Autoimmune Schilddrüsenerkrankungen

17.4.2018 in Bochum

Prof. Dr. med. B. L. Herrmann
Endokrinologie /// Diabetologie /// Innere Medizin
Facharztpraxis und Labor
Springorumallee 2 – 44795 Bochum

www.endo-bochum.de

2014-2018 Guidelines of the European Thyroid Association ETA of Thyroid Diseases

2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease

W, 51 Jahre, müde, abgeschlagen antriebslos

TSH 2,65 mU/l [0.3 – 4.0]

TPO-Ak zweifach erhöht

TG-Ak normal

normaler Stuhlgang

keine Hashimoto in der Fam.-Anamnese

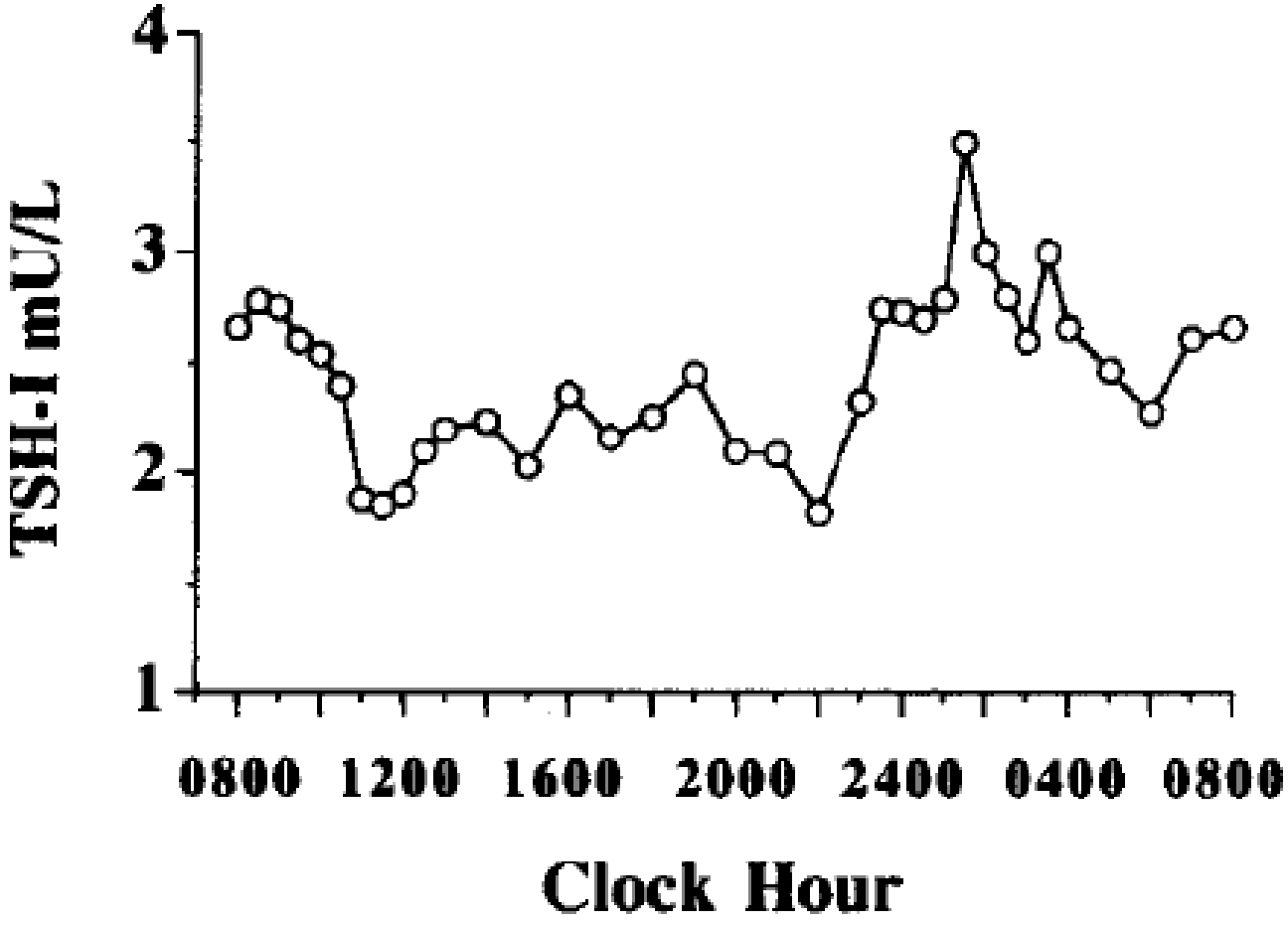
keine Herzrhythmusstörungen

Menopause seit 1 Jahren

Sonographie SD unauffällig

TSH im Verlauf 1,3 mU/l

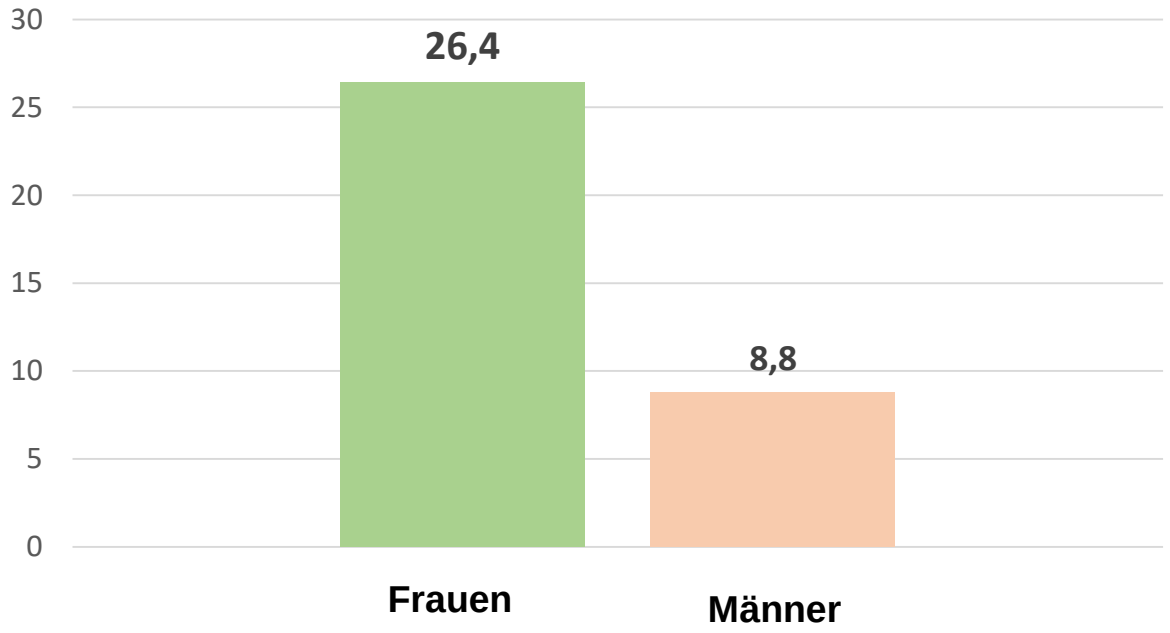
Circadian Variations of Thyrotropin (TSH) Bioactivity in Normal Subjects



Persani L et al.,J Clin Endocrinol Metub 80: 2722-2728, 1995

Prävalenz der SD-Autoantikörper [%]

Whickham Survey: 2 779 Personen untersucht und über 20 Jahre nachverfolgt



2% **0,5%**

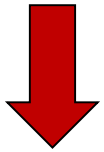
nicht mehr nachweisbar

Clin Endocrinol (Oxf). 2013 Mar;78(3):478

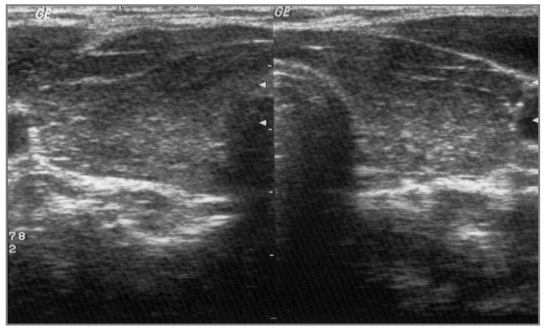
Hypothyreose – (Neigung)

TSH [mU/l]

