

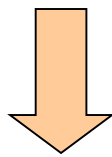
# Labor beim Schilddrüsenknoten

Georg Zettinig

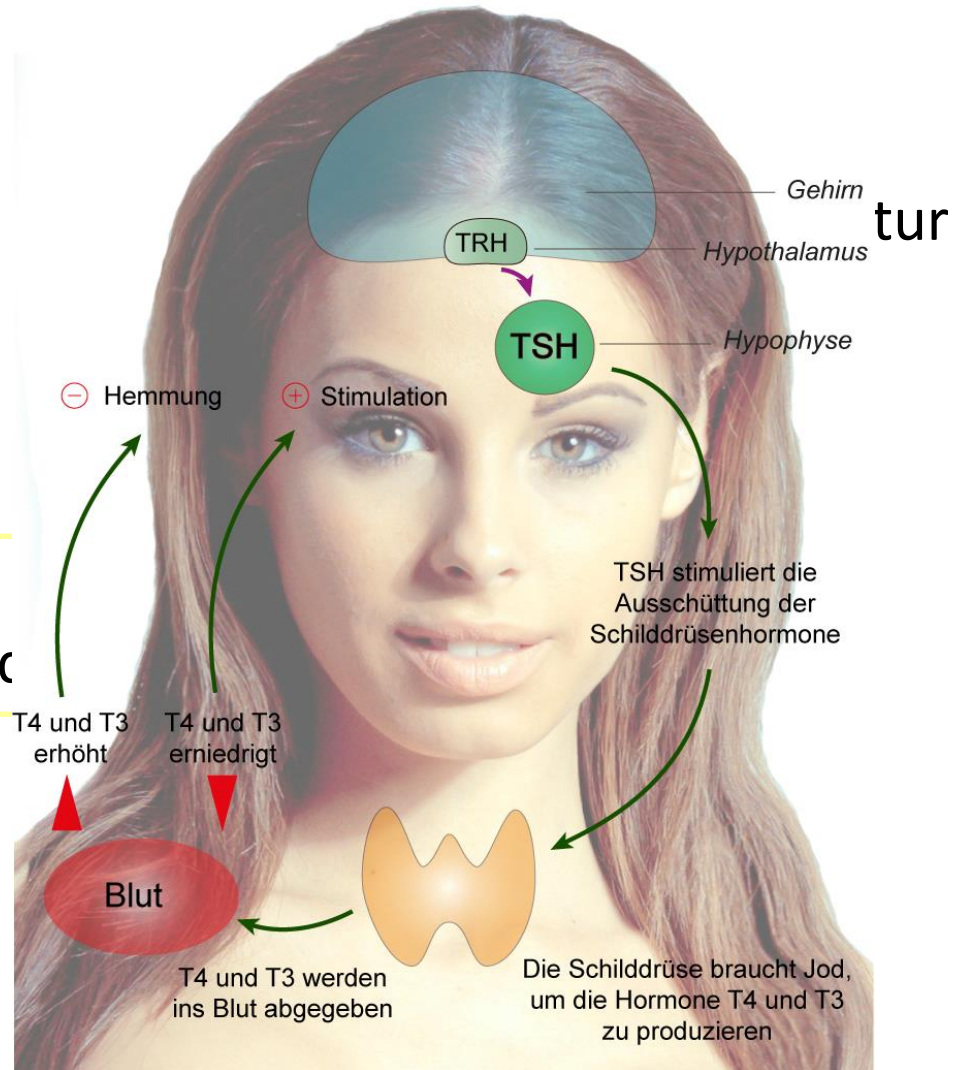


# Erkrankungen der Schilddrüse

Gestörte  
Funktion



der zugrunde



tur



# Erkrankungen der Schilddrüse

Ultraschall: primäre Screeningmethode beim Schilddrüsenknoten!!!

