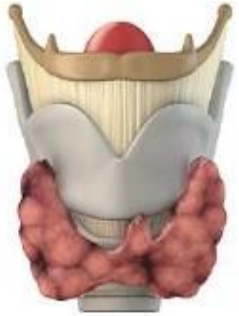
Update Schilddrüsenerkrankungen

9.4.2019 in Bochum



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

www.endo-bochum.de

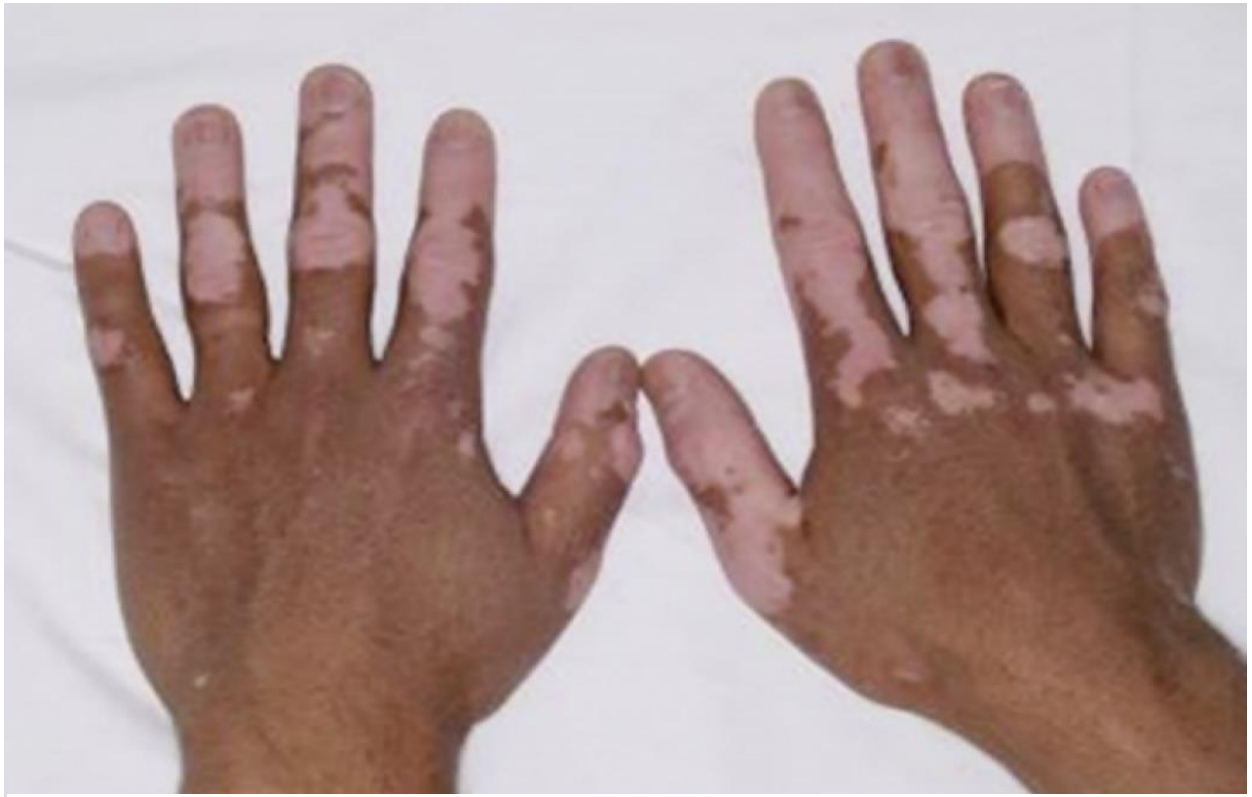
The Endocrine Society`s 101st Annual Meeting

New Orleans 23.-26. March 2019

Mon 594: Morbus Basedow und Autoimmunerkrankungen

MON-594 - **Report Of A Large Series Of Patients With Graves' Disease (with/without Graves' Ophthalmopathy) And Review Of The Literature, About The Association With Other Autoimmune Diseases**

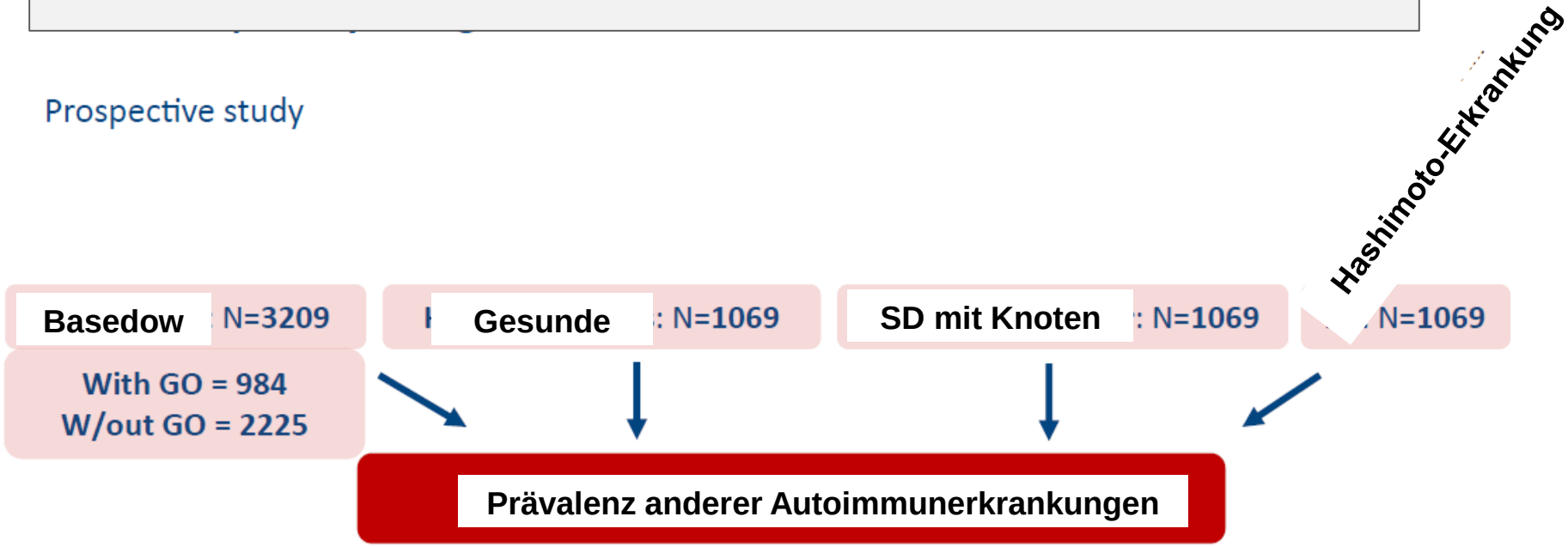
Alessandro Antonelli *et al.*, Pisa, Italy



Vitiligo

Assoziation
Morbus Basedow und Autoimmunerkrankungen

Prospective study



Patients and controls were matched by:

- Age
- Gender
- Same area of origin
- Similar iodine intake

Morbus Basedow und Autoimmunerkrankungen

Associations between GD and:	%
Vitiligo	**2.6%**
Chronic autoimmune gastritis	**2.4%**
Rheumatoid arthritis	1.9%
Polymyalgia rheumatica	1.3%
Multiple sclerosis	0.3%
Celiac disease	1.1%
Type 1 diabetes	**0.9%**
Systemic lupus erythematosus and Sarcoidosis	<0.1%
Sjogren disease	0.8%

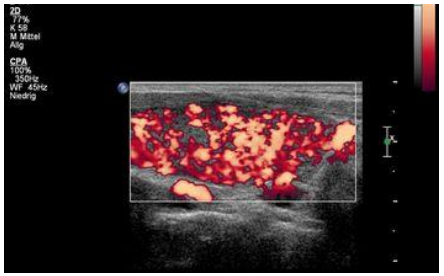
18.9% ⟷ 15.6% (keine)

- 'Significant' inc … nts VS controls
  - ➢ Prevalen… 8.9%
  - ➢ Prevalen… 5.6%

Höhere Prävalenz der Autoimmunerkrankungen bei Morbus Basedow mit Augenbeteiligung (endokrine Orbitopathie)