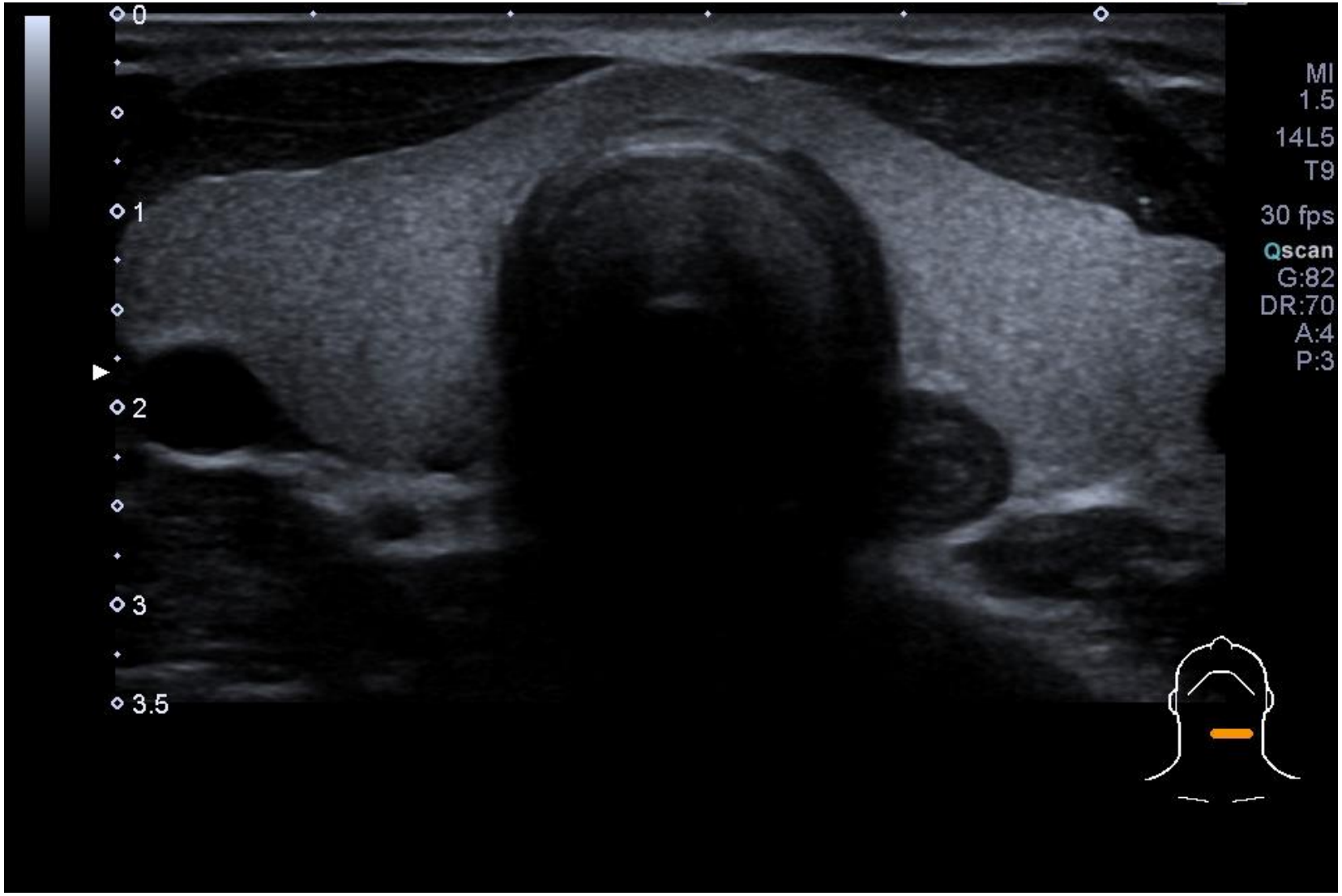
0,3 **4,0** **<10**



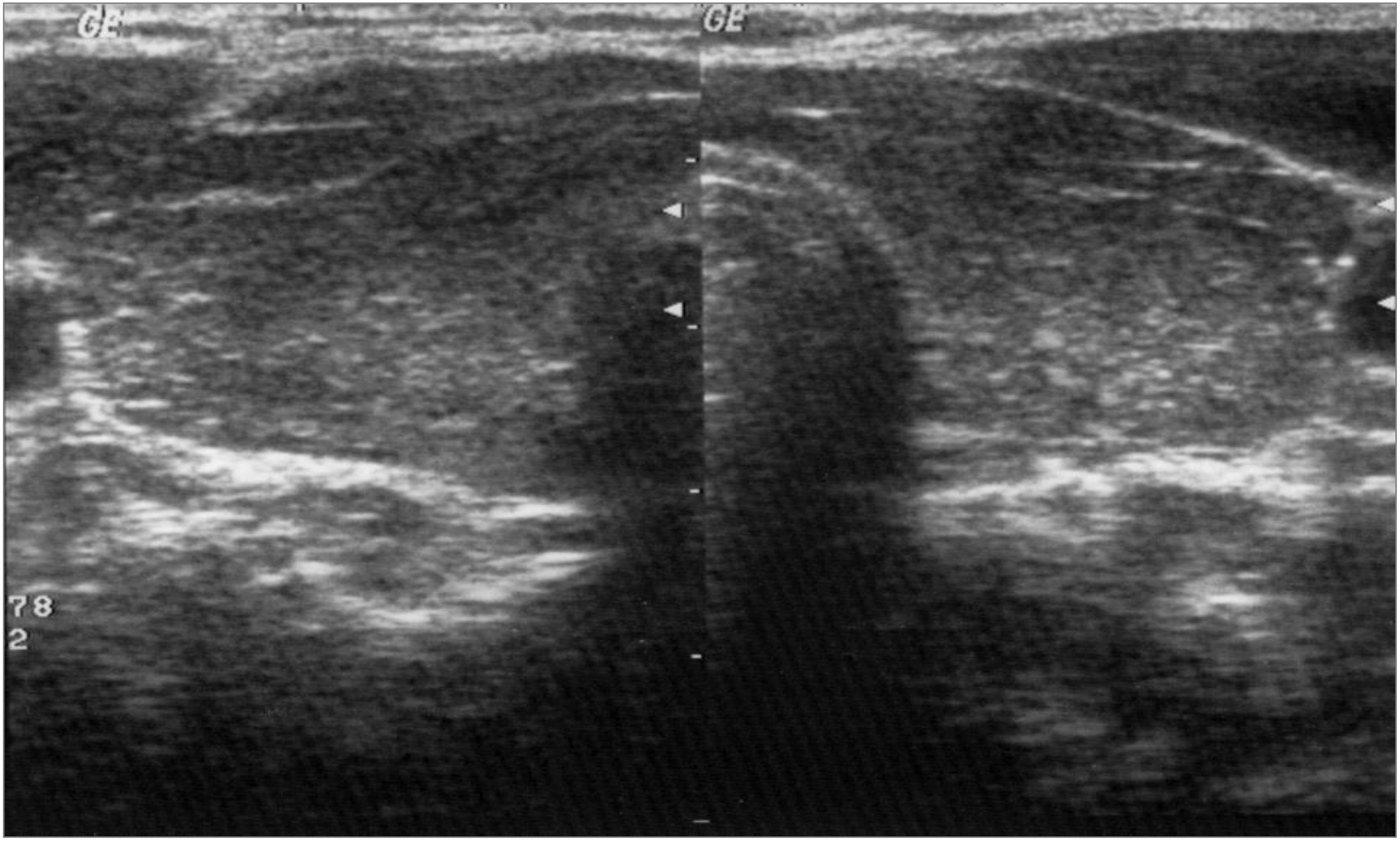
Symptome **Höhe der SD-Ak**



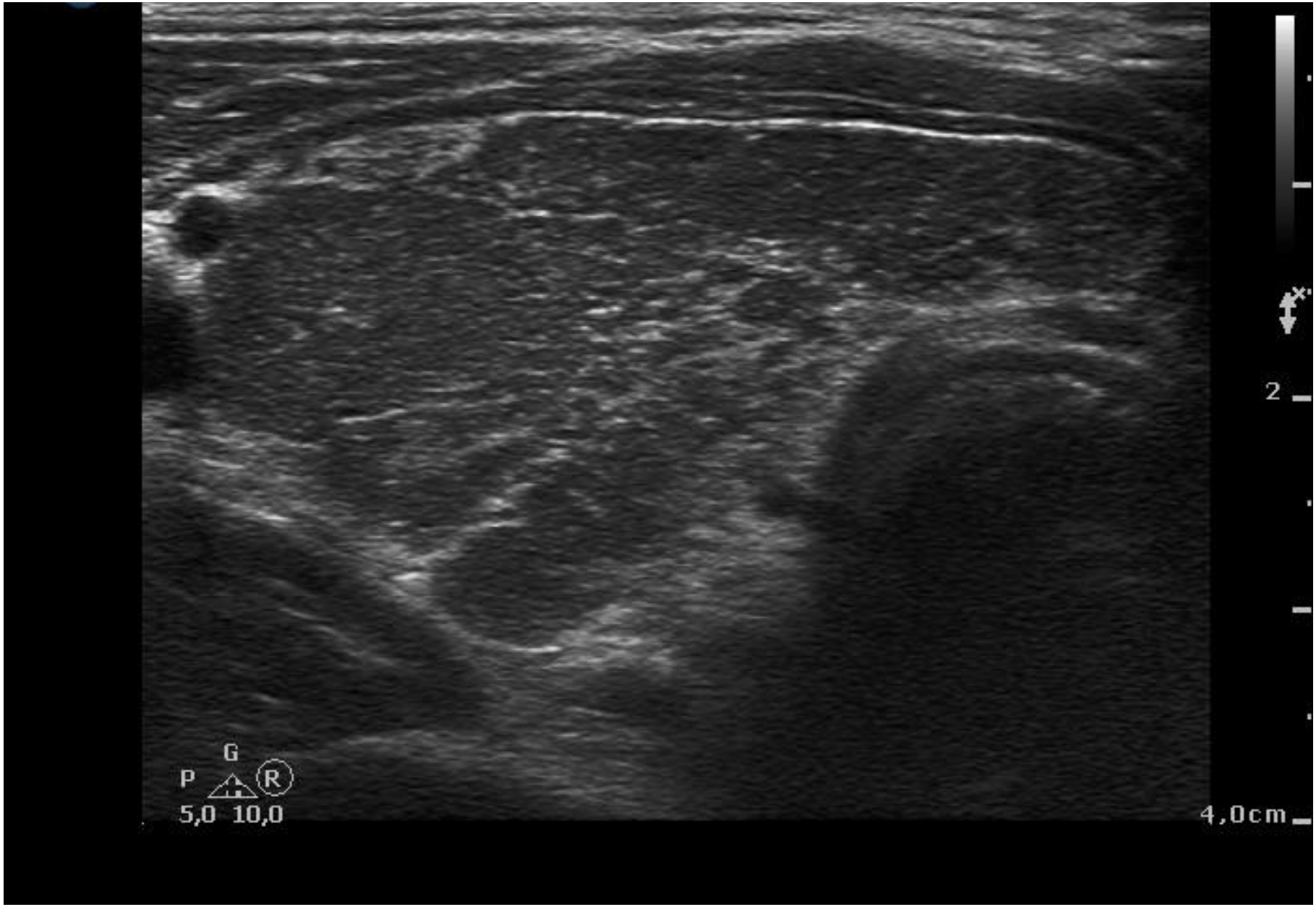
Normalbefund Schilddrüse



Autoimmunthyreoiditis

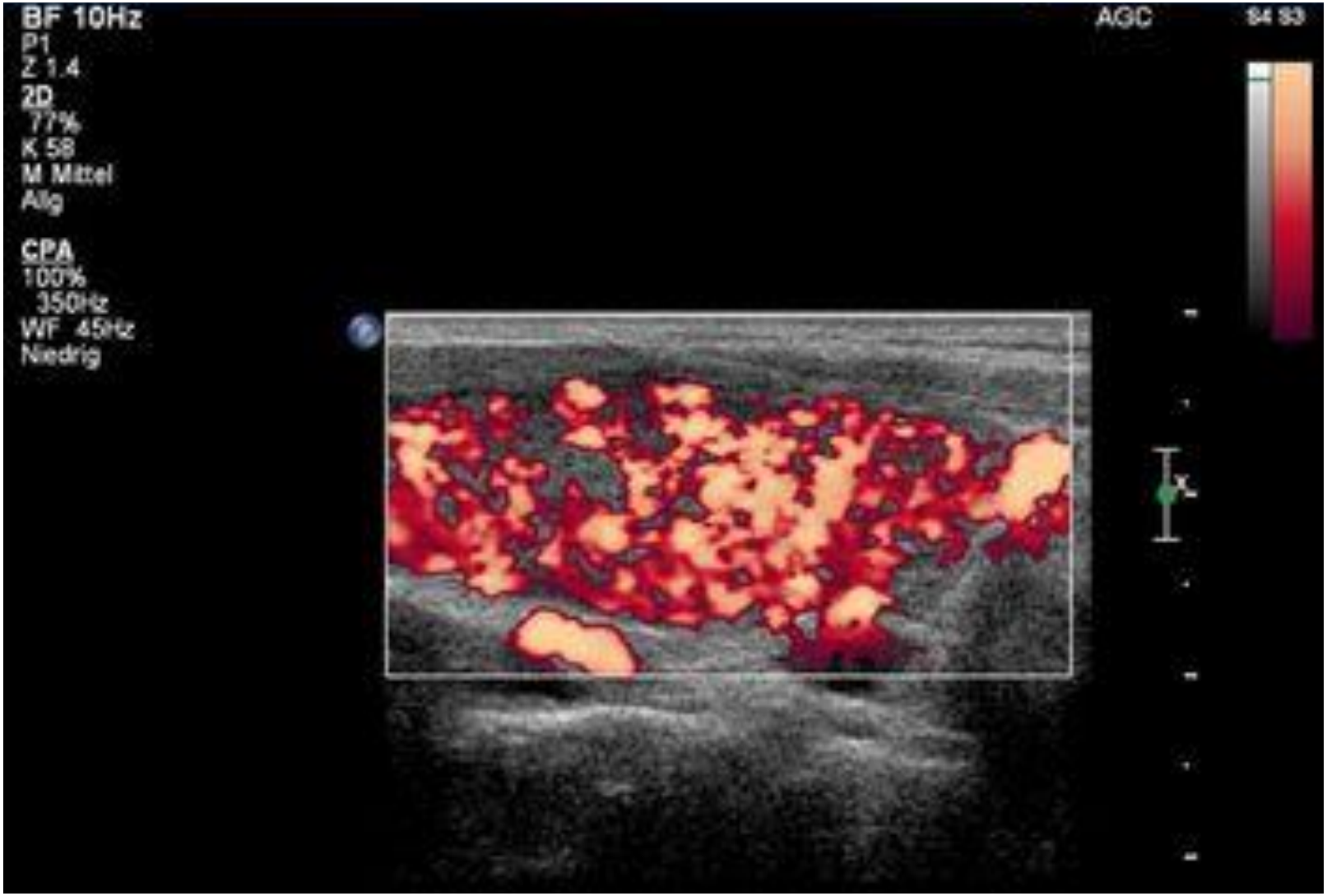