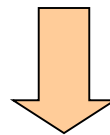


Gestörte  
Morphologie/Struktur



**DIAGNOSE**

Ursacheliegenden Erkrankung



Therapie

# Take Home Message 1

- Wichtigste Methode zur Abklärung von Schilddrüsenknoten ist die Sonografie
- Blutwerte sind bei SD Knoten meist unauffällig und nicht zur Dignitätsbeurteilung eines Knotens geeignet (einzige Ausnahme: die 10% medullären Karzinome)

*Thyroid* ©2015 American Thyroid Association DOI: 10.1089/thy.2015.0020

## **2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer**

The American Thyroid Association (ATA) Guidelines Taskforce  
on Thyroid Nodules and Differentiated Thyroid Cancer Bryan R. Haugen, M.D.<sup>1</sup> (Chair)\*,  
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M.D., M.P.H.<sup>5</sup>, Yuri E. Nikiforov, M.D., Ph.D.<sup>6</sup>,  
Furio Pacini, M.D.<sup>7</sup>, Gregory W. Randolph, M.D.<sup>8</sup>, Anna M. Sawka, M.D., Ph.D.<sup>9</sup>,  
Martin Schlumberger, M.D.<sup>10</sup>, Kathryn Schuff, M.D.<sup>11</sup>, Steven I. Sherman, M.D.<sup>12</sup>,  
Julie Ann Sosa, M.D.<sup>13</sup>, David L. Steward, M.D.<sup>14</sup>, R. Michael Tuttle, M.D.<sup>15</sup>,  
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\*Authors are listed in alphabetical order and were appointed by ATA to independently formulate the content of this manuscript. None of the scientific or medical content of the manuscript was dictated by the ATA.

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<sup>2</sup> Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

# Definition Knoten

- Läsion in der Schilddrüse, die sonografisch abgrenzbar ist
- Einzelne tastbare Läsionen können kein sonografische Korrelat zeigen (definitionsgemäß keine Knoten)
- Nicht palpable Knoten: Inzidentalom
- Diese haben gleich hohes Malignitätsrisiko wie tastbare Knoten

*[A2] What is the role of thyroid cancer screening in people with familial follicular-cell derived differentiated thyroid cancer?*

■ **RECOMMENDATION 1**

Screening people with familial follicular cell-derived differentiated thyroid cancer may lead to an earlier diagnosis of thyroid cancer, but the panel cannot recommend for or against ultrasound screening since there is no evidence that this would lead to reduced morbidity or mortality. (**No recommendation, Insufficient evidence**)

*[A4] Serum TSH measurement*

■ **RECOMMENDATION 2**

A) Serum TSH should be measured during the initial evaluation of a patient with a thyroid nodule. (**Strong recommendation, Moderate-quality evidence**)

B) If the serum TSH is subnormal, a radionuclide (preferably  $^{123}\text{I}$ ) thyroid scan should be performed. (**Strong recommendation, Moderate-quality evidence**)

C) If the serum TSH is normal or elevated, a radionuclide scan should not be performed as the initial imaging evaluation (**Strong recommendation, Moderate-quality evidence**)

*[A5] Serum thyroglobulin measurement*

■ **RECOMMENDATION 3**

Routine measurement of serum Tg for initial evaluation of thyroid nodules is not recommended. (**Strong recommendation, Moderate-quality evidence**)

*[A6] Serum calcitonin measurement*

■ **RECOMMENDATION 4**

The panel cannot recommend either for or against routine measurement of serum calcitonin in patients with thyroid nodules. (**No recommendation, Insufficient evidence**)

# Amerika vs. Mitteleuropa

- TSH zur Bestimmung der Schilddrüsenfunktion essentiell
- Thyreoglobulin hat beim nicht thyreoidektomierten / nicht radiojodtherapierten keinen Stellenwert als Routine-Laborparameter
- Kalzitonin-Screening: In Europa komplett gegenteilig
- Weitere Laborparameter haben in Europa ebenfalls wichtigen Stellenwert

# Welche Laborparameter

- TSH
  - basal / (nach TRH-Stimulation)
- Schilddrüsenhormone
  - die freien Schilddrüsenhormone (fT3, fT4)
  - Gesamt-T3, Gesamt-T4
- Schilddrüsenantikörper
  - gegen Thyreoglobulin (Tg-AK)
  - gegen Schilddrüsenperoxidase (anti-TPO)
  - gegen TSH-Rezeptor (TRAK)
- Kalzitonin