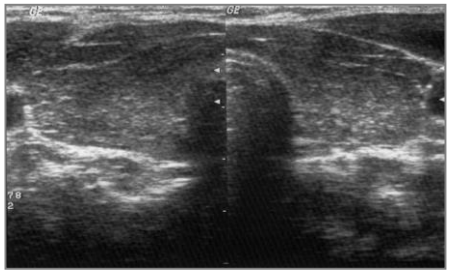
Gleiches Autoimmun-Muster

M. Basedow

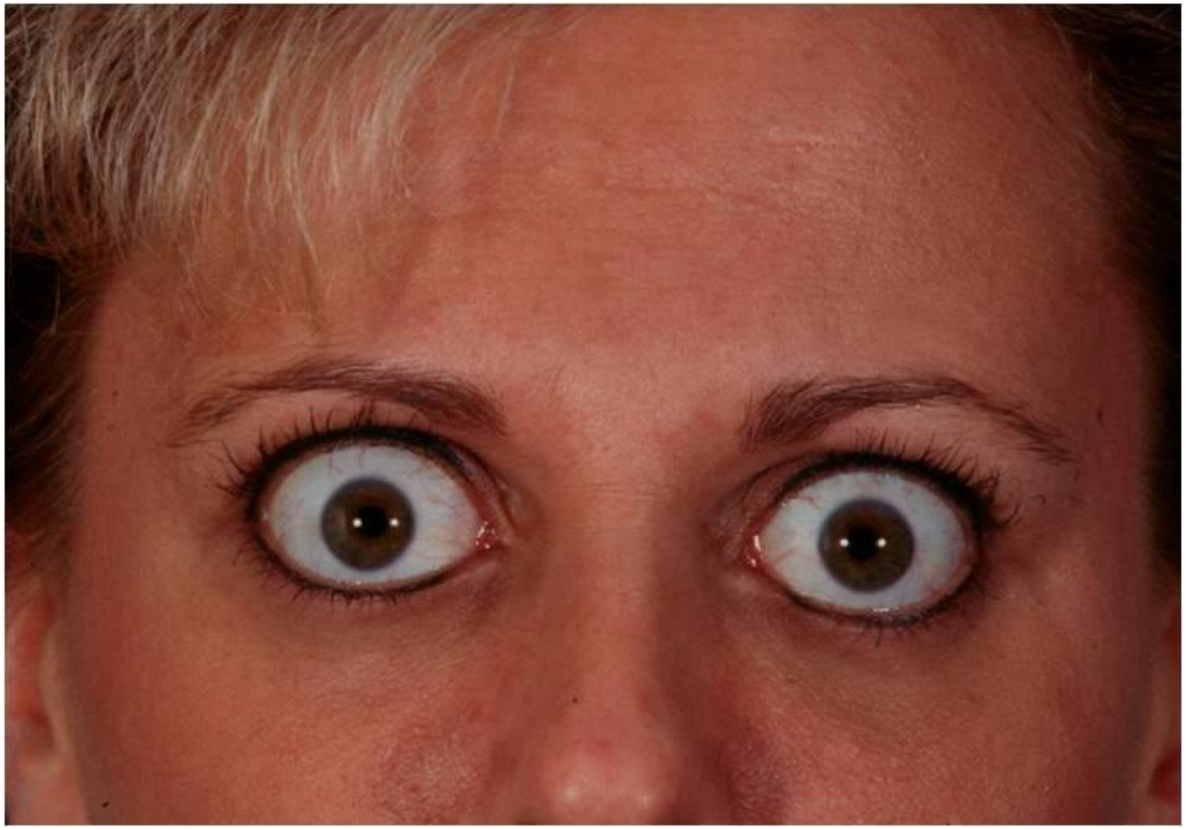


Associations between GD and:	%
Vitiligo	**2.6%**
Chronic autoimmune gastritis	**2.4%**
Rheumatoid arthritis	1.9%
Polymyalgia rheumatica	1.3%
Multiple sclerosis	0.3%
Celiac disease	1.1%
Type 1 diabetes	**0.9%**
Systemic lupus erythematosus and Sarcoidosis	<0.1%
Sjogren disease	0.8%

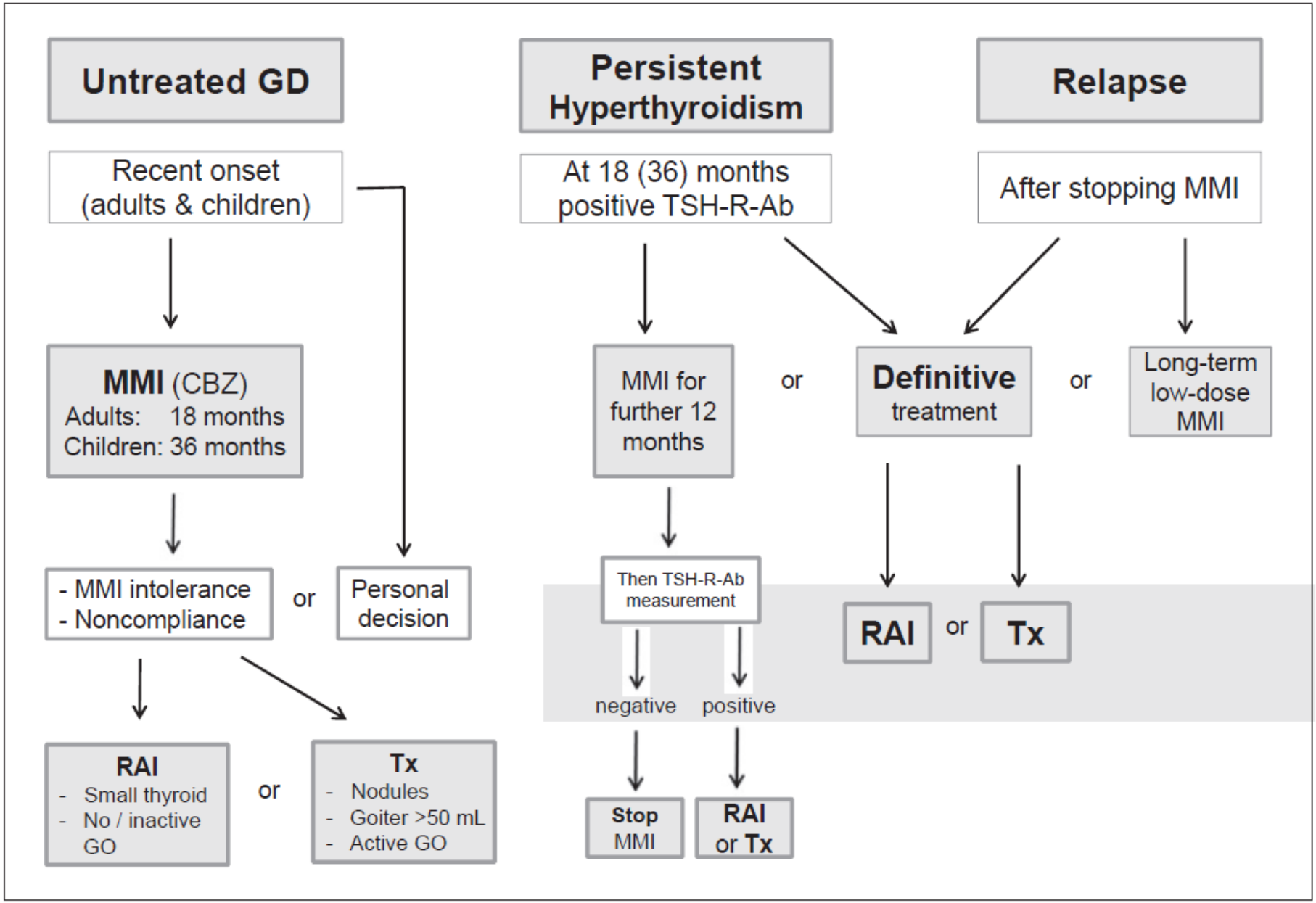
Hashimoto



2018 European Thyroid Association Guideline for the Management of Graves' Hyperthyroidism



Eur Thyroid J 2018;7:167–186



Eur Thyroid J 2018;7:167–186

Nahrungsergänzungsmittel

Haben Diäten / Nahrungsergänzungsmittel Einfluss auf Autoimmunerkrankungen ?

MON-013 - **Nutritional Approach To Autoimmune Thyroiditis (AIT) - The Patients' And Medical Professionals' View**
Malgorzata Trofimiuk-Muldner *et al.*, Krakow, Poland

- **Wunsch der Lebensqualitätsverbesserung**
- **Websides / Internet: Empfehlungen <u>ohne wiss. Evidenz</u>**

- **Wie gehen Ärzte und Patienten vor?**

In **Internet-Befragung** the recommendations for a nutritional approach in AIT

Internet-Befragung on the nutritional approach in own disease

„Mediziner“

- 30 physicians
- 32 nutritionists
- 35 medical Students
- 27 dietetics students

Patienten mit Hashimoto/Basedow =150

- Age: 18-70 years
- Females: N=146
- Males: N=4

Questions concerned: - Glu**Gluten-freie Kost**e diet **Vitamine und Mineralien**
- Source of patients' knowledge
- Recommending body behind their decision on changes in nutrition

	„Mediziner“	Patienten mit Hashimoto/Basedow
Selen bei Basedow - In Graves’ ophthalmopathy	**54%** 9.7%	**36.7%** (27.3% med. advice)
Jod Iodine supplements	**41.3%**	**8%** (All med. advice)
Vitamin D Vitamin D supplements	**92.3%**	74.7% (48.7% med. advice)
Gluten-freie Kost Gluten-free diet	6.4%*	**37.3%**
Laktose-freie Kost Lactose-free diet	4.8%**	**44.3%**
Diagnosed with celiac disease		2%
Therapieänderung nach Ärzteempfehlung		38%
Therapieänderung ohne Ärzteempfehlung		**62%**
Quellen: websides - Patienten-orientierte Publikation		**80.7%** 50.7%

* Regardless of gluten-related disorders

** Even in absence of intolerance

THYROID | Schlussfolgerung

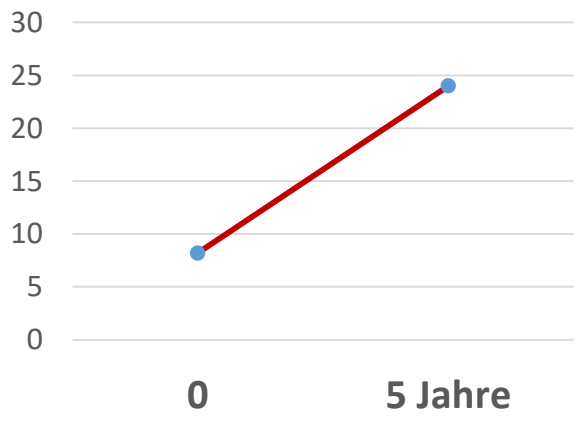
- ➢ **Sehr hohe Diät / Supplements-Einnahme**
  ➢ **ohne ärztlichen / medizinischen Rat**

- ➢ **Wenn ärztlicher / medizinischer Rat, dann häufig <u>ohne</u> wissenschaftliche Evidenz**

- ➢ **Einige Supplements / Diäten können schädlich sein (z.B. Gluten)**

Hashimoto-Prävalenz steigt trotz Gluten-freier Diät

- Prospective study of (n – 1255) **Zöliakie-Patienten**
  - Followed x **5 Jahre Gluten-freie Diät**
  - Prevalence of immune mediated disorders is high at diagnosis and increases despite the GFD
    - Hashimoto's increased from 8.2% to 24% over 5-years



Imperatore et al. Digest and Liver Disease 2016

Hashimoto-Prävalenz steigt trotz Gluten-freier Diät

- Prospective study of Zöliakie-Patiente
  (n – 1255)
  - Followed x 5 Jahre Gluten-fre
  - Prevalence of immune ... high
    at diagnosis and ... GFD
    - Hashimoto' ... 24% over 5-years

Keine prospektive Studie mit Gluten-freier Diät bei Patienten mit Hashimoto ohne Zöliakie

Imperatore et al. Digest and Liver Disease 2016

Role of Gluten in Autoimmune Disease

Gluten Intake and Risk of Islet Autoimmunity and Progression to Type 1 Diabetes in Children at Increased Risk of the Disease: The Diabetes Autoimmunity Study in the Young (DAISY)

Lund-Blix et al. Diabetes Care 2019

- No association between gluten intake > 4 months of age -> adolescents and the risk of islet cell autoimmunity or progression to T1DM
- No rationale to reduce amount of gluten even in high risk patients

Kein Hinweis eines Gluten-freien Einfluss bei Typ-1-Diabetes mellitus-Risiko und dessen Progression