Morbus Basedow

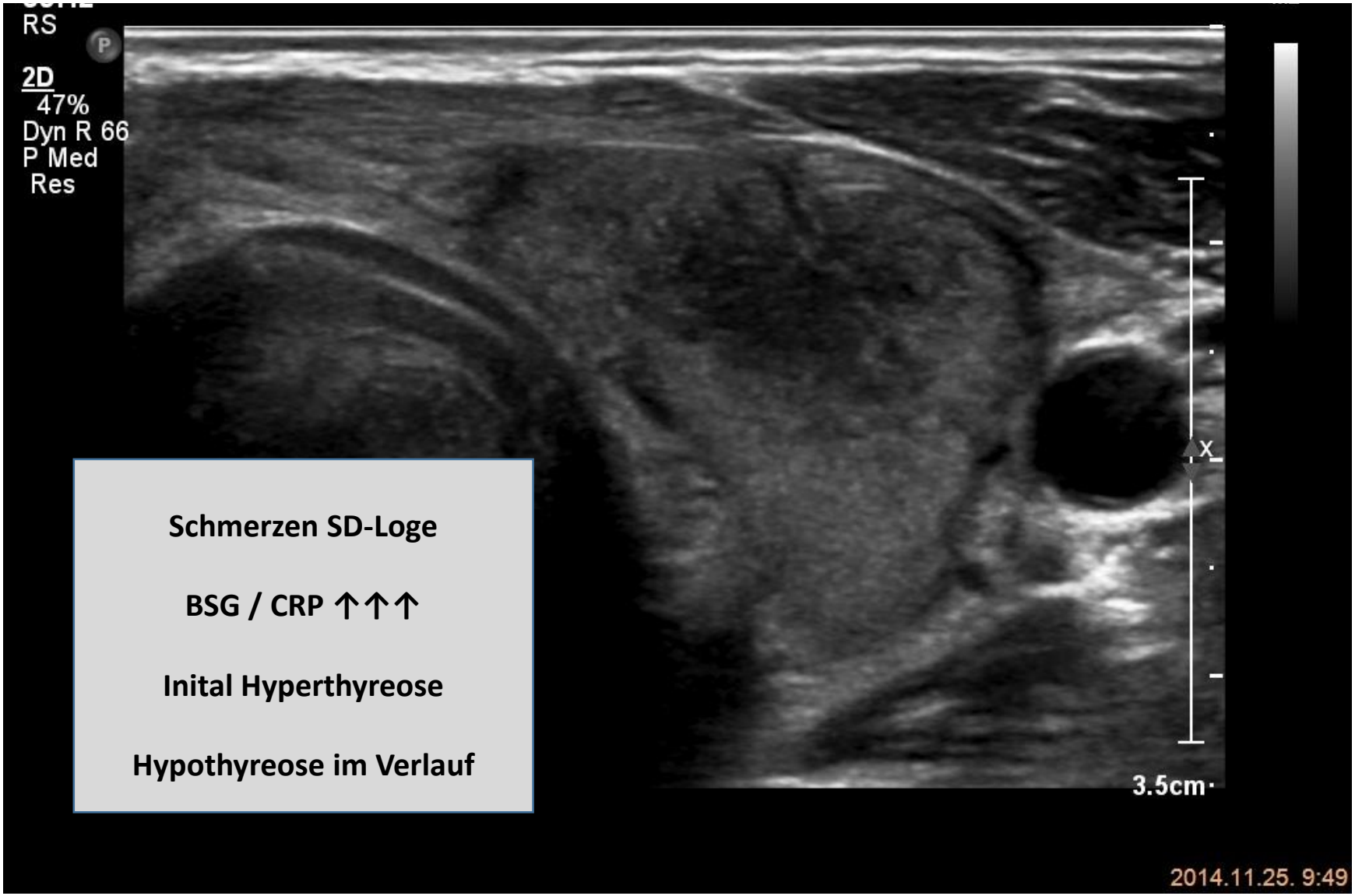


Morbus Basedow

Morbus Basedow



De Quervain Thyroiditis



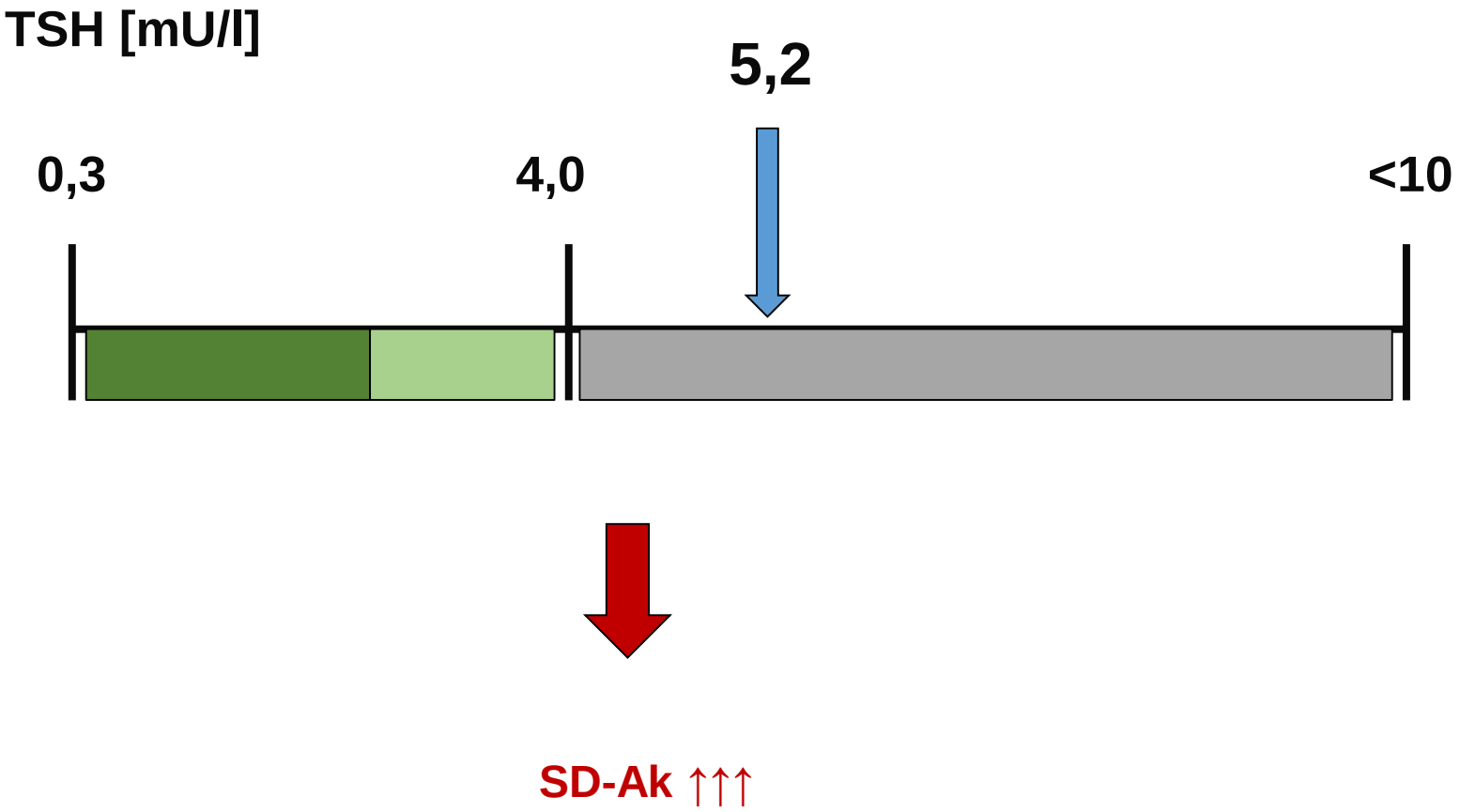
Schmerzen SD-Loge

BSG / CRP ↑↑↑

Inital Hyperthyreose

Hypothyreose im Verlauf

Hypothyreose – (Neigung)