# Welche Laborparameter

- TSH
  - basal / (nach TRH-Stimulation)
- Schilddrüsenhormone
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  - gegen Thyreoglobulin (Tg-AK)
  - gegen Schilddrüsenperoxidase (anti-TPO)
  - gegen TSH-Rezeptor (TRAK)
- Kalzitonin

# Personalisierte Medizin

- TSH - primärer Screeningparameter
- fT4, fT3
- Individuelle Setpoints für TSH, fT4, fT3
- Nach einer Operation kann die Befindlichkeit eingeschränkt sein, wenn die präoperativen fT4 und fT3 Werte nicht individuell substituiert werden

# Individuelle Postoperative Substitution - Korrelation der postop. T4 Dosis mit

- Gewicht
- BMI
- Alter
- Erythrozytenvolumen
- Präoperativer fT3 Wert

THYROID  
Volume 24, Number 12, 2014  
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DOI: 10.1089/thy.2014.0111

ORIGINAL STUDIES  
THYROID FUNCTION AND DYSFUNCTION

## A New Strategy to Estimate Levothyroxine Requirement After Total Thyroidectomy for Benign Thyroid Disease

Vincenzo Di Donna,<sup>1</sup> Mario Giannotti Santoro,<sup>1</sup> Chiara de Waure,<sup>2</sup> Maria Pia Ricciato,<sup>1</sup>  
Rosa Maria Paragliola,<sup>1</sup> Alfredo Pontecorvi,<sup>1</sup> and Salvatore Maria Corsello<sup>1</sup>

**Background:** The current approach for calculating the starting dose of levothyroxine (LT4) after total thyroidectomy is based on the patient's body weight (BW). The aim of the study was to identify the major predictive factors of LT4 requirement and to elaborate a new method to improve the accuracy of the LT4 starting dose after total thyroidectomy.

**Methods:** The study consists of two parts. The first part consisted of the retrospective identification of 92 adult patients (retrospective cohort) who had undergone a total thyroidectomy for benign disease and who had begun LT4 treatment at a dose of 1.6 µg/kg/day. Adjustments to optimize the LT4 dose were then performed at the post-surgery follow-up on the basis of serum thyrotropin (TSH) levels. The results of this retrospective analysis were used to formulate a nomogram for a proper calculation of the LT4 starting dose that was then used

## EFFECTS OF THYROXINE AS COMBINED WITH TRIIODOTHYRONINE IN PATIENTS WITH HYPOTHYROIDISM

ROBERTAS BUNEVIČIUS, M.D., PH.D., GINTAUTAS KAŽANAS, M.D., PH.D., AND ARTHUR J. PRADELLA, M.D.

## ABSTRACT

**Background** Patients with hypothyroidism are usually treated with thyroxine (levothyroxine) only, although both thyroxine and triiodothyronine are secreted by the normal thyroid gland. Whether thyroid secretion of triiodothyronine is physiologically important is unknown.

**Methods** We compared the effects of thyroxine alone with those of thyroxine plus triiodothyronine (liothyronine) in 33 patients with hypothyroidism. Each patient was studied for two five-week periods. During one period, the patient received his or her usual dose of thyroxine. During the other, the patient received a regimen in which 50  $\mu\text{g}$  of the usual dose of thyroxine was replaced by 12.5  $\mu\text{g}$  of triiodothyronine. The order in which each patient received the two treatments was randomized. Biochemical, clinical, and psychological tests were performed at the end of each treatment period.

**Results** The patients had lower serum thyroxine concentrations and higher triiodothyronine concentrations after treatment with thyroxine plus triiodothyronine than after treatment with thyroxine alone, whereas the serum thyrotropin concentrations were similar after both treatments. A mean

European  
Thyroid Journal

## Guidelines

Eur Thyroid J 2012;1:55–71  
DOI: 10.1159/000339444Received: 11/15/11  
Accepted: 1/10/12  
Published: 2/1/12

## 2012 ETA Guidelines: The Use of L-T4 + L-T3 in the Treatment of Hypothyroidism

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The Journal of Clinical Investigation