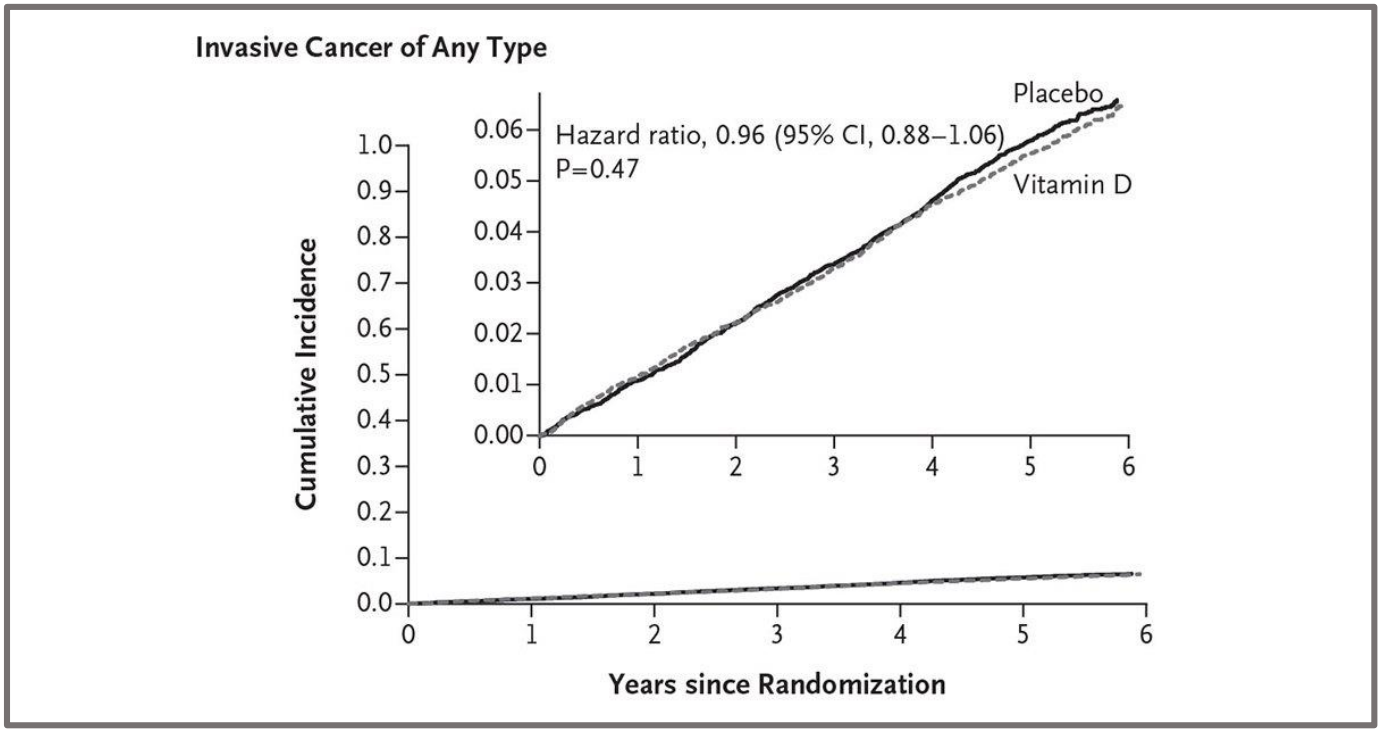
	„Mediziner“	Patienten mit Hashimoto/Basedow
Selenium supplements - In Graves’ ophthalmopathy	**54%** 9.7%	**36.7%** (27.3% med. advice)
Iodine supplements	**41.3%**	**8%** (All med. advice)
V**Vitamin D**	**92.3%**	74.7% (48.7% med. advice)
Gluten-free diet	6.4%*	**37.3%**
Lactose-free diet	4.8%**	**44.3%**
Diagnosed with celiac disease		2%
Changes following medical advice		38%
Changes **without** medical advice		**62%**
Sources: - Websites - Patient-oriented-publications		**80.7%** 50.7%

* Regardless of gluten-related disorders

** Even in absence of intolerance

Vitamin D verhindert keinen Krebs und keine KHK

25,871 participants - median follow-up of 5.3 years



Supplementation with vitamin D did not result in a lower incidence of invasive cancer or cardiovascular events than placebo.

N Engl J Med 2019; 380:33-44

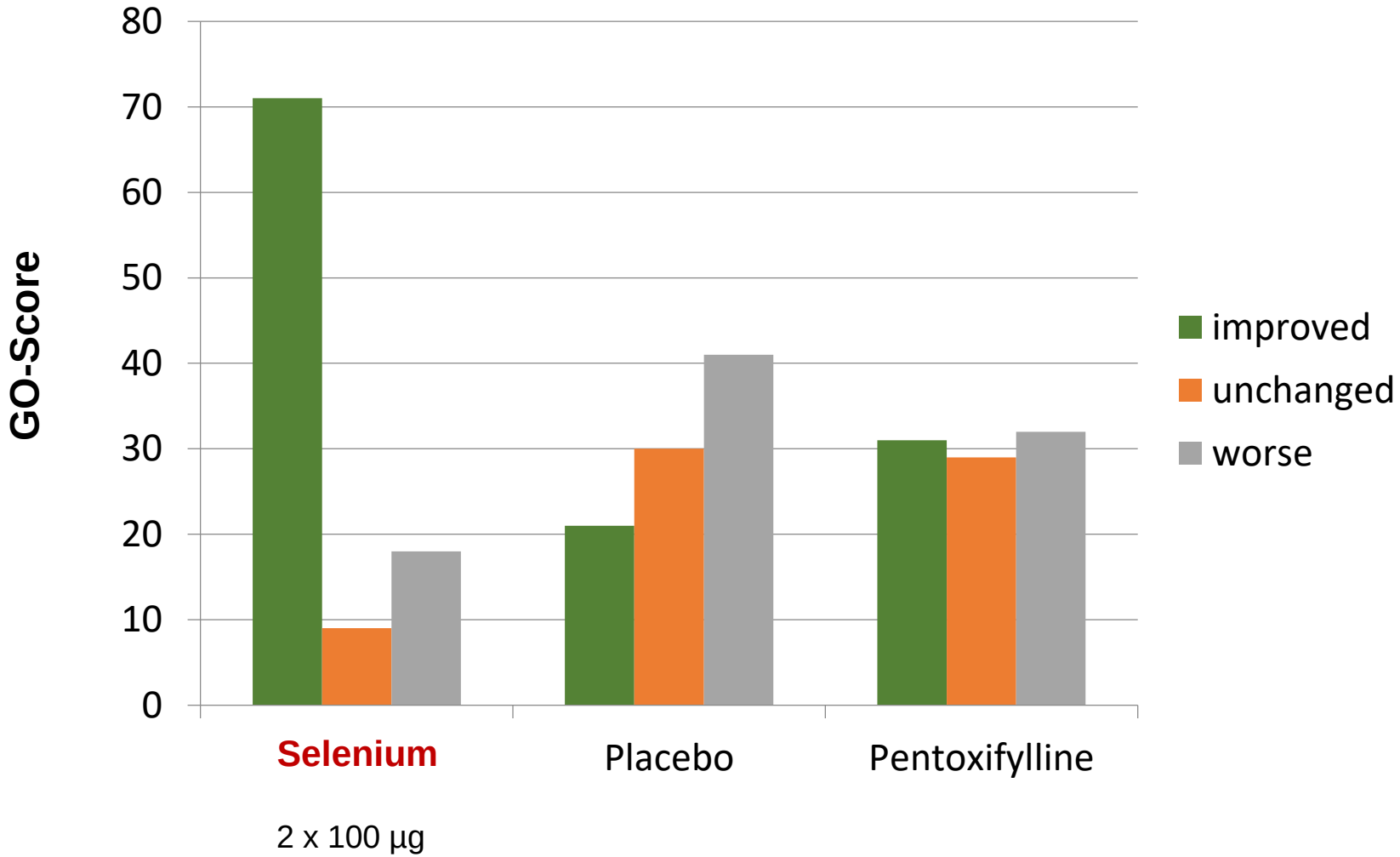
	„Mediziner“	Patienten mit Hashimoto/Basedow
Se	**54%**	**36.7%** (27.3% med. advice)
Iodine supplements	**41.3%**	**8%** (All med. advice)
Vitamin D supplements	**92.3%**	74.7% (48.7% med. advice)
Gluten-free diet	6.4%*	**37.3%**
Lactose-free diet	4.8%**	**44.3%**
Diagnosed with celiac disease		2%
Changes following medical advice		38%
Changes **without** medical advice		**62%**
Sources: - Websites - Patient-oriented-publications		**80.7%** 50.7%

Selen bei Basedow

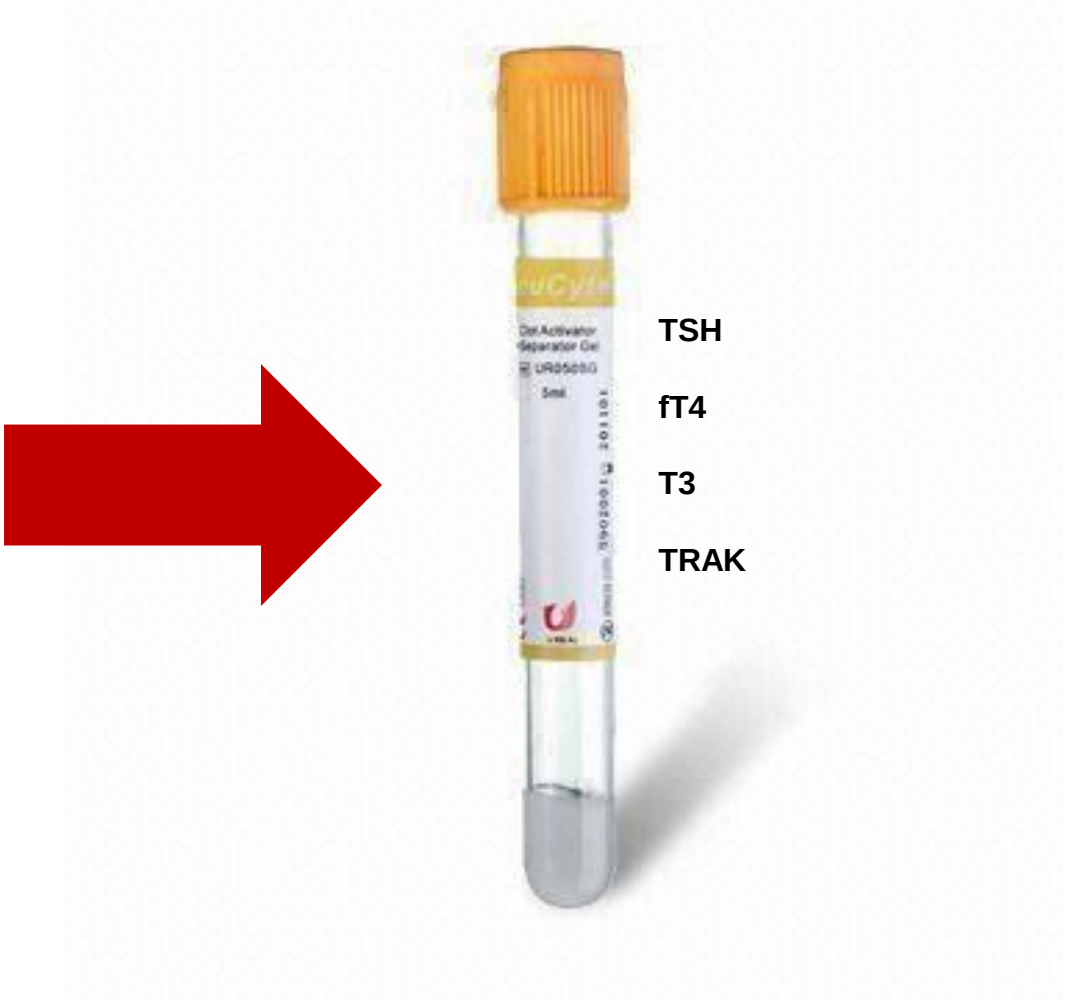
* Regardless of gluten-related disorders