Dermatologie

Psychiatrie

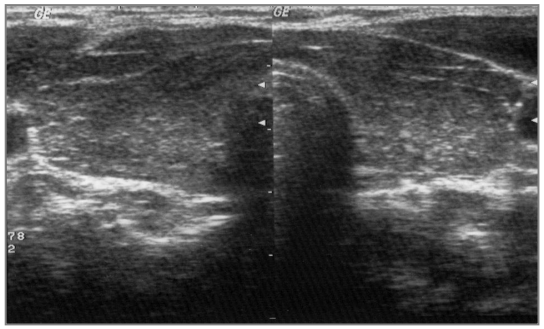
Depression

Fertilisation

Kinderwunsch

Kardiologie

Bradykardien
Perikarderguss



Hashimoto-Thyreoiditis

Hämatologie

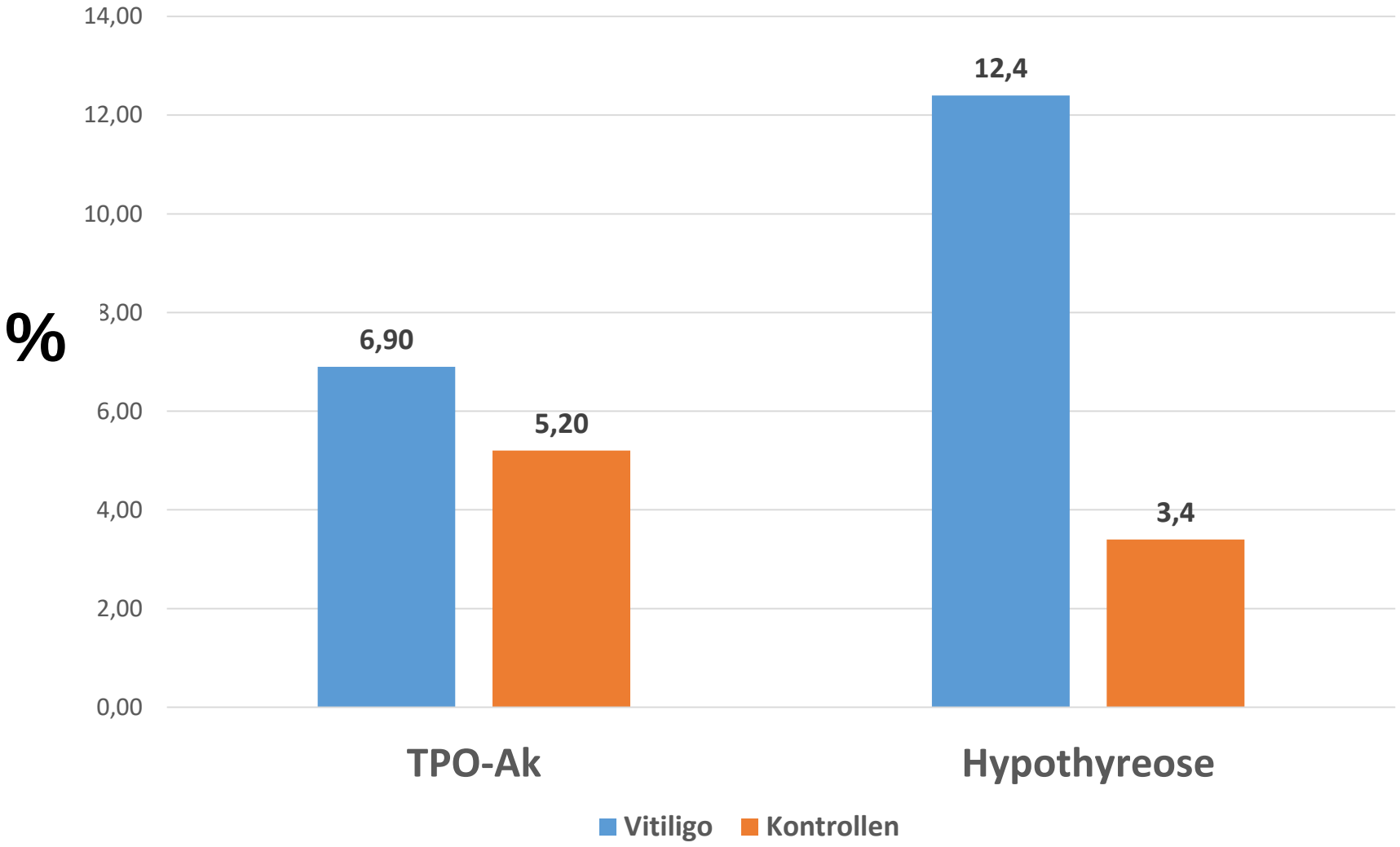
Anämie
Perniziöse Anämie

Gastro-Ent.

Zöliakie
Morbus Crohn

Polyglanduläre
Autoimmunsyndrome

Kinder mit Vitiligo (Hypothyreose und Ak)



Med Sci Monit, 2015; 21: 3216-3221

Dermatologie

Alopezie
Vitiligo
Neurodermitis

Psychiatrie

Depression

Fertilisation

Kinderwunsch

Kardiologie

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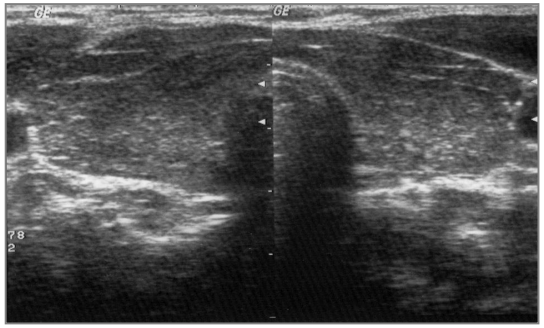
Perikarderguss



Hashimoto-Thyreoiditis

Hämatologie

Anämie
Perniziöse Anämie

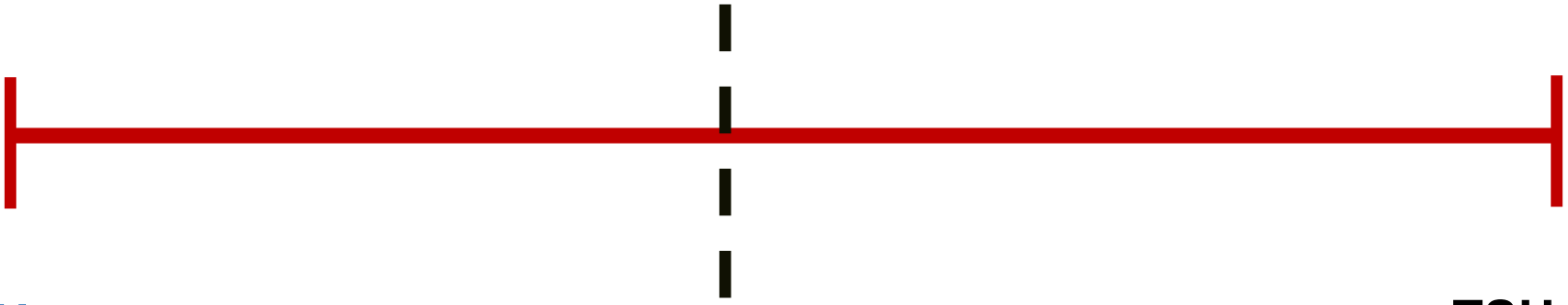
Gastro-Ent.

Zöliakie
Morbus Crohn

Polyglanduläre
Autoimmunsyndrome

Subklinische Hypothyreose ↔ Depression

prospektiv 220.454 Patienten über 2 Jahre Beobachtung



TSH ↑ **TSH ↔**

0,97

keine Korrelation

Kim et al., JCEM 2/2018

Levothyroxin-Gabe und Depression

POSITIV

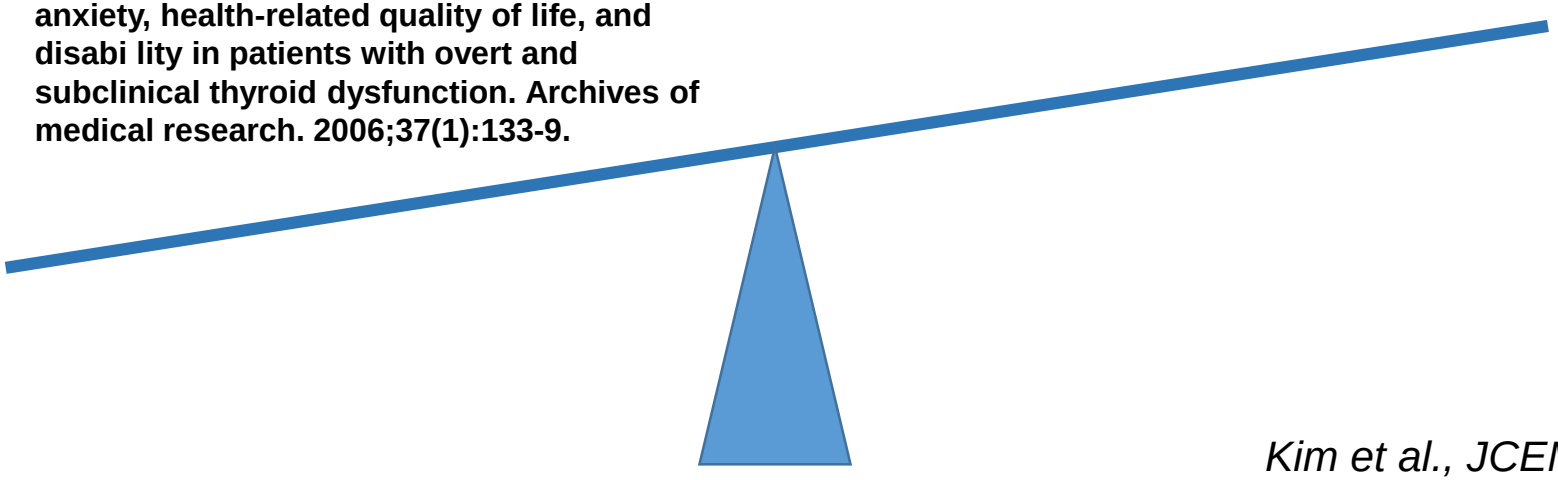
1. Monzani F, et al. Subclinical hypothyroidism: neurobehavioral features and benefi cial effect of L-thyroxine treatment. The Clinical investigator. 1993;71(5):367-71

2. Bono G et al., M. Cognitive and affective status in mild hypothyroidism and interactions with L-thyroxine treatment. Acta neurologica Scandinavica. 2004;110(1):59-66.

3. Gulseren S at el. Depression, anxiety, health-related quality of life, and disabi lity in patients with overt and subclinical thyroid dysfunction. Archives of medical research. 2006;37(1):133-9.

