JA

Woman to GP:

- **Tired**
- **Trouble concentrating**
- **Cold intolerance**
- **Thin hair**
- **Dry skin**
- **Weight increase**
- **Constipation**
- **Loss of appetite**
- **Sinus bradycardia**

Biokemisk thyroidea diagnostik

RegionHovedstaden

TSH

> 10 mIU/l

6,5 mIU/L **(< 4,0 mIU/L)**

FT4
TT4
T4indeks

→ **Subklinisk hypothyreose**

FT4: 12 pmol/L (10-22 pmol/L)

TT4: 80 nmol/L (67-134 nmol/L)

T3R: 0,70 (0,58-1,44)

Er behandling indiceret? **?**

Sampling time

Van Coevorden, 1989,

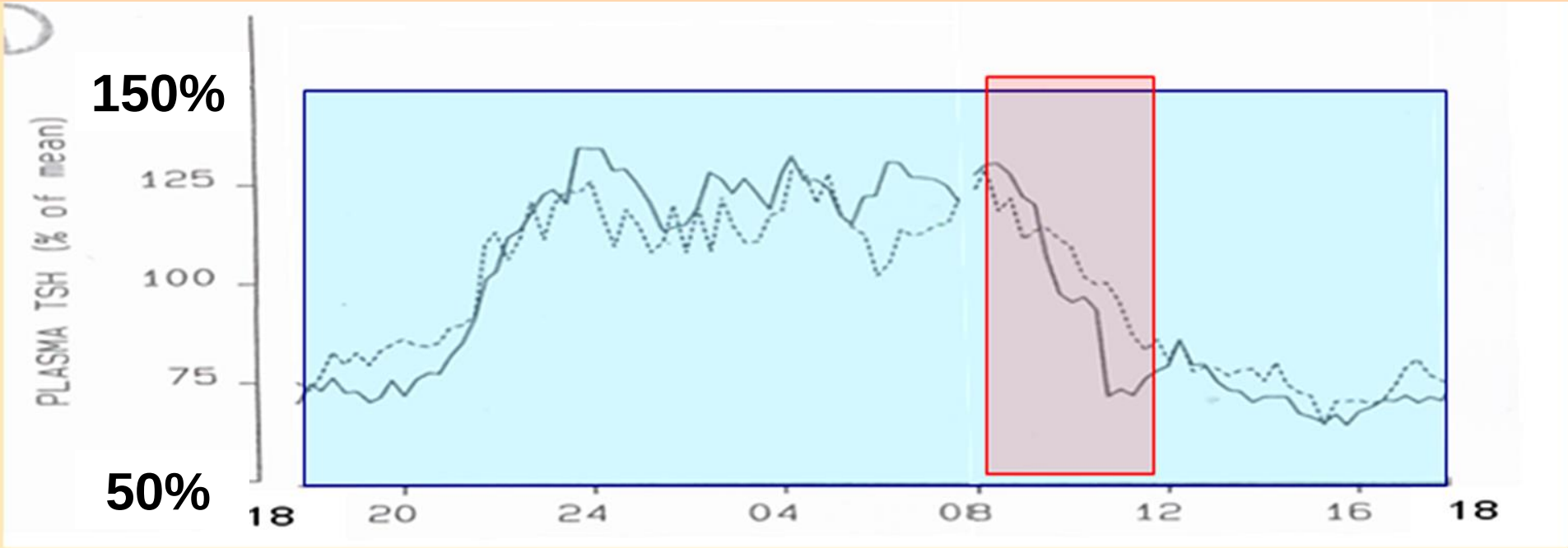
RIA, TSH detection limit 0,15 mU/L

8 M (20-27 years), 3 nights in sleep laboratory before test (——)

8 M (67-84 years), 5 nights in sleep laboratory before test (. . . .)

Polygrafical sleep registration

Blood Sampling every 15 minutes in room next door



Weeke, 1978,

RIA, TSH detection limit 0,20 mU/L
5 M (22-34 years),
In bed 23.00-06.30, no sleep registration
Blood Sampling every 30 minutes