** Even in absence of intolerance

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



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



TSH

fT4

T3

TRAK

Table 1. Characteristics of Six Children with Biotin-Induced Laboratory Indications of Autoimmune Hyperthyroidism.*

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Sex	Female	Female	Male	Male	Male	Male
Age	9 yr	2 yr	2 yr	5 mo	1 mo	1 mo
Primary disease	BTBGD	BTBGD	BTBGD	Infantile mitochondrial disease	Neonatal mitochondrial disease	Neonatal mitochondrial disease
Biotin dose (mg/kg/day)	10	14	15	2	7	8
Concomitant medication	Thiamine	Thiamine, methimazole, cholecalciferol, levetiracetam, chloral hydrate	Thiamine, methimazole, oxcarbazepine	Thiamine, sodium phenylbutyrate, propranolol, nystatin, cholecalciferol	CoQ10, thiamine, cholecalciferol, carnitine, riboflavin, bisoprolol, aspirin, furosemide	CoQ10, thiamine, methimazole, cholecalciferol, carnitine, riboflavin

6 Kinder mit Biotin-Induzierter hyperthyreoter Laboranalytik

* Serum biotin levels were highly elevated in all children during therapy (>3000 ng per liter). Levels of free thyroxine (T_4), total triiodothyronine (T_3), and thyrotropin were normalized within 24 to 48 hours after the discontinuation of biotin in all patients, whereas normalization of levels of anti–thyrotropin receptor antibodies took up to several days in some patients. Normal ranges are as follows: thyrotropin, 0.85 to 6.46 μIU per milliliter; free T_4, 0.94 to 1.71 ng per deciliter; anti–thyrotropin receptor antibodies, less than 1.7 IU per liter; and total T_3, 0.8 to 2.6 ng per deciliter. BTBGD denotes biotin–thiamine–responsive basal ganglia disease, CoQ10 coenzyme Q10, and ND not determined.

† After the discontinuation of biotin, mild hypothyroidism became evident, with spontaneous recovery after the discontinuation of methimazole. Possible long-term complications due to transient hypothyroidism are unclear in this patient.

‡ Methimazole treatment intermittently normalized laboratory values during biotin treatment. After the discontinuation of biotin and methimazole, all values normalized completely. There was no evidence of long-term complications due to transient hypothyroidism.

N Engl J Med 2016; 375:704-706

Table 1. Characteristics of Six Children with Biotin-Induced Laboratory Indications of Autoimmune Hyperthyroidism.*

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Sex	Female	Female	Male	Male	Male	Male
Age	9 yr	2 yr	2 yr	5 mo	1 mo	1 mo
Primary disease	BTBGD	BTBGD	BTBGD	Infantile mitochondrial disease	Neonatal mitochondrial disease	Neonatal mitochondrial disease
Biotin dose (mg/kg/day)	10	14	15	2	7	8
Concomitant medication	Thiamine	Thiamine, methimazole, cholecalciferol, levetiracetam, chloral hydrate	Thiamine, methimazole, oxcarbazepine	Thiamine, sodium phenylbutyrate, propranolol, nystatin, cholecalciferol	CoQ10, thiamine, cholecalciferol, carnitine, riboflavin, bisoprolol, aspirin, furosemide	CoQ10, thiamine, methimazole, cholecalciferol, carnitine, riboflavin
Laboratory results						
During biotin treatment						
Thyrotropin (μIU/ml)	0.05	0.02	0.04	0.02	0.08	0.03
Free T_4 (ng/dl)	6.24	>7.77	>7.77	>7.77	>7.77	>7.77
Anti–thyrotropin receptor antibodies (IU/liter)	38.6	>40.0	>40.0	>40.0	>40.0	>40.0
Total T_3 (ng/dl)	>6.5	ND	>6.5	>6.5	>6.5	ND

* Serum biotin levels were highly elevated in all children during therapy (>3000 ng per liter). Levels of free thyroxine (T_4), total triiodothyronine (T_3), and thyrotropin were normalized within 24 to 48 hours after the discontinuation of biotin in all patients, whereas normalization of levels of anti–thyrotropin receptor antibodies took up to several days in some patients. Normal ranges are as follows: thyrotropin, 0.85 to 6.46 μIU per milliliter; free T_4, 0.94 to 1.71 ng per deciliter; anti–thyrotropin receptor antibodies, less than 1.7 IU per liter; and total T_3, 0.8 to 2.6 ng per deciliter. BTBGD denotes biotin–thiamine–responsive basal ganglia disease, CoQ10 coenzyme Q10, and ND not determined.

† After the discontinuation of biotin, mild hypothyroidism became evident, with spontaneous recovery after the discontinuation of methimazole. Possible long-term complications due to transient hypothyroidism are unclear in this patient.

‡ Methimazole treatment intermittently normalized laboratory values during biotin treatment. After the discontinuation of biotin and methimazole, all values normalized completely. There was no evidence of long-term complications due to transient hypothyroidism.

Table 1. Characteristics of Six Children with Biotin-Induced Laboratory Indications of Autoimmune Hyperthyroidism.*

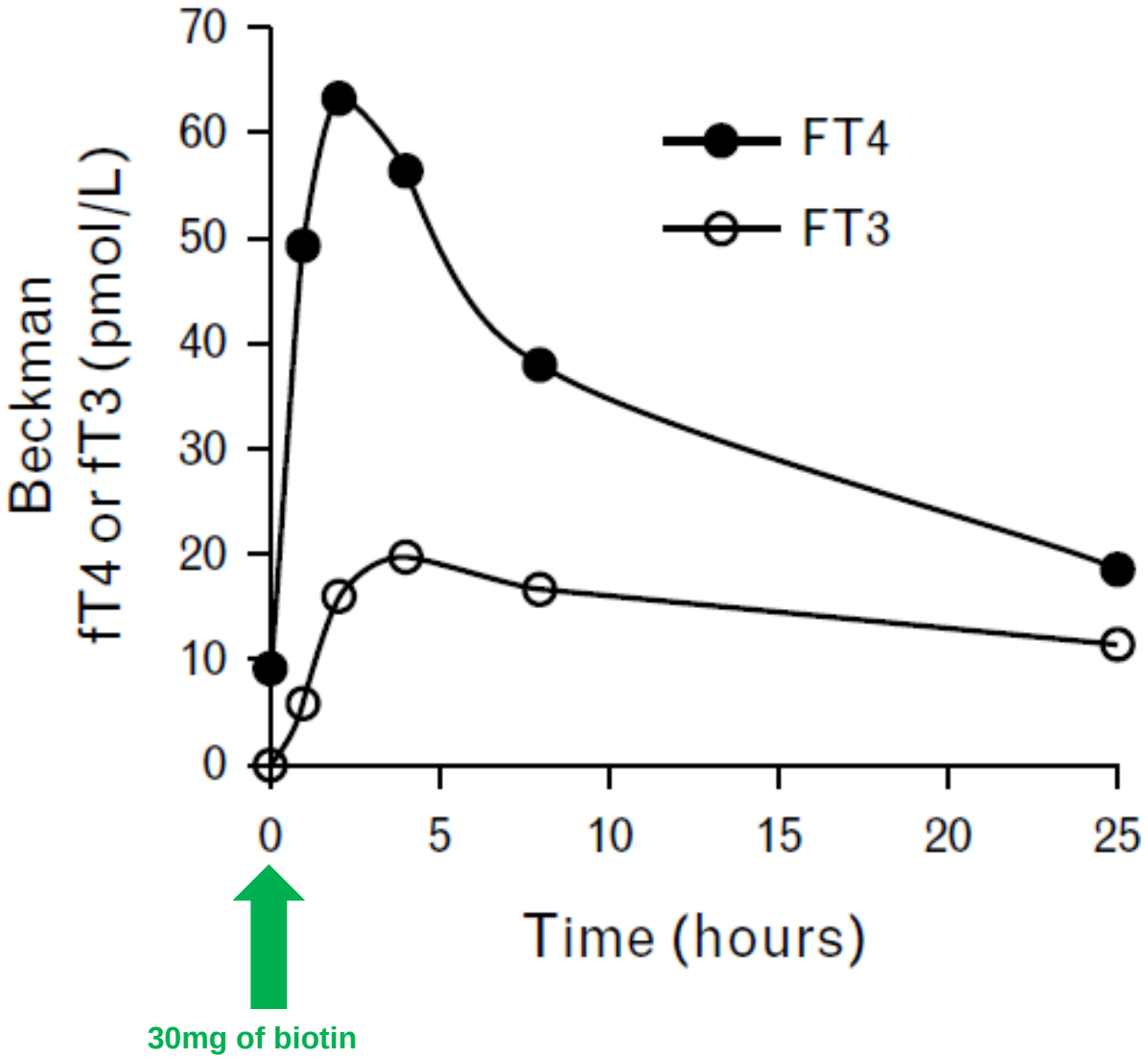
Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Sex	Female	Female	Male	Male	Male	Male
Age	9 yr	2 yr	2 yr	5 mo	1 mo	1 mo
Primary disease	BTBGD	BTBGD	BTBGD	Infantile mitochondrial disease	Neonatal mitochondrial disease	Neonatal mitochondrial disease
Biotin dose (mg/kg/day)	10	14	15	2	7	8
Concomitant medication	Thiamine	Thiamine, methimazole, cholecalciferol, levetiracetam, chloral hydrate	Thiamine, methimazole, oxcarbazepine	Thiamine, sodium phenylbutyrate, propranolol, nystatin, cholecalciferol	CoQ10, thiamine, cholecalciferol, carnitine, riboflavin, bisoprolol, aspirin, furosemide	CoQ10, thiamine, methimazole, cholecalciferol, carnitine, riboflavin
Laboratory results						
During biotin treatment						
Thyrotropin (μIU/ml)	0.05	0.02	0.04	0.02	0.08	0.03
Free T_4 (ng/dl)	6.24	>7.77	>7.77	>7.77	>7.77	>7.77
Anti–thyrotropin receptor antibodies (IU/liter)	38.6	>40.0	>40.0	>40.0	>40.0	>40.0
Total T_3 (ng/dl)	>6.5	ND	>6.5	>6.5	>6.5	ND
1–7 Days after discontinuation of biotin						
Thyrotropin (μIU/ml)	1.80	3.75	6.07	2.20	8.12	2.87
Free T_4 (ng/dl)	1.58	1.70	1.16	1.13	1.84	1.91
Anti–thyrotropin receptor antibodies (IU/liter)	<0.3	ND	0.7	1.0	0.4	<0.3
Total T_3 (ng/dl)	2.0	ND	1.8	ND	1.8	2.3
Antithyroid medication	No	Methimazole treatment for 14 mo with up to 1.9 mg/kg/day†	Methimazole treatment for 3.5 mo with up to 0.9 mg/kg/day‡	No	No	Methimazole treatment for 2 wk