NEGATIV

Baldini IM et al. Psychopathological and cognitive features in subclinical hypothyroidism. Progress in neuro-psychopharmacology & biological psychiatry. 1997;21(6):925-35



Kim et al., JCEM 2/2018

Dermatologie

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Psychiatrie

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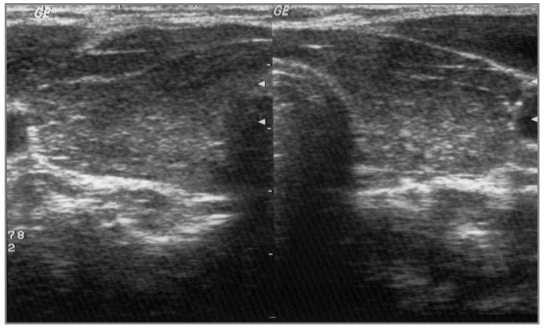


Hashimoto-Thyreoiditis

Hämatologie

Anämie
Perniziöse Anämie

Gastro-Ent.

Zöliakie
Morbus Crohn

Polyglanduläre Autoimmunsyndrome

normal
Morbus Addison

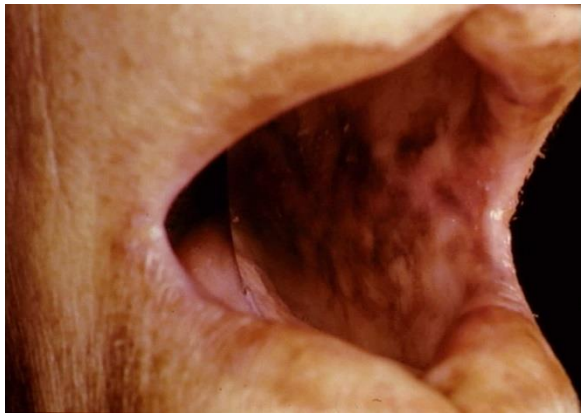
Hormonanalytik, w, 38 Jahre, müde und hypoton

Parameter	Ergebnis		Referenzbereich
ACTH	1145 pg/ml	+	10.0 - 46.0
Cortisol	2,48 µg/dl	-	6.5 - 23.0 morgens
Androstendion	<0,3 ng/ml	-	0.3 - 3.3 bis 1,0 Postmenopause
DHEAS	<15 µg/dl		65 - 380
Nebennierenrinde Ak IFT	positiv .	+	negativ
Renin	>128 pg/ml	+	3,0 - 35
Aldosteron	29,52 pg/ml	-	40 - 310
Aldosteron / Renin Quotient	0,2306 .		<20

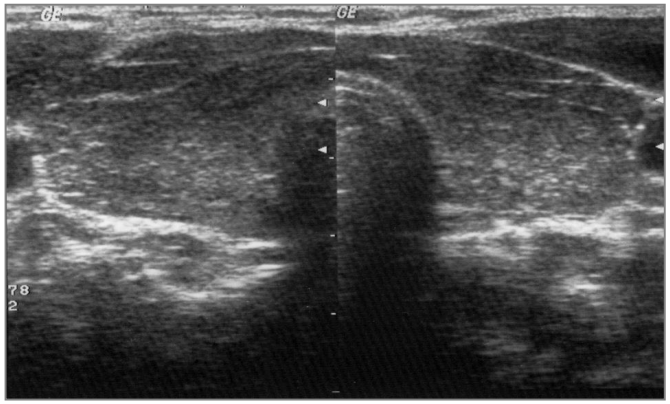
ACTH-Test

Cortisol	3,38 µg/dl	-	6.5 - 23.0 morgens
Cortisol n. 30 min.	3,21 µg/dl		
Cortisol n. 60 min.	3,08 µg/dl		

Addison



Hashimoto



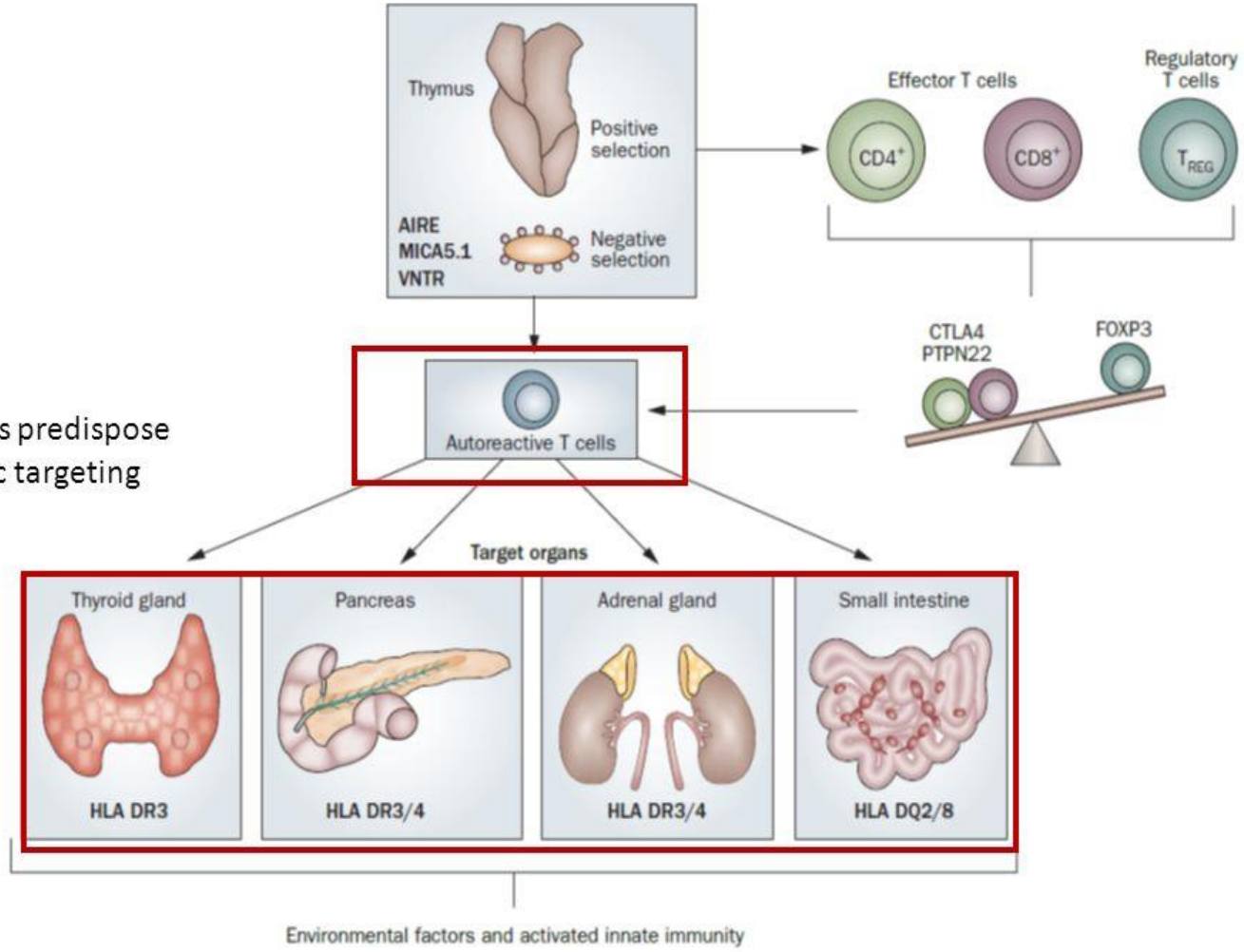
Schmidt-Syndrom

CAVE: Erst Hydrocortison, dann Levothyroxin geben !!!

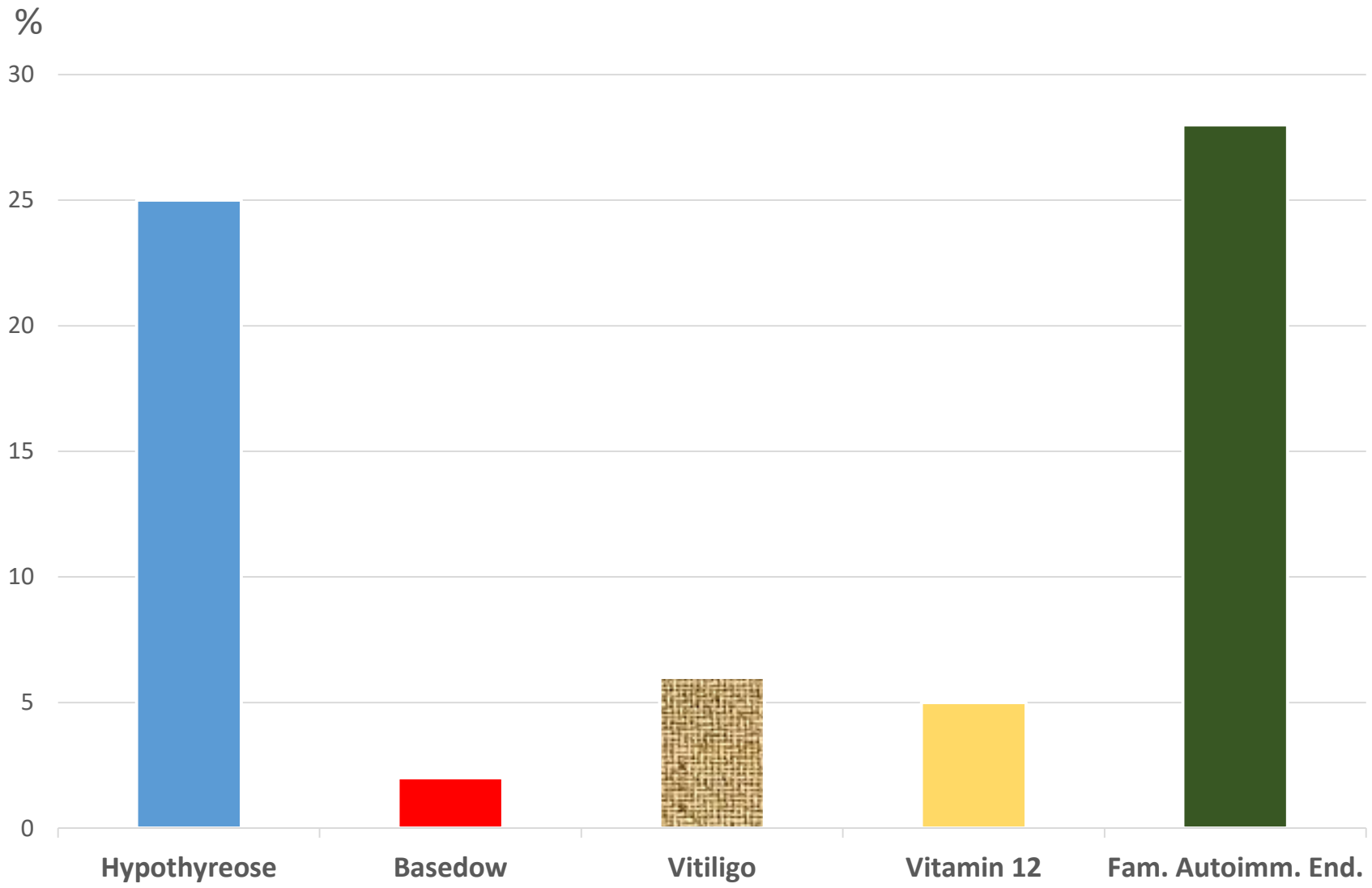
Polyglanduläres Autoimmun-Syndrom

Autoimmune Polyglanduläre Syndrome

HLA-II molecules predispose to tissue specific targeting



Typ-1-Diabetes mellitus und Autoimmunopathien



Journal of Clinical and Diagnostic Research. 2014 Feb, Vol-8(2):70-72

Polyglanduläres Autoimmunsyndrom

Klassifikation nach Neufeld und Blizzard 1980

APS-1: **Candidiasis, Hypoparathyreoidismus, Morbus Addison (>2/3)**

APS-2: **Morbus Addison (immer) + Hashimoto und /oder Typ 1 Diabetes mellitus**

APS-3: **Hashimoto mit anderen Autoimmopathien außer Morbus Addison / Hypopparathyreoid.**

and/or hypoparathyroidism)

APS-4: Combinations not included in the previous groups

Modifiziert Betterle et al. 2003

TABLE 2.