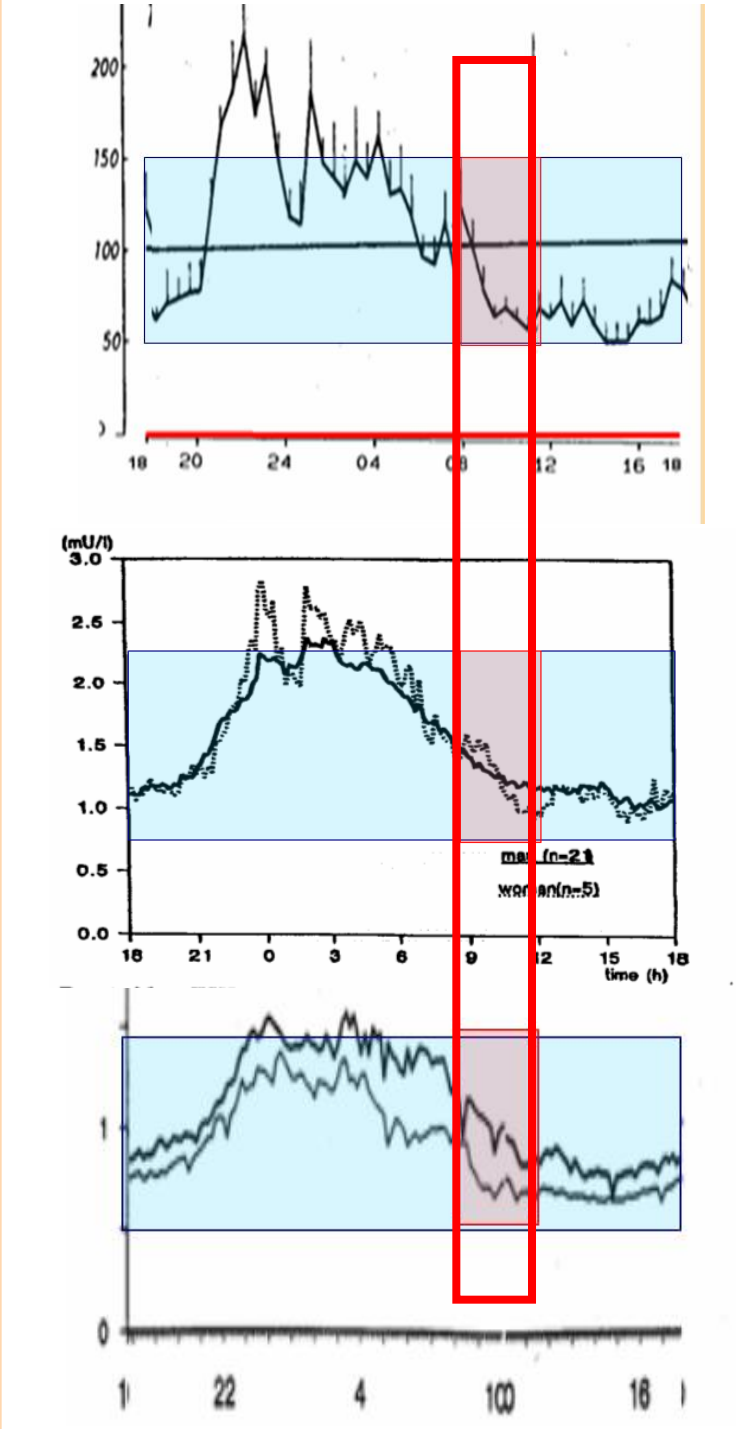
Brabant, 1990

Henning IRMA, TSH detection limit ? mU/L
21 M (———)
5 F (.....)
Staying in bed 24 hours
Sleep allowed 23.00-07.00. No sleep registration
Blood Sampling every 10 minutes