RESEARCH ARTICLE

## Differences in hypothalamic type 2 deiodinase ubiquitination explain localized sensitivity to thyroxine

Joao Pedro Werneck de Castro,<sup>1,2</sup> Tatiana L. Fonseca,<sup>1,2</sup> Cintia B. Ueta,<sup>1</sup> Elizabeth A. McAninch,<sup>1,2</sup> Sherine Abdalla,<sup>1</sup> Gabor Wittmann,<sup>3</sup> Ronald M. Lechan,<sup>3</sup> Balazs Gereben,<sup>4</sup> and Antonio C. Bianco<sup>1,2</sup>

<sup>1</sup>Division of Endocrinology, Diabetes and Metabolism, University of Miami School of Medicine, Miami, Florida, USA. <sup>2</sup>Division of Endocrinology and Metabolism, Rush University Medical Center, Chicago, Illinois, USA. <sup>3</sup>Department of Medicine, Division of Endocrinology, Diabetes and Metabolism, Tufts Medical Center, Boston, Massachusetts, USA. <sup>4</sup>Department of Endocrine Neurobiology, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary.

The current treatment for patients with hypothyroidism is levothyroxine (L-T4) along with normalization of serum thyroid-stimulating hormone (TSH). However, normalization of serum TSH with L-T4 monotherapy results in relatively low serum 3,5,3'-triiodothyronine (T3) and high serum thyroxine/T3 (T4/T3) ratio. In the hypothalamus-pituitary dyad as well as the rest of the brain, the majority of T3 present is generated locally by T4 deiodination via the type 2 deiodinase (D2); this pathway is self-limited by ubiquitination of D2 by the ubiquitin ligase WSB-1. Here, we determined that tissue-specific differences in D2 ubiquitination account for the high T4/T3 serum ratio in adult thyroidectomized (Tx) rats chronically implanted with

# TSH, fT4, fT3

- TSH ist der wichtigste Parameter zur Beurteilung der Schilddrüsenfunktion
- Dokumentation präoperativer fT4 und fT3 Werte wichtig falls postoperativ Probleme mit der Schilddrüsenhormonsubstitution
- Kombinationspräparate nur dort einsetzen wo indiziert
- Großzügiger Einsatz von Kombinationspräparaten ohne entsprechende Indikation fahrlässig

# Welche Laborparameter

- TSH
  - basal / (nach TRH-Stimulation)
- Schilddrüsenhormone
  - die freien Schilddrüsenhormone (fT3, fT4)
  - Gesamt-T3, Gesamt-T4
- Schilddrüsenantikörper
  - gegen Thyreoglobulin (Tg-AK)
  - gegen Schilddrüsenperoxidase (anti-TPO)
  - gegen TSH-Rezeptor (TRAK)
- Kalzitonin

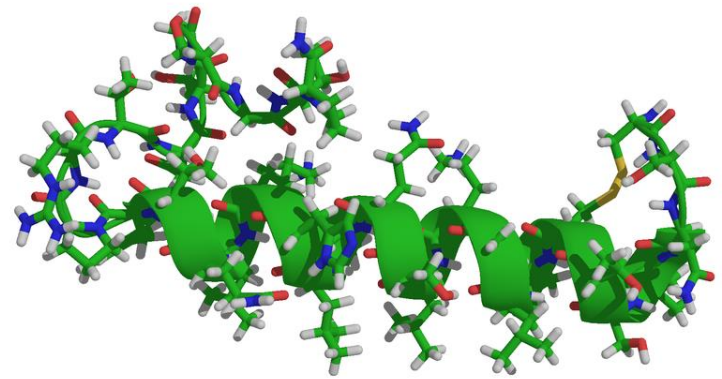
# Antikörper

- TPO Antikörper, Tg Antikörper
  - Ausdruck einer chronischen Immunthyreoiditis
  - Radiologisch beschriebene "Knoten" oft nur fokale Thyreoiditis
- TRAK (TSH Rezeptor Antikörper)
  - Beim Schilddrüsenknoten TRAK nicht nachweisbar.
  - Stimmt die Diagnose?