Main Features of APS Types

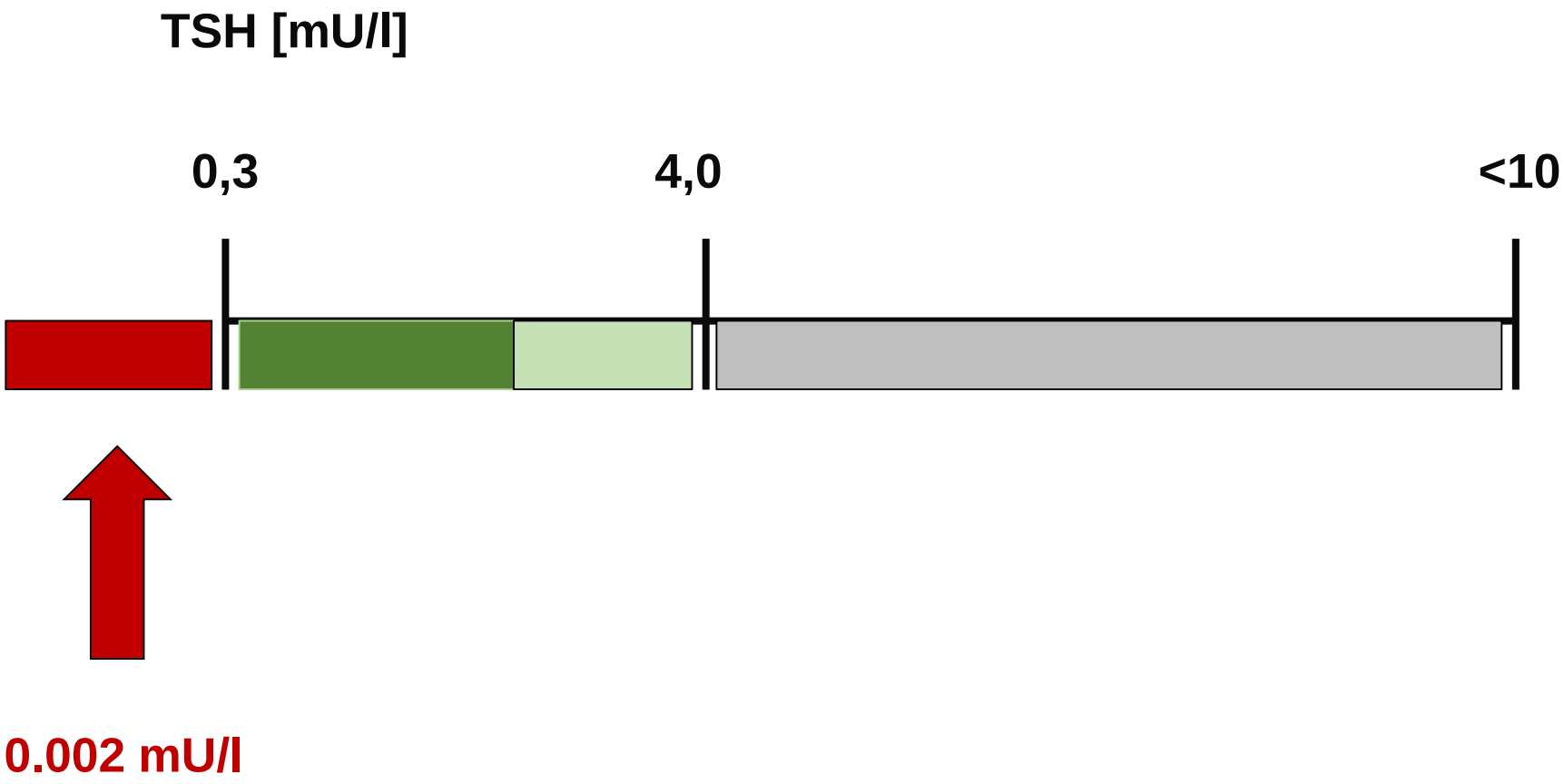
	APS Type I	APS Type II	APS Type IV
Gender	F > M	F > M	F > M
Mean age of onset (y)	13	36	36
Family history	APS type 1 (25%)	AD (rare), other autoimmune diseases (frequent)	AD (rare), other autoimmune diseases (rare)
Genetic	*AIRE* gene mutations	HLA-DR3	HLA-DR3
Major component of disease	Candidiasis, hypo-parathyroidism, AD	AD, thyroid autoim-mune disease, type 1 diabetes mellitus	AD
ACA and/or 21-OH Abs (at onset of AD)	100%	100%	100%
Minor autoimmune diseases*	11%-60%	0%-11%	100%

Abs = autoantibodies; ACA = adrenal cortex autoantibodies; AD = Addison's disease; APS = autoimmune polyendocrine syndrome.

**Minor autoimmune diseases include gonadal failure, vitiligo, alopecia, atrophic gastritis, pernicious anemia, celiac disease, chronic hepatitis, hypophysitis, malabsorption, cholelithiasis, and asplenia.*

Adapted from Betterle et al[10]