Weber, 1991

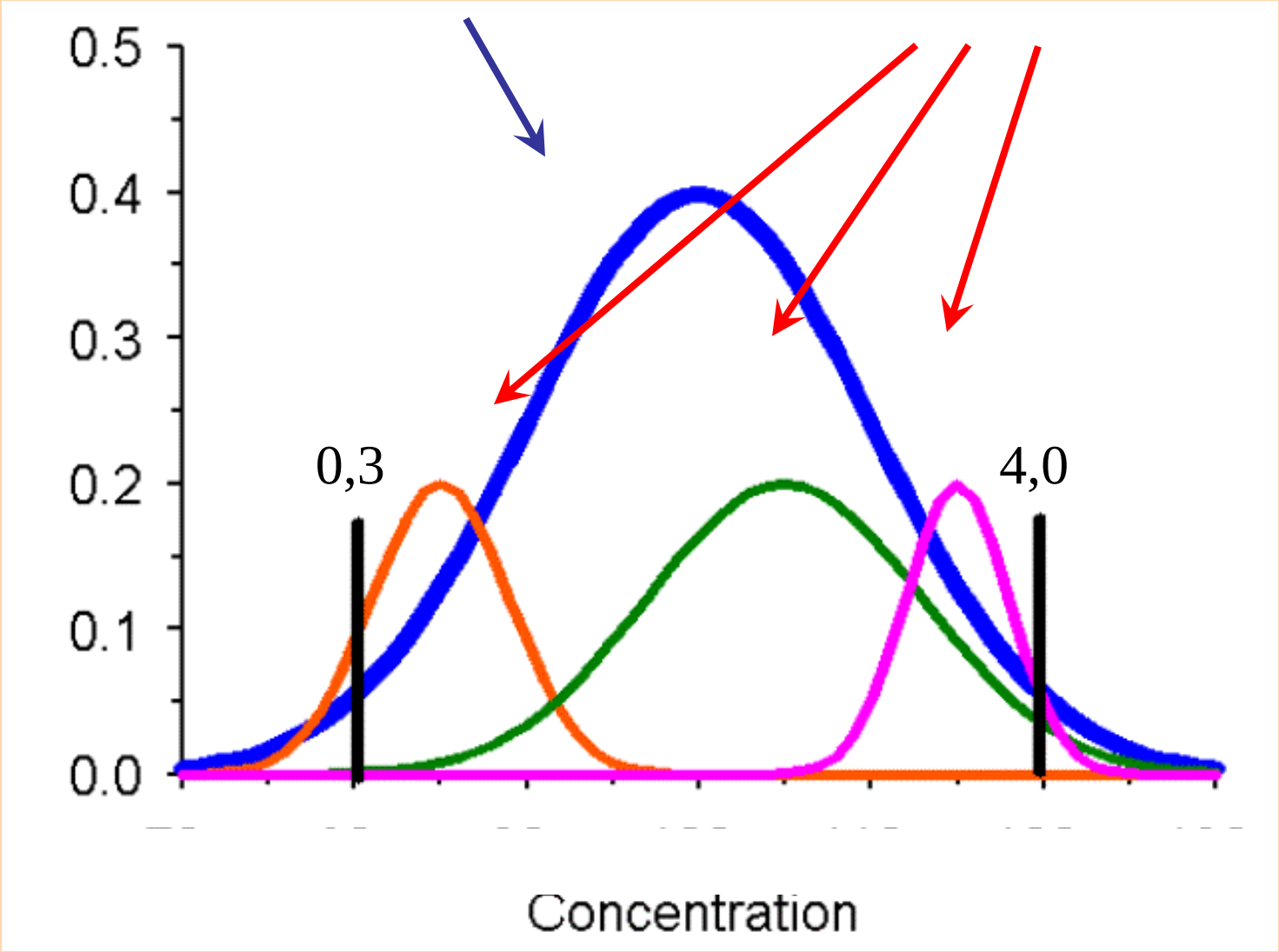
Henning IRMA, TSH detection limit ? mU/L