The results were falsely increased or decreased according to whether a competitive method of measurement (for free T_4 and total T_3,) or noncompetitive method (for thyrotropin) was used.

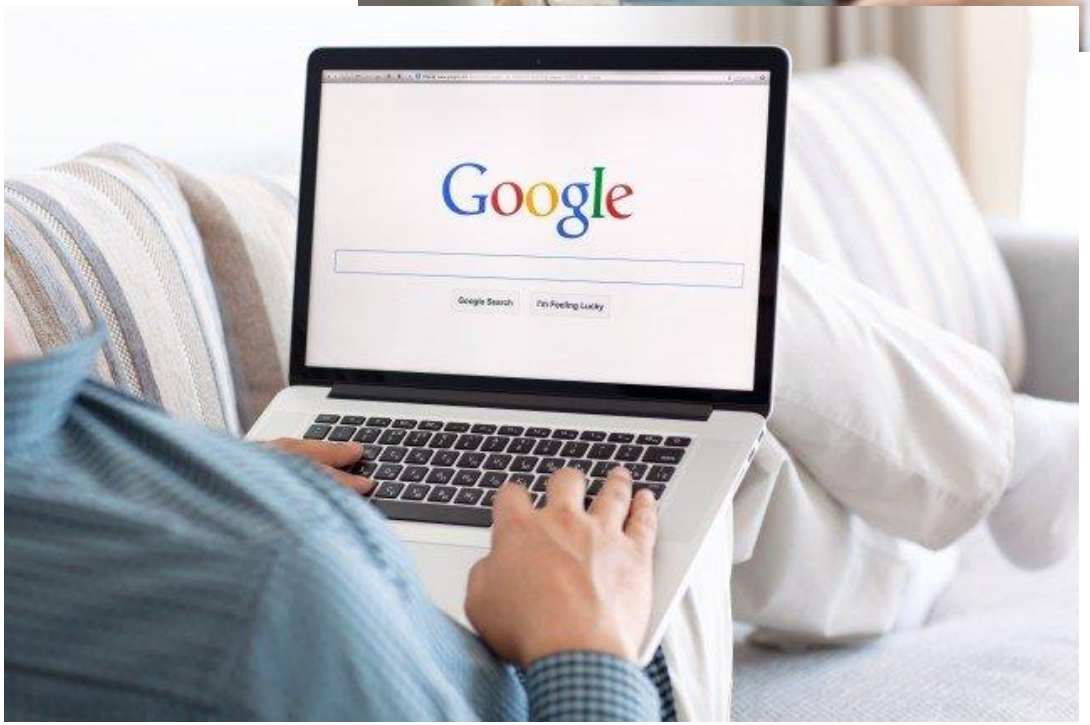
(T_3), and thyrotropin were normalized
took up to several days in some patients.
dies, less than 1.7 IU per liter; and total T_3,
. Possible long-term complications due to
ole, all values normalized completely.

N Engl J Med 2016; 375:704-706

Interference of the Ingested Biotin on fT4 and fT3



Wijeratne NG et al., Pathology · October 2012


Google
Google Search
I'm Feeling Lucky

?

DIE ZEIT

PREIS DEUTSCHLAND 3,50 €

WOCHENZEITUNG FÜR POLITIK WIRTSCHAFT WISSEN UND KULTUR

28. MÄRZ 2019 N° 14

Werden wir immer dümmer?

In fast allen westlichen Ländern sinkt der Intelligenzquotient. Woran das liegt – und was dagegen hilft DOSSIER

Macht mal langsam!

Die Schriftstellerin Thea Dorn kritisiert die Intoleranz vieler vermeintlich Toleranter SEITE 3

Das System der Täter

Odenwaldschule: Ein Opfer über neue Erkenntnisse im Missbrauchsskandal

Kultur & Gesellschaft, Seite 37

Das Massaker von Kerala

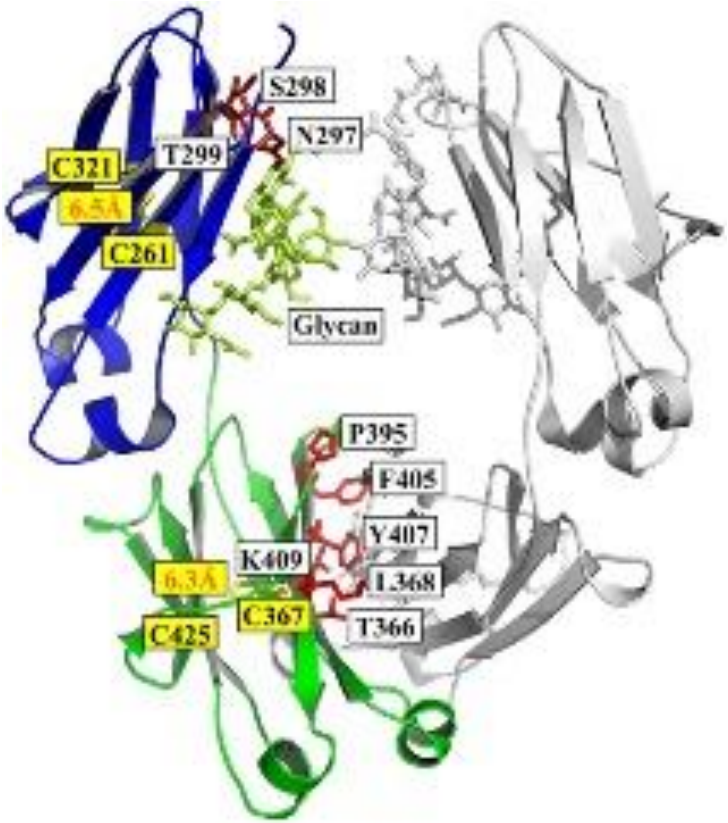
DOSSIER

Wir waren mal schlauer

Jahrzehntelang stieg der IQ in den meisten Industrienationen an, auch in Deutschland. Seit einigen Jahren aber sinkt er. Warum?

VON NATALY BLEUEL, NIKE HEINEN UND TANJA STELZER

Der erste therapeutische monoklonale Antikörper wurde im Jahr 1986 zugelassen. Muromonab-CD-23(Orthoclone OKT3®) ….



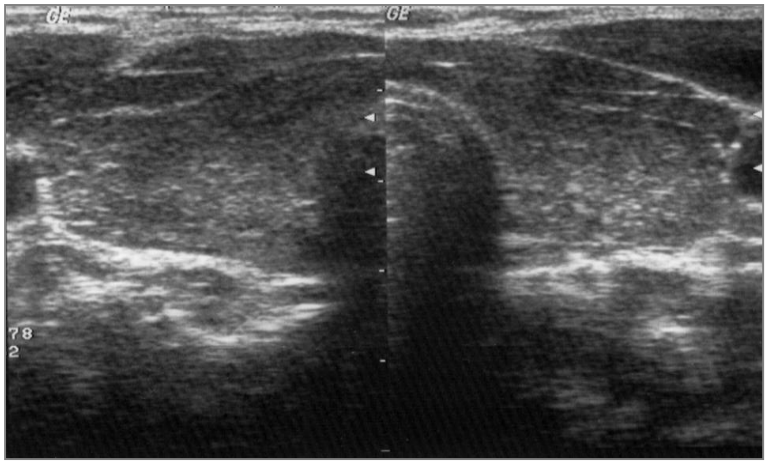
… bindet an den CD3-Rezeptor auf T-Zellen und wurde in der Transplantationsmedizin verwendet.