Hyperthyreose



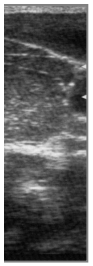
TSH <0,3 mU/l: Hyperthyreose

Levothyroxinüberd

Jodexposition (Her

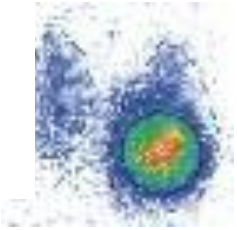
Morbus Basedow

oto-Thyreoiditis



in-Thyreoiditis

utonomien

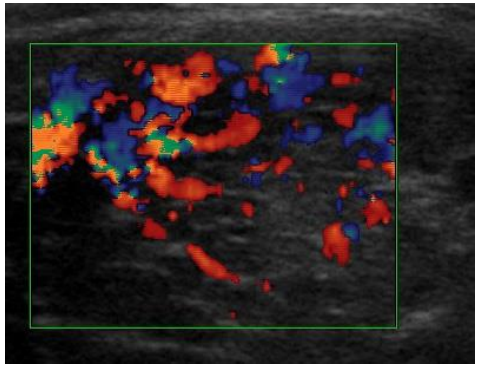


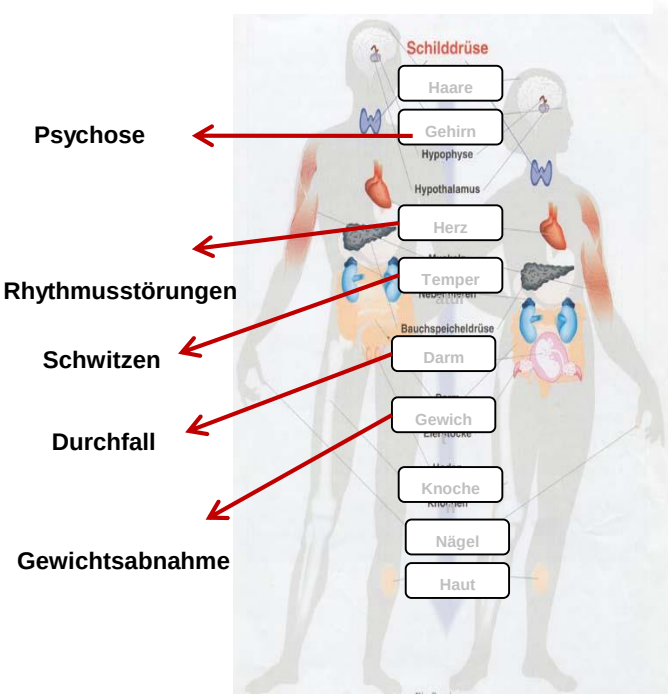
Morbus Basedow

TSH <0,3 mU/l

fT4 ↑↑

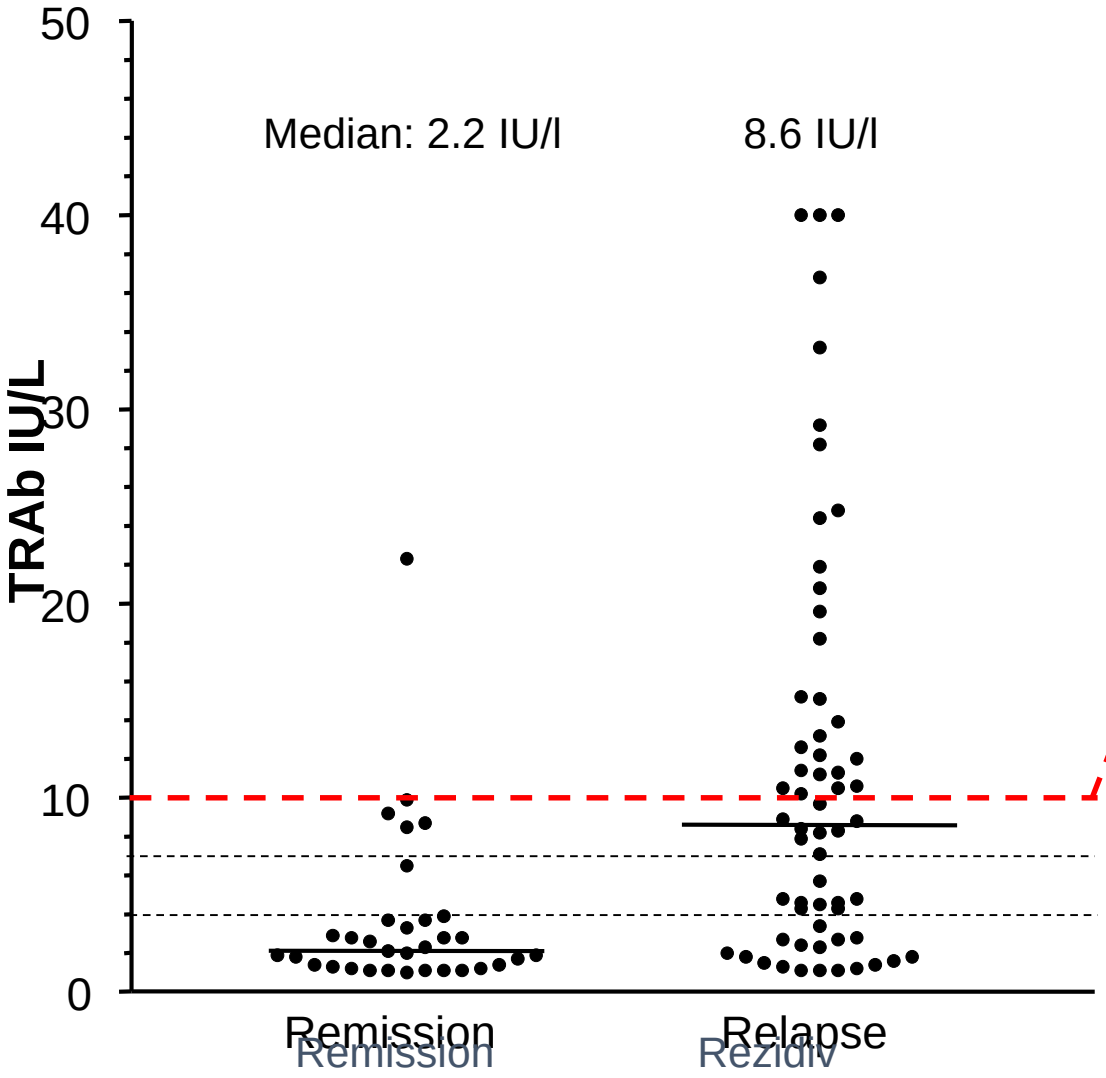
fT3 ↑↑





TRAK ↑

Hyperthyreose-Rezidiv in Abhängigkeit der TRAK-Spiegel



n = 93 Patienten

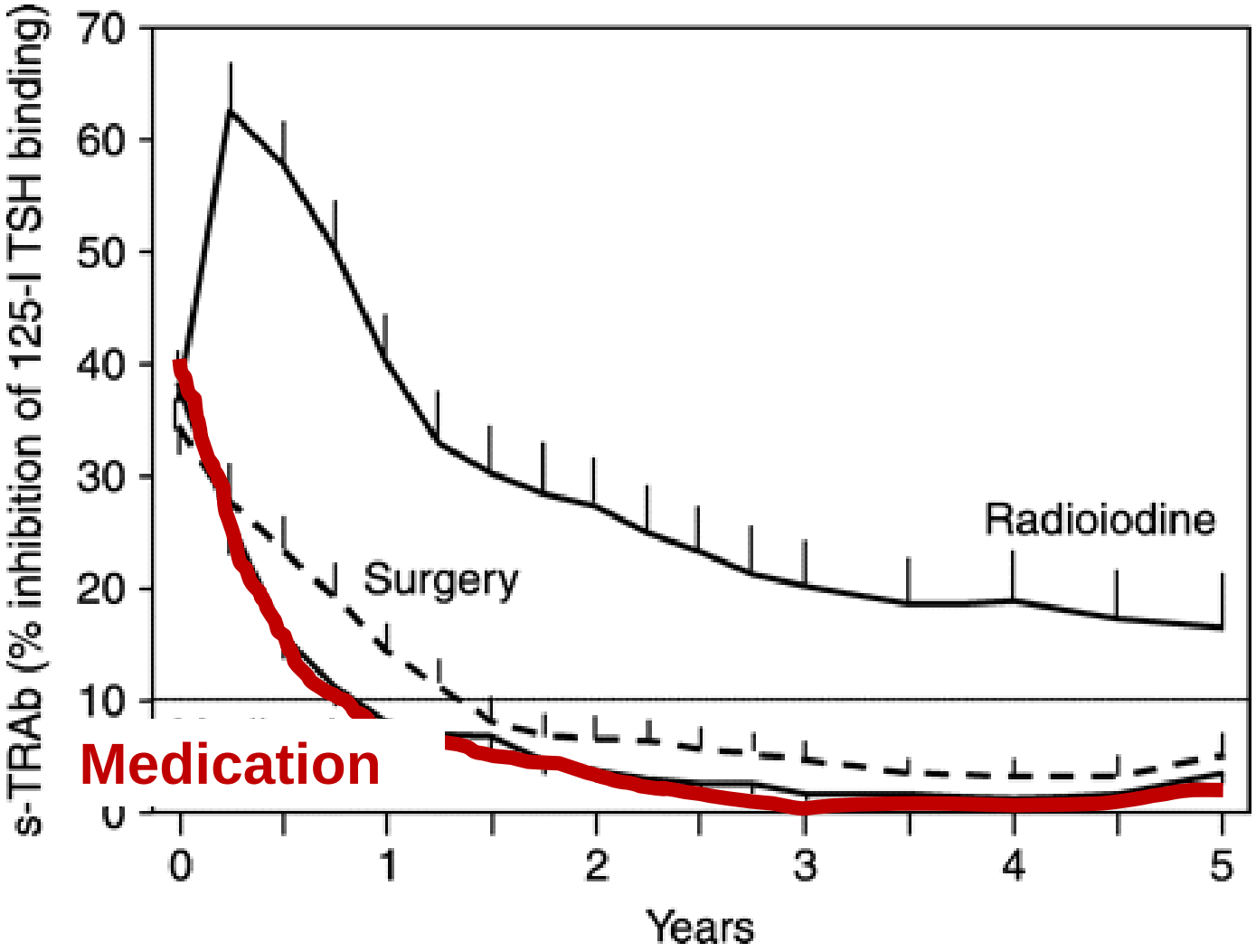
Mittlere Dauer der thyreostatische Therapie

insgesamt:	∅ 5,1 Mon
- Rez.:	∅ 5,4 Mon
- Rem:	∅ 4,6 Mon
follow-up:	∅ 21,7 Mon
Dauer der Rem:	∅ 17,0 Mon

TRAb (IU/l)	Wahrscheinlichkeit einer **Remission**
> 10	***3,4%* (1/29)** **Spez. für Rezidiv 97%** **PPV für Rez. 96,4%**
> 7	*13,9%* (5/36)
> 4	*15,6%* (7/45)

Schott M et al., Horm Metab Res 2004;36:92-96

TRAK-Verlauf unter Therapie



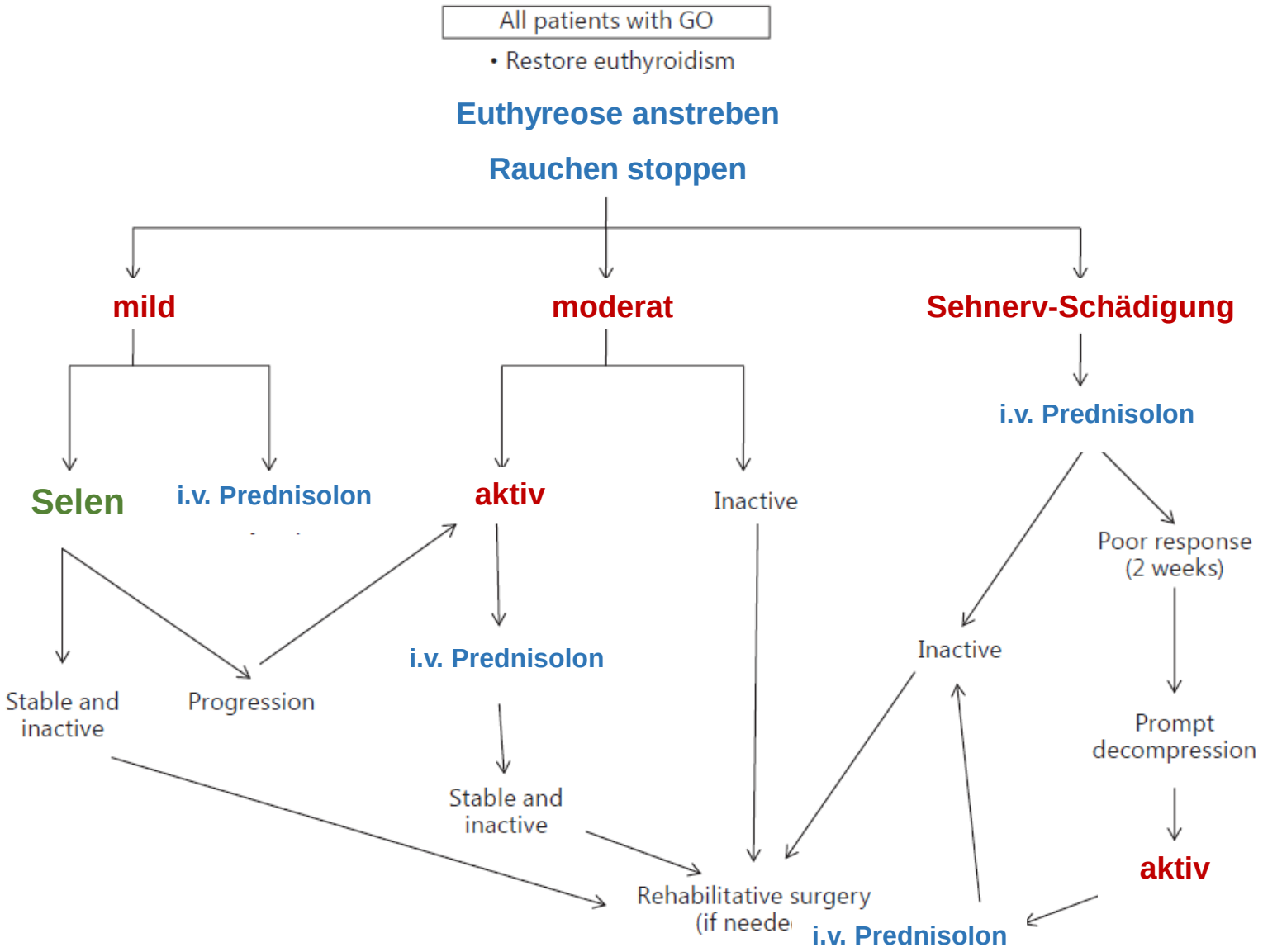
Laurberg P et al. Eur J Endocrinol 2008;158(1):69-75