# Welche Laborparameter

- TSH
  - basal / (nach TRH-Stimulation)
- Schilddrüsenhormone
  - die freien Schilddrüsenhormone (fT3, fT4)
  - Gesamt-T3, Gesamt-T4
- Schilddrüsenantikörper
  - gegen Thyreoglobulin (Tg-AK)
  - gegen Schilddrüsenperoxidase (anti-TPO)
  - gegen TSH-Rezeptor (TRAK)
- Kalzitonin

# Kalzitonin



- 1961 erstmals in isolierten Schild- und Nebenschilddrüsen von Hunden postuliert (Copp und Cameron),
- 1967 Produktion in parafollikulären Zellen erkannt
- Senkt den Blutkalziumspiegel
- Antagonist zum Parathormon
- Im Vergleich zu PTH und Vitamin D Effekt gering

# Vierhapper JCEM 1997

n=1062

## Routine Measurement of Plasma Calcitonin in Nodular Thyroid Diseases

H. VIERHAPPER, W. RABER, C. BIEGLMAYER, K. KASERER, A. WEINHÄUSL,  
 AND B. NIEDERLE

*Division of Endocrinology and Metabolism, Department of Internal Medicine III, Institute for Medical and Chemical Laboratory Diagnostics, Institute of Pathology, and the Department of Surgery, Division of General Surgery, University of Vienna, and St. Anna Kinderspital, Vienna, Austria A-1090*

### ABSTRACT

In a prospective study, plasma concentrations of human calcitonin (hCT) were determined in 1062 consecutive patients with thyroid nodular disease. Basal plasma hCT was above the normal range (>6

a small (diameter, 3 mm) medullary thyroid carcinoma (MTC). Including this patient, MTC was found in 6 of the 12 patients. We conclude that the routine determination of hCT in all patients with thyroid nodular disease should be supplemented by pentagastrin-

Plasma hCT (pg/ml)	basal	Anstieg auf > 100 nach Pentag.	Diagnose			
			unklar	benigne	CCH	MTC
<1.0	767					
1.0 - 5.0	223					
5.0 – 10.0	38	1/38		1		
10 - 20	20	4/20	1		3	
20 - 100	11	6/11			3	3
> 100	3	3/3				3

# SMENA - Kriterien

- Nichols Diagnostics
- basal > 100: MTC wahrscheinlich
- basal > 10: Pentagastrin Stimulation nüchtern
- basal sowie 2 min, (3 min,) 5 min, (10 min) nach 0,5 µg/kg KG Pentagastrin

## CHAPTER 25 Sporadic Medullary Thyroid Microcarcinoma

BRUNO NIEDERLE, CHRISTIAN SCHEUBA

### Introduction

Thorough experience has been gained from biochemical screening programs for the early diagnosis of C-cell disease in families with hereditary medullary thyroid cancer (MTC).<sup>1,2</sup> Based on such research, several study groups outside North America have considered routine calcitonin (CT) measurements (CT screening) worthwhile in patients with nodular thyroid disease with the objective of diagnosing sporadic MTC in an early and therefore potentially curable stage (see Chapters 23, Sporadic Medullary Thyroid Carcinoma and 24, Sporadic Medullary

### Definition and Clinical and Biochemical Characteristics of Medullary Thyroid Microcarcinoma and C-Cell Hyperplasia

#### Definition

MTC refers to malignant tumors of the thyroid gland show-

# Calcitonin Screening



## Conclusion

- Basal Calcitonin measurements „must“ be performed in all patients independent the „thyroid morphology“
- bCT >10pg/ml → Pentagastrin stimulation
- sCT > 100 pg/ml → Surgery
- Genetic Screening!

Sporadic / Medullary Thyroid Cancer.  
B. Niederle 2006, [www.gep-net.com](http://www.gep-net.com)

# Stand der Dinge

- Testverfahren wurden verändert
  - es gibt keinen Goldstandard
- Pentagastrin nicht verfügbar



# Bieglmayer et al., 2007

- Vergleich Nicols (NID) mit Diagnostic Products Corporation (DPC), Diasorin (DS), Scantibodies (SC)
- DPC = Immulite = Siemens
  - DPC misst bei Thyreoidektomierten kein Kalzitinin
  - Basal:  $DPC = 0.78 * NID - 0.3$
  - Pentagstrin: DPC entspricht NID
- Diasorin
  - $DS \approx NID + 3.1$
  - $DS = DPC / 0.8 + 3.4$

Clin Chem Lab Med 2007;45(5):662-666 © 2007 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2007.124