Checkpoint-Inhibitors (Antikörpertherapie) und Hashimoto

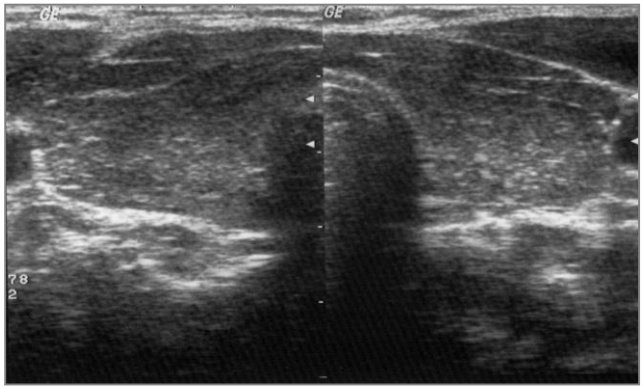
MON-575 - **Clinical Implication of Sonographic Evaluation for Immune Checkpoint Inhibitor-Related Thyroiditis: A Case Series Study**
A Ram Hong *et al.*, Gwangjui, South Korea

Monoclonale Antikörper

LIGANDS		
Benralizumab	IL-12	Lebrikizumab
Brodalumab	IL-13	Mepolizumab
Dupilumab	IL-17A	Nitric oxide (NO)
Eotaxin (CCL11)	IL-17F	Omalizumab
GM-CSF	IL-22	Pascolizumab
IL-1β	IL-23	Reslizumab
IL-4	IL-25	Secukinumab
IL-5	IL-31	TSLP
IL-9	IL-33	Ustekinumab



Checkpoint-Inhibitors (Antikörpertherapie) und Hashimoto



- Destructive and Immune-related **thyroiditis**: - induced by immune checkpoint inhibitors (ICIs)
  - Natural course are not well understood
- Study: **Patienten mit Thyreotoxikosis nach Antikörpertherapie**
  - → **Sonographische Charakteristika**
  - → **Klinischer Wert und Verlauf**

Study in single tertiary cancer center:

5 Patienten

"Thyrotoxicosis associated with ICI"

Modulation of:
- Cytotoxic T-lymphocyte antigen-4
- Programmed cell death
- Protein-1
- It ligand PD-L1

Normale SD-Funktion

Normal thyroid function at baseline (Prior to ICI-treatment)

→

Evaluation der SD-Funktion nach Ak-Therapie

Evaluation of thyroid function after initiation of ICIs

Included ICIs: - Pembrolizumab - Durvalumab - Atezolizumab	 n=2 n=2 n=1
Observed cancer diagnoses - Lung cancer - Cervix cancer - Transitional cell carcinoma	 n=3 n=1 n=1

Painless thyroiditis	Schmerzlose Thyreoiditis	100% (n = 5)
Asymptomatic thyrotoxicosis	Asymptomatische Thyreotoxikosis	n=3 (60.0%)
Median time from ICI-initia	Median der Ak-Gabe zur Thyreotoxikosis	**4 weeks**
Ultrasound features of thyroiditis	Sonogr. Zeichen der Thyreoiditis	**n=4 (80%)**
→ Mean time untill developement	Zeit bis zur Hypothyreose*	**6.8 weeks**
Positive Anti-thyroglobulin Abs (**TgAbs**) & **Anti-TP**	SD-Ak-positiv	n=3 (**75%**)
Normal thyroid gland (Echo) + positive TgAb**		n=1 (20%)
Grave's disease		n=0

*Patients remained on levothyroxine at 24 weeks after ICI treatment

**Patient developed hypothyroidism at 18 weeks after thyrotoxicosis & remained on levothyroxine at 24 weeks after ICI

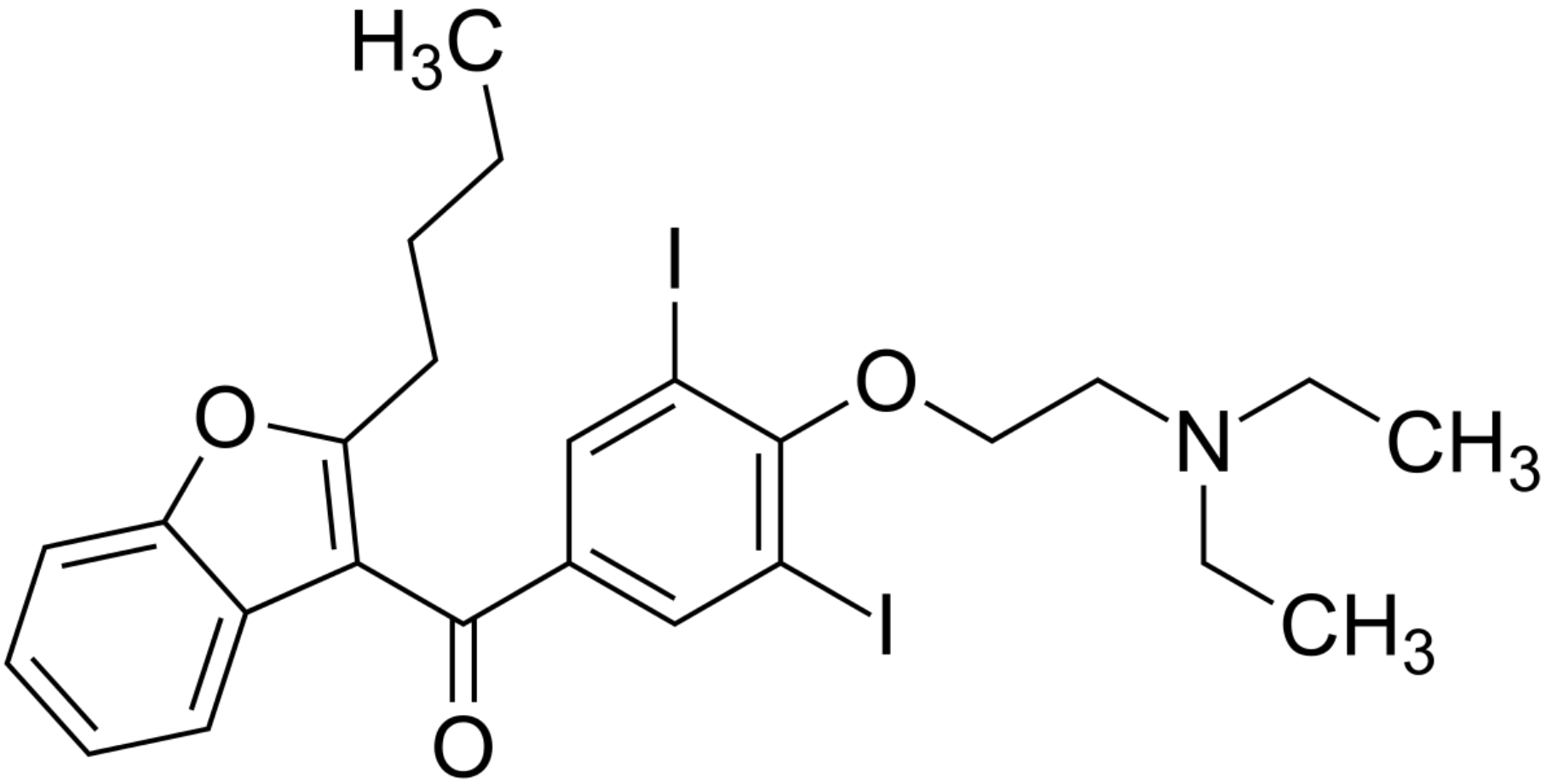
Zusammenfassung

- **Ak-Therapie induzierte Thyreotoxikose ist mit einer schmerzlosen Thyreoiditis assoziiert**

- **Sonographische Zeichen einer Thyreoiditis sind mit der Entwicklung einer Hypothyreose assoziiert**

- **Merke:**
- **Wenn die Sonographie unauffällig ist, kann die Entwicklung einer Hypothyreose nicht ausgeschlossen werden**

- **Monitoring der SD-Funktion muss in die Verlaufsuntersuchungen der Patienten mit einer Ak-Therapie eingeschlossen werden**


H3C
O
O
I
I
O
N
CH3
CH3

SD-Monitoring unter Amiodaron

MON-607 - **Monitoring Thyroid Function in Patients on Amiodarone: A Review of Practice Patterns and Adherence to the Recommended Guidelines in a Health Care System**

Ariane Davis *et al.*, Baltimore, USA

Background

SD-Dysfunktion in 15-20%

- Amiodarone has complex effects on thyroid, including thyroid dysfunction 15-20% of cases
- Spectrum of disease

Amiodaron-induzierte Hypothyreose (AIH)

Amiodaron-induzierte Hyperthyreose (AIT)

- The American Thyroid Association and **North American Society of Pacing** *recommend*:
  - **TFT at baseline** (before starting) and **then at regular intervals – baseline, 1 month, 3 months and then every 3-6 months (ATA)**

fT4: 0, 1, 3, 3-6 Monate

- Hypothesis: **Thyroid function in these patients may not be evaluated and monitored per recommendations in American health care system**

Studie-Einschluss:
Pat. mit Vorhofflimmern und ventrikulären Tachykardien

ICD 9/10 diagnosis of: Atrial and/or ventricular tachyarrhythmias

Retrospective review of medical charts
from outpatient clinic
January 2012 – December 2017

Patienten unter Amiodaron

Patients	N=1218
No baseline TSH: kein TSH vor Therapie	N=867 (71.2% 71%
Baseline TSH: - 3-month follow-up - 6-month follow-up	N=137 (11.24%) N=21/137 (15.3%) N=23/137 (16.8%)
Unknown amiodarone start date:	N=214 (17.5%)
≥1 TSH during amiodarone treatment:	N=484 (39.7%)
Abnormal TFTs after starting amic Abnormale fT4-Level - Mild thyroid function abnormalities - Preexisting hypothyroidism - Develo Amiodaron-induzierte Hypothyreose (AIH) - Develop Amiodaron-induzierte Hyperthyreose (AIT) - Development of subclinical hypothyroidism	N=152 (12%) 12% N=52/152 (34.21%) N=20/152 (13.15%) N=54/152 (35.5%) 36% N=10/152 (6.6%) 7% N=9/152 (21%)
Followed by cardiologist	93%
Followed by other healthcare providers	6.6%

Zusammenfassung: Patienten unter Amiodaron

- Findings revealed that **majority of patients**:
  - Were not appropriately evaluated before starting amiodarone therapy
  - Were not subsequently followed with T
    (As recommended in guidelines)
    - **Amiodaron-induzierte Hypothyreose (AIH) - 35%** (54/152)
      - Previous studies – 7-10%

Benjamins et al. Eur J Endo 2017
Martino et al. Horm Res 1987

- Further study is needed to understand the reasons behind the lack of appropriate evaluation