6 M + 5 F control (———)
11 non-toxic goitre (------)
No sleep registration
Blood Sampling every 10 minutes

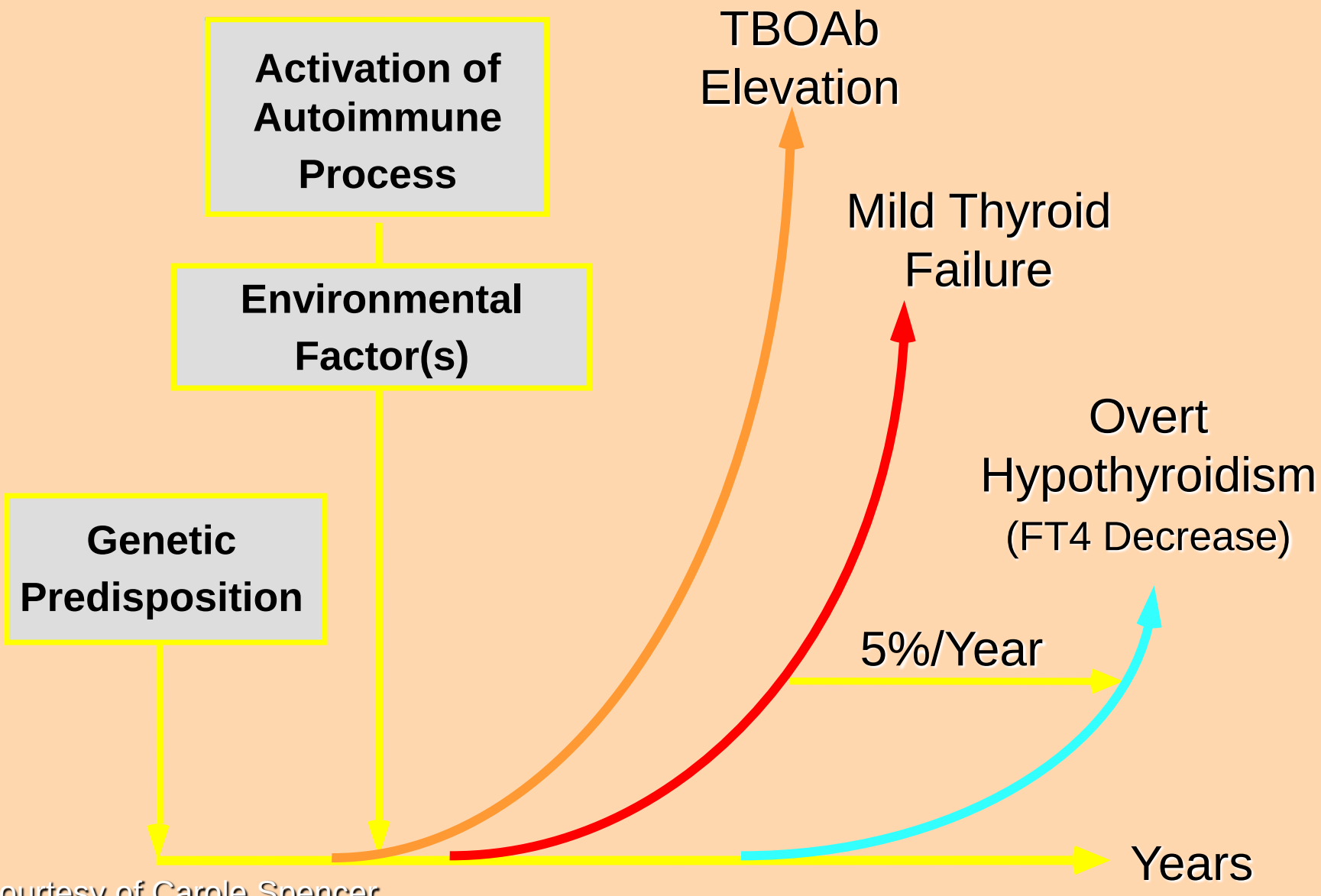


TSH and biological variation

Population **Within-subject**



Developing Autoimmune Thyroid Dysfunction



Courtesy of Carole Spencer.