## Measurement of calcitonin by immunoassay analyzers

Christian Bieglmayer<sup>1,\*</sup>, Heinrich Vierhapper<sup>2</sup>,  
Robert Dudczak<sup>3</sup> and Bruno Niederle<sup>4</sup>

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<sup>2</sup> Department for Endocrinology and Metabolism,

**Keywords:** auto-analyzer; calcitonin; method  
comparison.

### Introduction

Analysis of calcitonin (CT) in patients with nodular  
thyroid disease is an important tool in the early detec-

# Kratsch et al., Clin Chem Endocrinol 2009

- Immulite 2000, Diasorin (LIA), Medipan (IRMA), sowie PCT Kryptor
- viermal Einfrieren / Auftauen hat keinen Einfluss
- -40°C: > 7 Tage stabil
- 4-8°C (Kühlschrank):
  - nach 6 h reduzierte Konzentrationen bei allen Assays
  - nach 12h Konzentration um 23% reduziert
  - nach 7 Tagen 65% (IL), 33.5% (LIA), 91% (IRMA)
- Raumtemperatur: nur 2 h stabil

# Kratsch et al., Clin Chem Endocrinol 2009

- Verschiedene Assays geben unterschiedliche Konzentrationen an.

		IL	LIA	IRMA
Hashimoto		1.0	3.1	0
PPI		6.8	11.4	31.8
Interne Patienten		2.0	10	26

mäßig erhöht in %

# Kratsch et al., Clin Chem Endocrinol 2009

- 31% der Nierenpatienten mit PPI hatten erhöhte Kalzitoninwerte
- Signifikante Korrelation mit Schwere der Niereninsuffizienz

		IL	LIA	IRMA
CNI		13	9.8	24.4
Dialyse		11.1	1.6	71.4
NTX		23.7	18.2	23.7

in %

# Thyreoidektomierte

- IL: alle unter Nachweisgrenze
- LIA: 97% unter Nachweisgrenze
- IRMA: 3 % unter Nachweisgrenze

# Pentagastrin

- IL und LIA höher stimulierbar als IRMA
- Beim basalen CT Overlap MTC/NINS
  - IL n=2, LIA n=3, IRMA n=0
- Pentagastrin: alle MTC klar von den Niereninsuffizienten abgrenzbar in allen Assays

Acta Radiol Oncol. 1980;19(2):85-9.

## **Pentagastrin, calcium and whisky stimulated serum calcitonin in medullary carcinoma of the thyroid.**

Emmertsen KK, Nielsen HE, Mosekilde L, Hansen HH.

### **Abstract**

The efficiency of pentagastrin, calcium and whisky in raising serum immunoreactive calcitonin (S-iCT) concentrations was analysed in 6 patients with medullary carcinoma of the thyroid and in 8 healthy controls. All 6 patients responded to pentagastrin with a significant increase in S-iCT, 5 responded to calcium and only 3 to whisky. In the 8 controls no or only a modest increase in S-iCT occurred following pentagastrin, calcium and whisky with no difference between the three. It is concluded that pentagastrin is the most useful stimulative agent for ICT secretion in patients with C-cell neoplasms. In selected cases the additional use of calcium could be advantageous.

## Refining Calcium Test for the Diagnosis of Medullary Thyroid Cancer: Cutoffs, Procedures, and Safety

Caterina Mian, Michela Perrino, Carla Colombo, Elisabetta Cavedon, Gianmaria Pennelli, Stefano Ferrero, Simone De Leo, Cristiano Sarais, Chiara Cacciatore, Gloria Irene Manfredi, Uberta Verga, Maurizio Iacobone, Loredana De Pasquale, Maria Rosa Pelizzo, Leonardo Vicentini, Luca Persani, and Laura Fugazzola

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**Context:** Calcitonin (CT) measurement is crucial to the early diagnosis and the follow-up of medullary thyroid cancer (MTC). If the evaluation of stimulated CT levels is required, a provocative test can be performed, being the high-dose Ca test recently reintroduced in clinical practice.

**Objective:** Our objective was to identify gender-specific thresholds for MTC diagnosis in a large series of patients who underwent the Ca test.