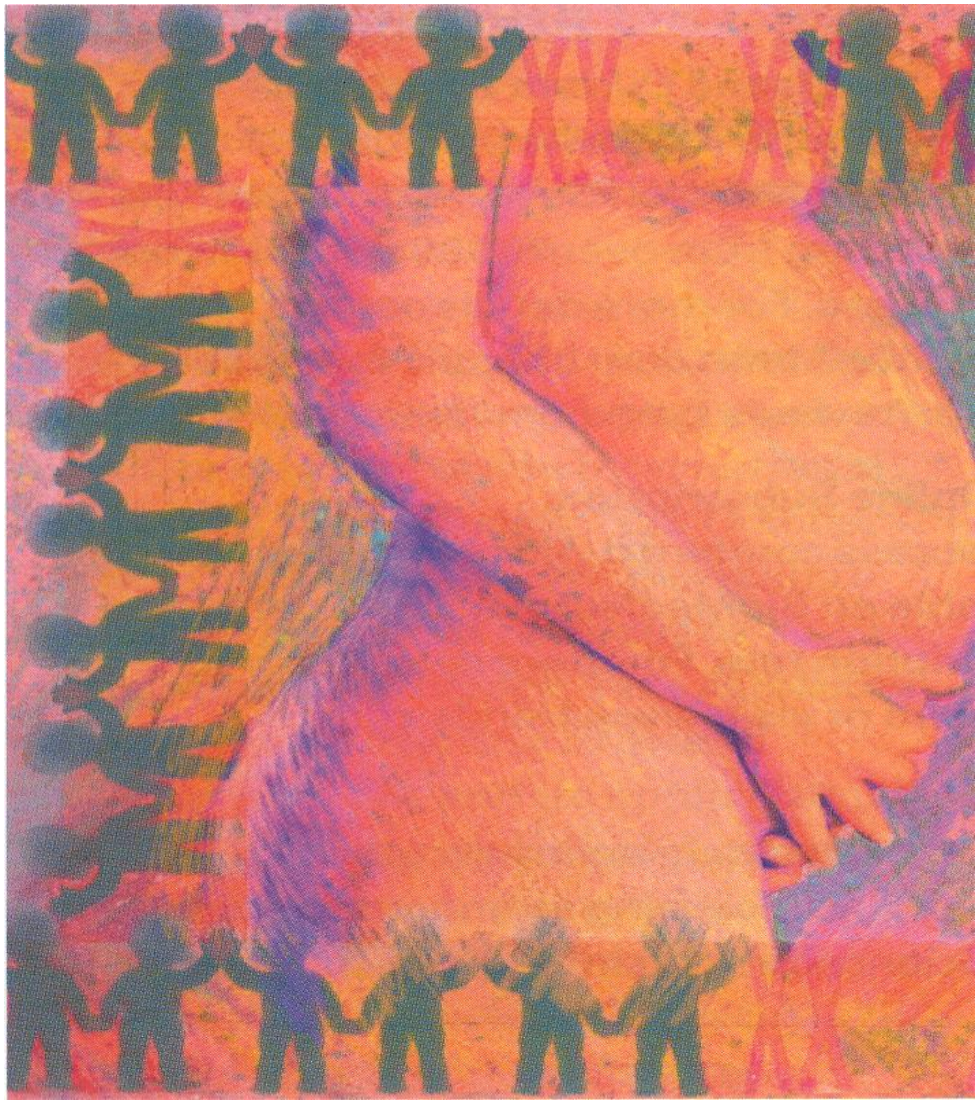
- Education of providers regarding the guidelines may be helpful

71% nur basales TSH, fT4

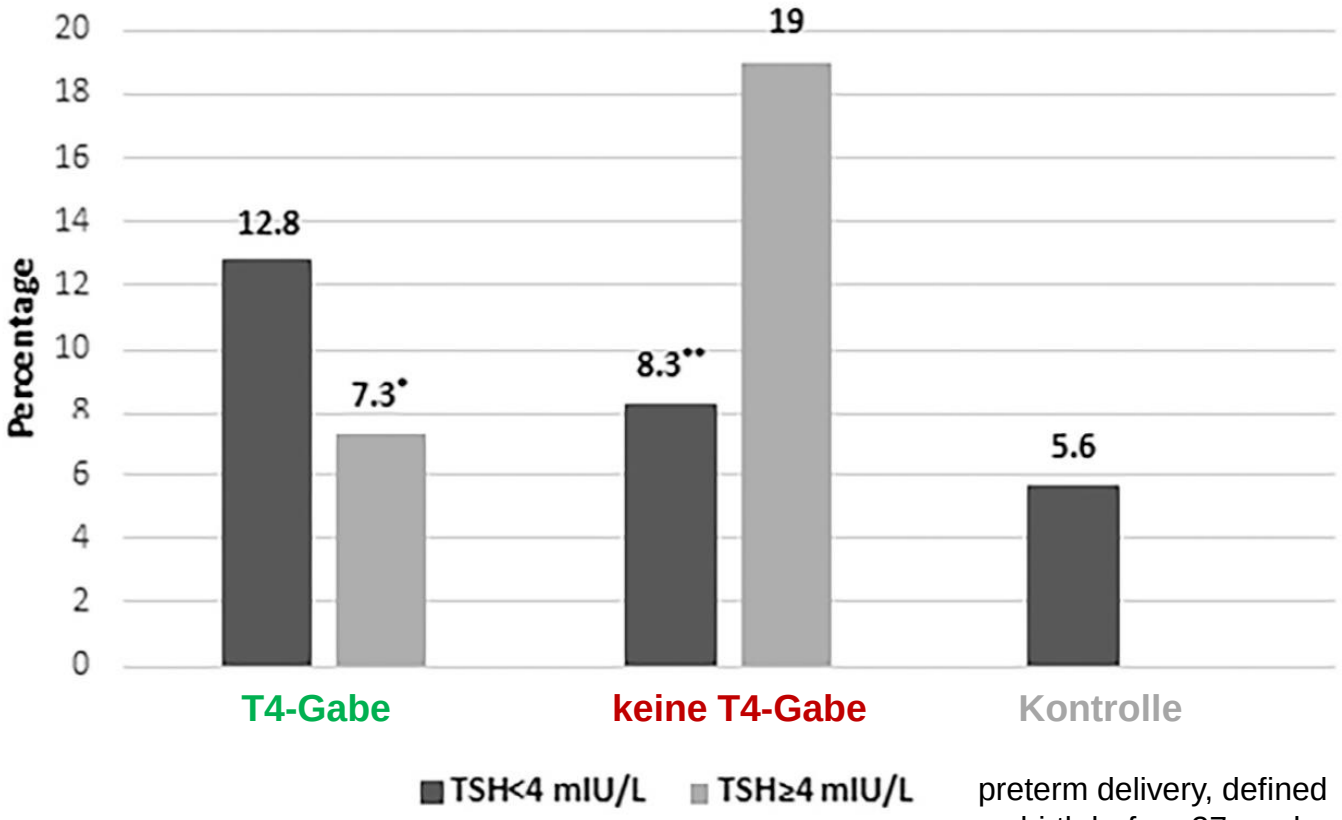
unzureichendes follow-up mit fT4

Leitlinien mehr beachten

Schilddrüse und Schwangerschaft



Effects of Levothyroxine on Pregnant Women With Subclinical Hypothyroidism, Negative for Thyroid Peroxidase Antibodies



preterm delivery, defined as birth before 37 weeks of gestation

In conclusion, this study provides evidence that replacement therapy with LT_4 in pregnant women with TSH concentrations of 2.5 to 4.0 mIU/L who are negative for TPOAb could not improve pregnancy outcomes, whereas treatment in women with TSH concentrations ≥4.0 mIU/L was beneficial in reducing preterm delivery.

The Journal of Clinical Endocrinology & Metabolism, Volume 103, Issue 3, March 2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Levothyroxine in Women with Thyroid Peroxidase Antibodies before Conception

Rima K. Dhillon-Smith, M.B., Ch.B., Ph.D., Lee J. Middleton, M.Sc., Kirandeep K. Sunner, M.Sc., Versha Cheed, M.Sc., Krys Baker, Samantha Farrell-Carver, Ruth Bender-Atik, B.A., Rina Agrawal, M.B., B.S., Ph.D., Kalsang Bhatia, M.B., B.S.,

a history of miscarriage or infertility.

Khashia Mulbagal, M.B., B.S., Natalie Nunes, M.B., B.S., M.D., Caroline Overton, M.D., Siobhan Quenby, M.D., Raj Rai, M.D., Nick Raine-Fenning, M.B., Ch.B., Ph.D., Lynne Robinson, M.B., Ch.B., M.D., Jackie Ross, M.B., B.S., Andrew Sizer, M.D., Ph.D., Rachel Small, B.Sc., F.R.C.O.G., Alex Tan, M.B., Ch.B., Martyn Underwood, M.B., Ch.B., Mark D. Kilby, D.Sc., M.D., Kristien Boelaert, M.D., Ph.D., Jane Daniels, Ph.D., Shakila Thangaratinam, Ph.D., Shiao Y. Chan, M.B., Ch.B., Ph.D., and Arri Coomarasamy, M.B., Ch.B., M.D.

N Engl J Med 2019;380:1316-25.