Behandling?

TSH → **4-10 mIU/L** → **FT4**, **TT4**, **T4indeks** → **Subklinisk hypothyreose**

Thyroidea PerOxidase Antibody (TPOAb)	**nej**
eller	
Thyroglobulin Antibody (TgAb)	**nej**

Er behandling indiceret?

Nej

Behandling?

TSH

4-10 mIU/L

FT4
TT4
T4indeks

→ **Subklinisk hypothyreose**

Thyroidea PerOxidase Antibody (TPOAb)	**ja**
eller	
Thyroglobulin Antibody (TgAb)	**ja**

Er behandling indiceret? **?**

Case # : 35 year old woman

History: Inability to become pregnant. Clinically euthyroid. No medication

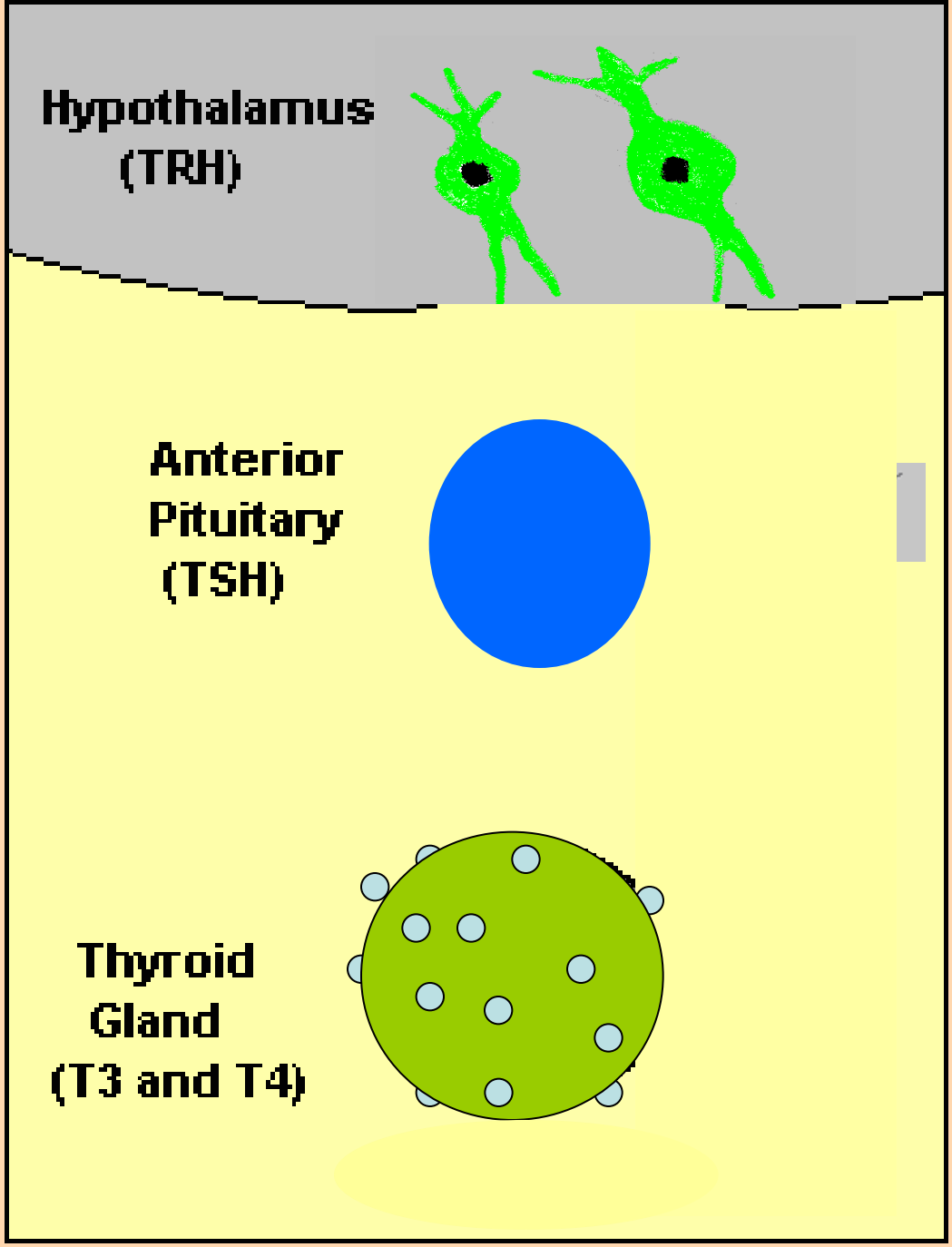
Thyroid peroxidase antibodies (TPOAb)	230	(<10 kIU/L)
Thyroglobulin antibodies (TgAb)	95	(<20 kIU/L)