**Patients and Methods:** A total of 91 patients (49 females and 42 males) underwent the Ca test (calcium gluconate, 25 mg/kg) before thyroidectomy and both basal CT (bCT) and stimulated CT (sCT) were compared with histological results by receiver operating characteristic plot analyses. To evaluate possible side effects of Ca administration, cardiac function has been extensively studied.

**Results:** bCT levels were found to harbor the same accuracy as sCT in the preoperative diagnosis of MTC. The best Ca thresholds for the identification of MTC were  $>26$  and  $>68$  for bCT and  $>79$  and  $>544$  pg/mL for sCT in females and males, respectively. The high tolerability and safety of the Ca test was demonstrated and advice offered to be followed before and during the test.

**Conclusions:** Gender-specific bCT and sCT cutoffs for the identification of C-cell hyperplasia and/or MTC have been defined. The bCT and sCT were found to have a similar accuracy, indicating that serum CT assays with improved functional sensitivity may likely decrease the relevance of the stimulation test in several conditions. Finally, systematic cardiac monitoring confirms the safety of the Ca test. (*J Clin Endocrinol Metab* 99: 1656–1664, 2014)

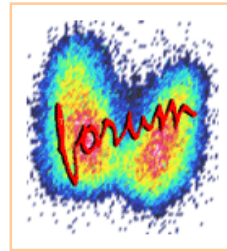
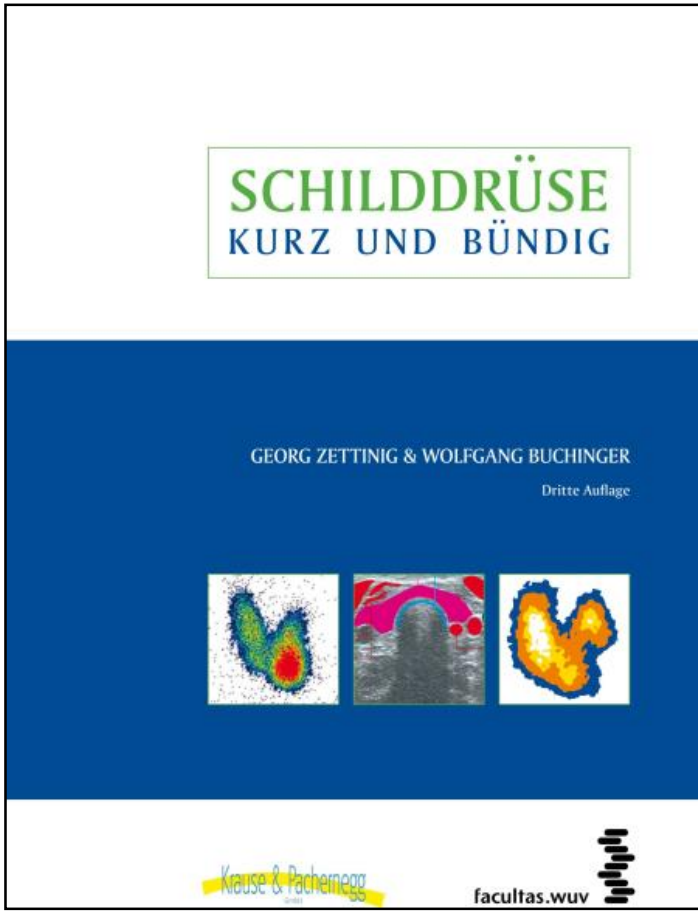
# Kalzitonin

- Das medulläre Schilddrüsenkarzinom ist das einzige Schilddrüsenmalignom, das durch veränderte Blutwerte erkannt werden kann
- Präanalytik wichtig
- Interpretation mäßig erhöhter Kalzitoninwerte erfordert viel Erfahrung



# Succus

- TSH zur Bestimmung der Schilddrüsenfunktion essentiell
- fT4 und fT3 im Sinne der personalisierten Medizin
- Thyreoglobulin hat beim nicht thyreoidektomierten / nicht radiojodtherapierten keinen Stellenwert als Routine-Laborparameter
- Wichtigste Methode zur Abklärung von Schilddrüsenknoten ist die Sonografie
- Blutwerte sind bei SD Knoten meist im Normbereich



[www.schilddruesenforum.at](http://www.schilddruesenforum.at)




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Ihr Team von Experten