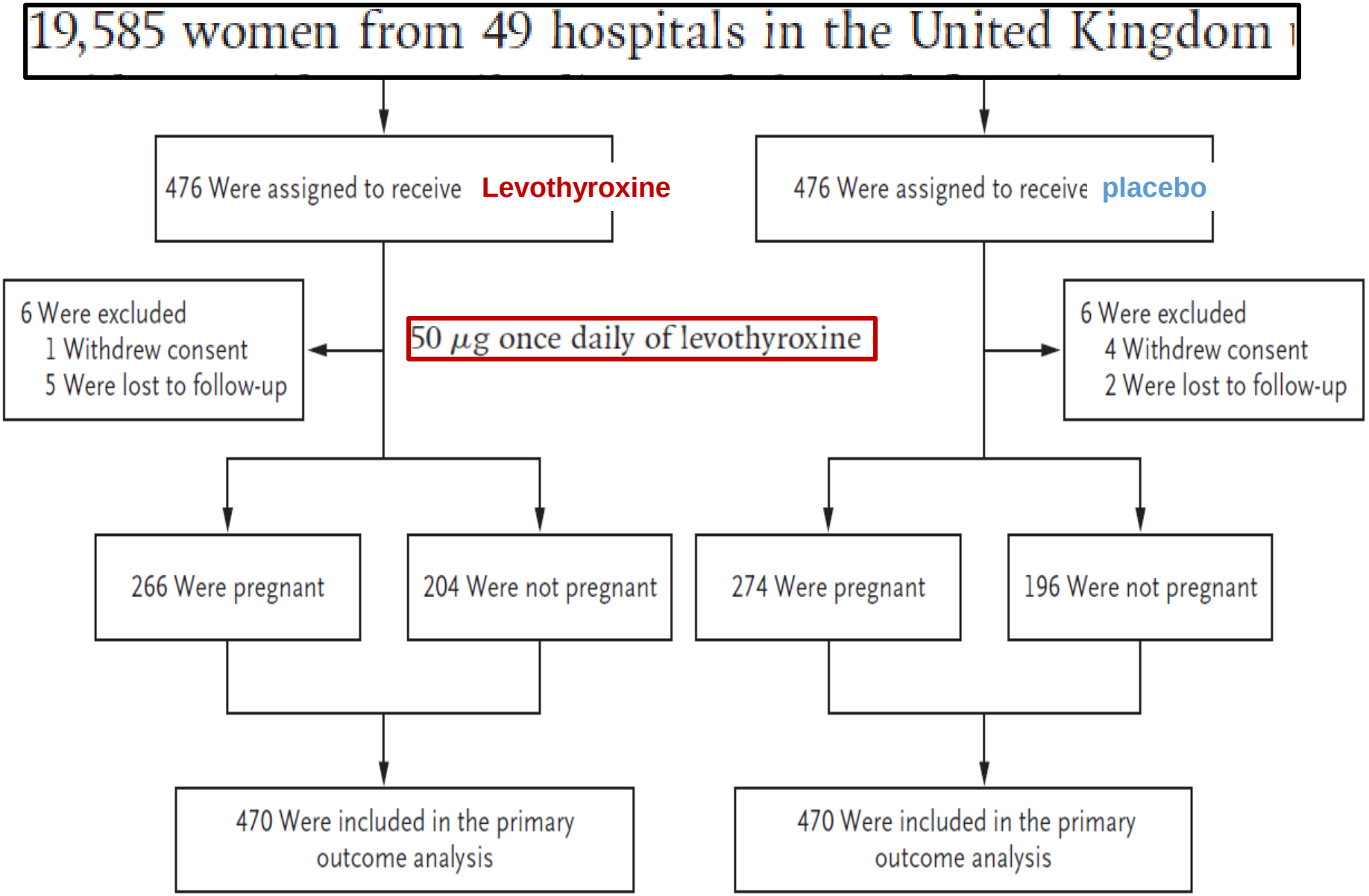


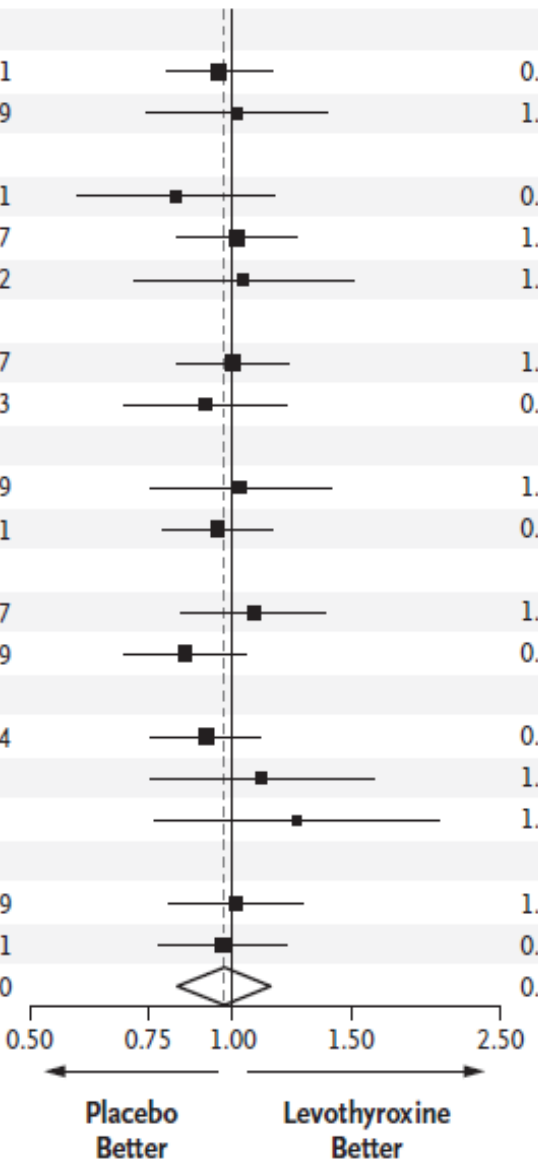
Figure 1. Enrollment, Randomization, Follow-up, and Analysis.

Table 1. Baseline Characteristics of the Participants.*

Characteristic		Levothyroxine Group (N = 476)	Placebo Group (N = 476)
Prerandomization thyroid hormone concentrations			
Serum thyrotropin level†			
≤2.5 mIU/liter — no. (%)		329 (69.1)	330 (69.3)
>2.5 mIU/liter — no. (%)		147 (30.9)	146 (30.7)
Median level (IQR) — mIU/liter	**TSH**	2.10 (1.51–2.74)	2.01 (1.45–2.70)
Level on log scale — mIU/liter		0.674±0.422	0.652±0.418
Mean serum free thyroxine level — pmol/liter		14.6±1.9	14.5±2.0
Median serum thyroid peroxidase antibody level (IQR) — IU/ml§	**TPO-Ak**	170 (83–428)	202 (94–417)

Outcome	Levothyroxine Group	Placebo Group	Relative Risk or Mean Difference (95% CI)††
Primary outcome			
Live birth at ≥34 wk — no./total no. (%)	176/470 (37.4)	178/470 (37.9)	0.97 (0.83 to 1.14)
Secondary outcomes			
Pregnancy at ≤12 mo after enrollment — no./total no. (%)	266/470 (56.6)	274/470 (58.3)	0.97 (0.88 to 1.07)

Subgroup	Levothyroxine	Placebo	Relative Risk (95% CI)	P Value for Interaction
	no. of women/total no.			
Maternal age				0.74
<35 yr	123/302	124/301	0.96 (0.80–1.15)	
≥35 yr	53/168	54/169	1.02 (0.75–1.38)	
No. of previous miscarriages				0.55
0	44/157	51/151	0.83 (0.59–1.16)	
1 or 2	98/219	91/217	1.02 (0.83–1.25)	
≥3	34/94	36/102	1.04 (0.72–1.51)	
Thyrotropin concentration at baseline				0.59
≤2.5 mIU/liter	121/325	120/327	1.00 (0.83–1.22)	
>2.5 mIU/liter	55/145	58/143	0.91 (0.69–1.20)	
Infertility treatment at time of randomization				0.67
Yes	61/215	58/209	1.03 (0.76–1.40)	
No	115/255	120/261	0.95 (0.79–1.15)	
Thyroid peroxidase antibody concentration at baseline				0.16
Very high (≥50th percentile)	79/217	82/247	1.08 (0.84–1.38)	
High (<50th percentile)	93/247	95/219	0.85 (0.69–1.05)	
Race or ethnic group				0.40
White	121/324	132/334	0.91 (0.76–1.10)	
South Asian	37/108	30/92	1.11 (0.76–1.62)	
Chinese, black, or other	18/38	16/44	1.25 (0.77–2.03)	
BMI				0.78
≥25	87/237	88/239	1.01 (0.81–1.27)	
<25	87/219	88/221	0.97 (0.78–1.21)	
All participants	176/470	178/470	0.97 (0.83–1.14)	0.74



Hormonanalytik nach partieller Thyreoidektomie

MON-609 - **Hormonal Outcomes after Partial Thyroidectomy: The Cleveland Clinic Experience**

Keren Zhou *et al.*, Cleveland, USA

Background

- Partial thyroidectomies (PT):
  - Frequent surgical procedure
  - Controversy about thyroid hormonal outcomes
- Large number of patients start thyroid hormone replacement (THR) immediately post PT
- Study: Examination of Cleveland Clinic (CC) data to provide insight to these questions

Häufiges Prozedere

Kontroverse über Hormonstatus-Interpretation

viele starten die Levothyroxintherapie direkt nach der OP

Inclusion criteria:
- PT performed at Cleveland Clinic
- Between 2000-2010

Exclusion criteria:
- Unexplained thyrotoxicosis
- Lost to follow-up in 1st year
- Completion thyroidectomy/RAI in follow-up

→ **Data collection: (5 years post PT)**
- Baseline variables
- Thyroid hormone levels/replacemen

- Classification based on hormonal outcomes:

Overt hypothyroidism (OH, TSH >10 uU/mL or TSH >4.2 uU/mL started on THR)

Subclinical hypothyroidism (SH, TSH >4.2-10 uU/mL with no THR)

Euthyroid (Eu, TSH 0.4-4.2 uU/mL with no THR)

Second cohort: Immediate start on THR (TSH<0.4 uU/nL)

↓ Follow up for 5 years (longer if patient was Eu)

Patients	N=**380**
Average age at surgery	51 years
Female	77.4%
Follow-up	58.4 months
No immediate start of THR: - Development - Deve - Continuing E	N=244 N=73 (**29.9%**) N=29 (11.9%) N=142 **(58.2%)**

Hypothyreose TSH >10 mU/l

Subklin. Hypothyreose TSH 4.2 – 10 mU/l

Euthyreose TSH 0.4-4.2 mU/l

TSH (mU/l)	>10	4.2 – 10	0.4 - 4.2	
	OH	**SH**	**Eu**	**P-value**
Euthyroid vs. **Overt Hypothyroid**:				
- Weight adjusted remaining gland			**Larger lobe**	P=0.015
- History of Lymphocytic infiltrate			**Lower rate**	P=0.021
			AITD	P<0.001
- TSH	1.9 [1.5,2.3]		1.1 [0.84,1.6]	
- Positive antibody status - Family history of thyroid disorders - Radiation history	Similar			
Subclinical hypothyroid group during follow-up		**48.1%** *normalized with* final TSH 3.4 [2.2,3.7]		

Zusammenfassung: Patienten nach part. SD-Resektion

- **Mehrheit (58%) bleibt euthyreot**
- **Niedriger Ausgangs-TSH macht eine post-OP-Euthyreose wahrscheinlich**
- **Viele Patienten erreichen nach einer post-OP-subklin. Hypothyreose eine Euthyreose**

DOSSIER

Jahrzehntelang stieg der IQ in den meisten Industrienationen an, auch in Deutschland. Seit einigen Jahren aber sinkt er. Warum?

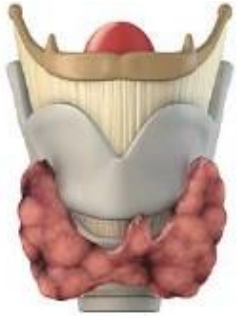
VON NATALY BLEUEL, NIKE HEINEN UND TANJA STELZER

Werden wir wieder schlauer ???

Ja, … es fragt sich nur wann????

Update Schilddrüsenerkrankungen

9.4.2019 in Bochum



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

www.endo-bochum.de