Exophthalmus

Konjunktivitis

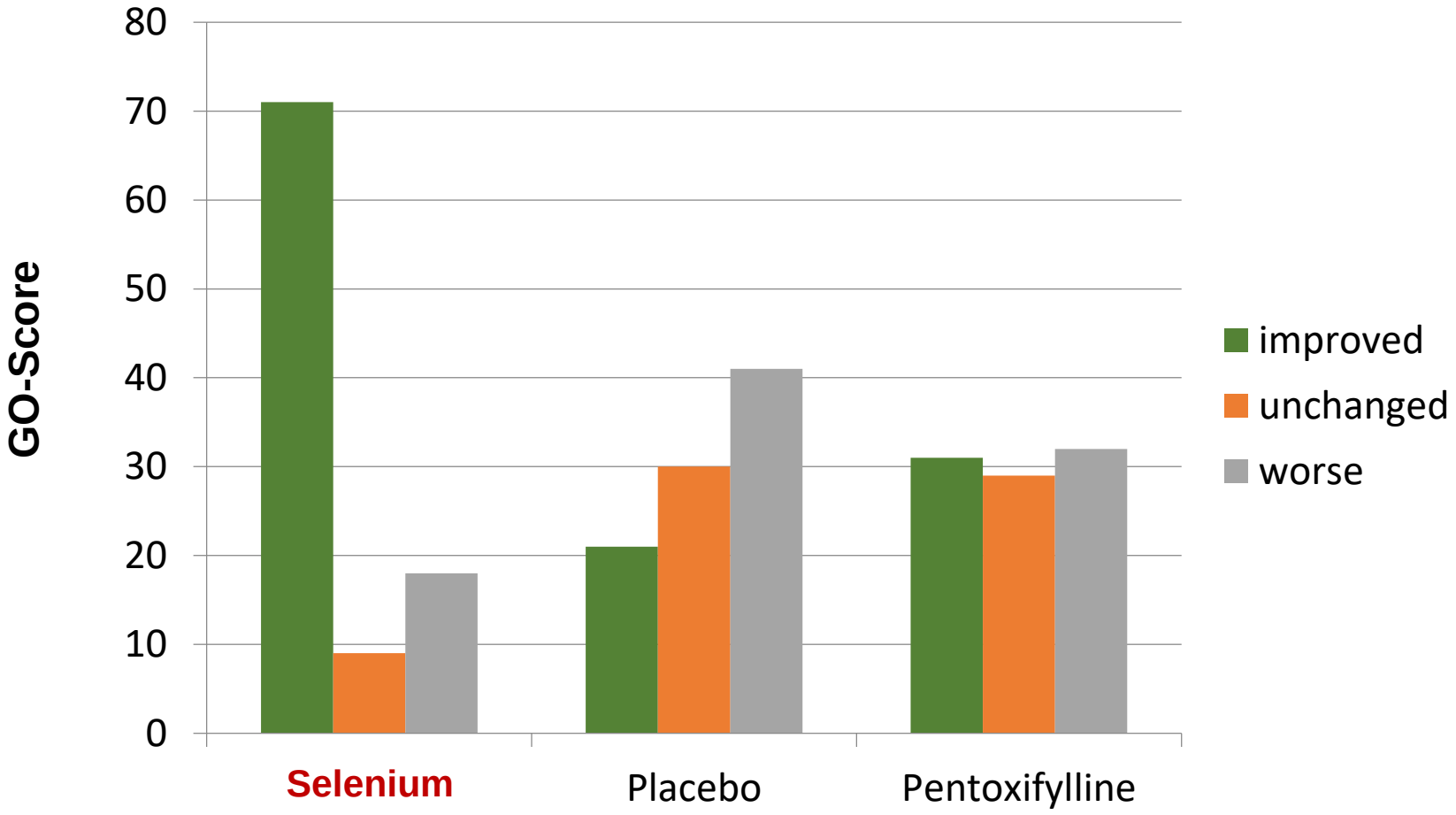
Doppelbilder

Europäische Richtlinie Endokrine Orbitopathie



Eur Thyroid J 2016;5:9–26

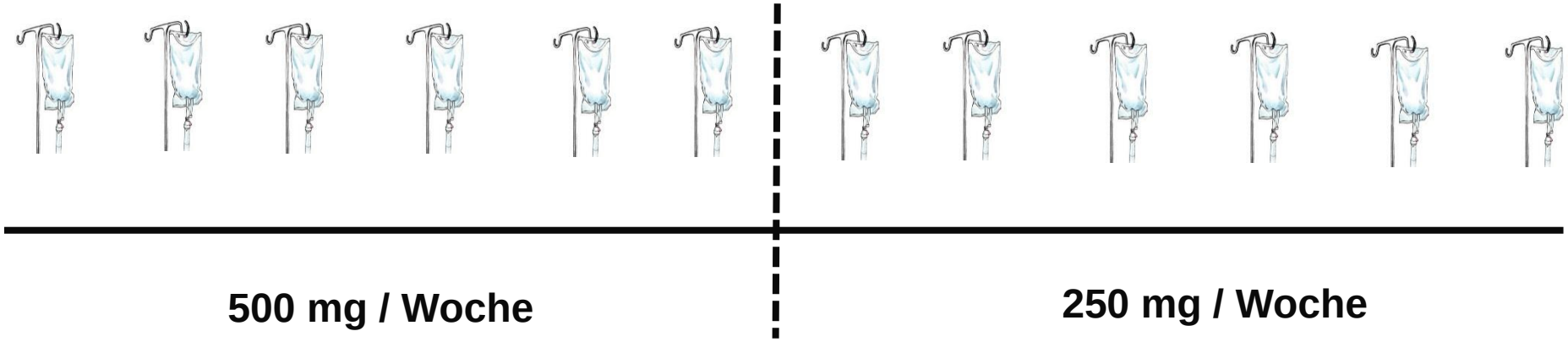
Selen verbessert die Augensymptomatik (E.O.) bei M. Basedow



2 x 100 µg

Marcocci C et al. N Engl J Med 2011; 364(20):1920-193

i.v.-Prednisolon



Summe: 4,5 g

Kummulative Dosis [g]	**7.47**	**4.98**	**2.25**
Verbesserung E.O. [%]	**52**	**35**	**28**

Eur Thyroid J 2016;5:9–26

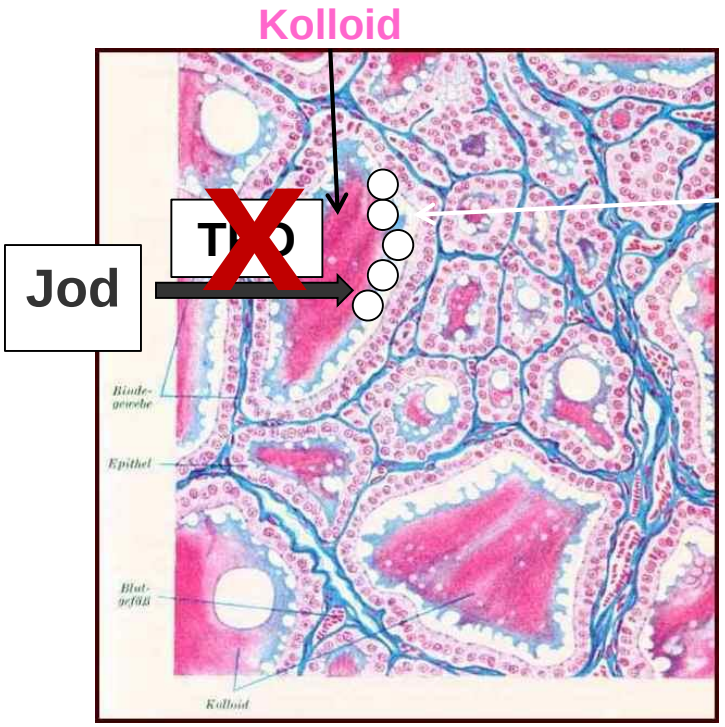
Thyreostatika

Propylthiouracil	**3 x tgl.**
Thiamazol	**1 x tgl.**
Carbimazol	**1 x tgl.**

Carbimazol ist ein «Prodrug» von Thiamazol.

Es wird im Körper vollständig zu Thiamazol umgewandelt.

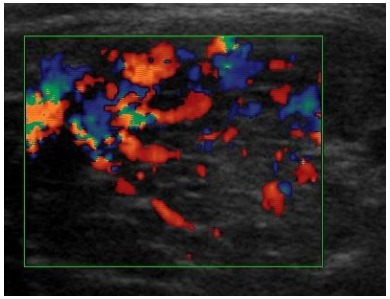
15 mg Carbimazol = 10 mg Thiamazol.



Dies beruht auf einer reversiblen Blockierung der Schilddrüsen- Peroxydase, des für den Einbau von Jodid in das Thyreoglobulin verantwortlichen Enzymes.

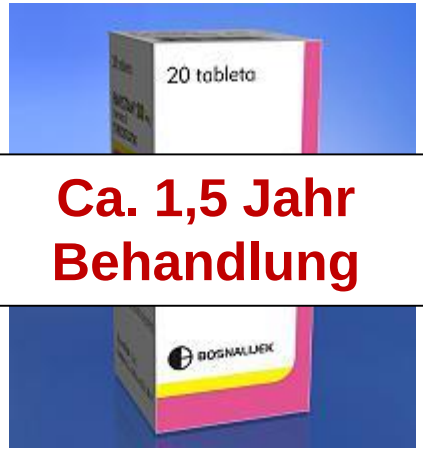
In hohen Dosen vermindert Propylthiouracil zudem die periphere Konversion von Thyroxin (T_4) zu Trijodthyronin (T_3).

Therapie des Morbus Basedow



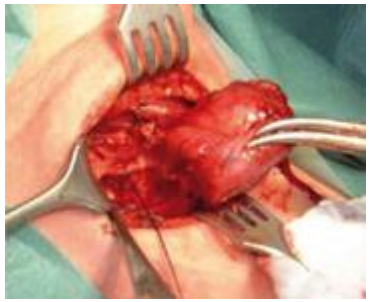
Radiojodtherapie

Thyreostatika



Ca. 1,5 Jahr Behandlung

Operation



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