All other thyroid parameters normal

Is this patient free of disease?

	Men		Women		in total
Age	< 40yr	≥ 40yr	< 40yr	≥ 40yr	
Healthy individuals	315	212	299	161	987
Only medication	19	27	27	17	90
Only Familiy history	18	24	39	24	105
Only one Thyroid antibody					
TPOab	20	13	24	19	76
Tgab	5	7	16	10	38
TRab	4	4	3	4	15
Two autoantibodies					
TPOab and Tgab	9	9	24	28	70
TRab and TPOab or Tgab	2	1	1	1	5
Three autoantibodies					
TRab and TPOab and Tgab	3	1	4	4	12
Two or more risk factors					
One antibody and family history	2	4	6	6	18
Two antibodies and family history	0	1	4	9	14
Three antibodies and family history	0	0	0	2	2
Analysis not complete	3	3	1	2	9
	400	306	448	287	1441
TPOAb	33/397	24/303	52/447	53/285	162/1432

Thyreotropin
Receptor
Anti
body



Hvad er TRAb?

Hæmmende TRAb

Kontrol hypothyreose

algoritme RegionHovedstaden

AHH	**TSH, FT4**
BBH/FB	**TSH, TT4**
Gentofte	**TSH, FT4**
Herlev	**TSH, TT4 eller FT4**
NOH	**TSH, T4 indeks (TT4 x TUP)**

Thyreoidea artikler

- Jensen E, Petersen PH, Blaabjerg o, Hansen PS, Brix th, Kyvik KO, Hegedüs L. Establishment of a serum TSH reference interval in healthy adults. The importance of environmental factors, including thyroid antibodies. Clin Chem Lab Med 2004; 42:824-832
- Petersen PH, Blaabjerg O, Andersen M, Jørgensen LGM, Schousboe K, Jensen E. Graphical Interpretation of Confidence Curves in Rankit Plots. Clin Chem Lab Med 2004; 42:715-724
- Jensen E, Petersen PH, Blaabjerg O, Hansen PS, Hegedüs L. Improved sensitivity of a **thyreotropin receptor antibody method**. Clin Chem. 2005;51, 2186-2187
- Jensen EA, Petersen PH, Blaabjerg O, Hansen PS, Brix TH, Hegedüs L. Establishment of reference distributions and decision values for thyroid antibodies against thyroid peroxidase (TPOAb), thyroglobulin (TgAb) and the **thyrotropin receptor (TRAb).** *Clin Chem Lab Med 2006; 44:991-998*
- Jensen E, Blaabjerg O, Petersen PH, Hegedüs L. Sampling time is important but may be overlooked in establishment and use of thyroid-stimulating hormone reference intervals.Clin Chem. 2007;53, 355-356
- Jensen E, Petersen PH, Blaabjerg O, Hegedüs L. Biological variation of thyroid autoantibodies and thyroglobulin. Clin Chem.Lab Med 2007; 45: 1058-1064
- Hyltoft Petersen P, Jensen EA, Brandslund I. Analytical performance, reference values and decision limits. A need to differentiate between reference intervals and decision limits and to define analytical quality specifications CCLM 2012:50;(5)819-31.