Das Kind mit erniedrigtem TSH

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Hyperthyreose bei Kindern

- Schwerer Verlauf
- Höhere Nebenwirkungsrate
- Niedrigere Remissionsrate
- Mehr Life Events
- Längere Lebenszeit mit/nach Hyperthyreose

Nach Tim Cheetham, ESPE 2019

TABLE 1.
Signs and Symptoms of Graves' Disease in Children.

Signs	Symptoms
Goiter	Hyperactivity
Tachycardia	Moodiness and emotional lability
Tremor	Decreased concentration
Weight loss	Poor school performance
Hyperreflexia	Fatigue
Warm, moist skin	Sleep disturbance
Ophthalmopathy – lid lag, proptosis	Increased appetite
Systolic hypertension	Weight loss
Advanced bone age – if long-standing	Palpitations
Thymic hyperplasia	Diarrhea
	Heat intolerance

Bauer et al JCEM 2011

Hyperthyreose – DD & Symptomatik

Neonaten & Säuglinge

- Transiente Hyperthyreose bei mat. Mb. Basedow
- Aktivierende *TSHR*-Mutationen

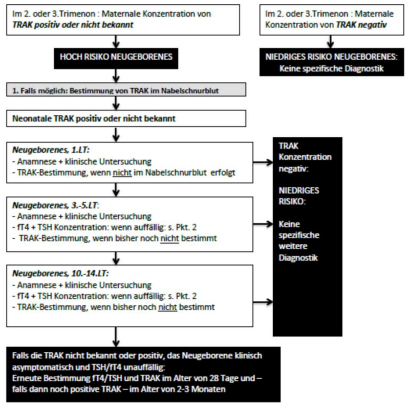
Kinder & Jugendliche

- Mb Basedow
- Hashitoxikose
- Toxisches Adenom
- Exogene Zufuhr
- Amiodaron-induzierte Thyreotoxikose
- Toxische multinoduläre Struma
- McCune Albright Syndrom

Neonatale Hyperthyreose

- 1:70 bei materalem Mb. Basedow
- Mortalität 10-20%

- Laborchemische Manifestation:
  - 3-5.LT fT4
  - Bei Erhöhung
    - Thiamazol
    - Betablocker
    - Lugol'sche Lösung (1gtt / 8h)



S2k Leitlinie 174-024, nach Kaay et al 2006

Autonome Schilddrüsenknoten

- 7% der Kinder & Jugendlichen mit Hyperthyreose
- Karzinomrate
  - 29% (Niedziela et al JPEM 2002)
  - 0% (Ly et al JCEM 2016) →
- Therapie ident zu adultem Vorgehen

	Autonomous (n = 31)	Nonautonomous (n = 125)	
Age	15 yr (range 3 to 18 y)	15 yr (range 5 to 18 yr)	.73
Gender			.25
Female	29 (94%)	105 (84%)	
Male	2 (6%)	20 (16%)	
Size of largest nodule, mm	39 mm (range 18–67 mm)	25 mm (range 10–64 mm)	<.0001
Nodules ≥1 cm per patient			.016
Solitary (=1)	18 (58%)	101 (81%)	
Multiple (>1)	13 (42%)	24 (19%)	
Thyroid cancer			.001
Patients with thyroid cancer	0 (0%)	28 (22%)	
Patients without thyroid cancer	31 (100%)	97 (78%)	

Ly et al JCEM 2016

Therapieoptionen

Thyreostatika		Radiojodtherapie		Thyroidektomie	
Nur eine Tablette	Nebenwirkungen	Einfach	Strahlung	Schnell	Narbe
Günstig	Häufigere Kontrollen	Sicher (?)	Hypothyreose Ophtalmopathie	Endgültig	Anästhesie Komplikationen Hypothyreose

JAMA Internal Medicine

View Article

Association of Radioactive Iodine Treatment With Cancer Mortality in Patients With Hyperthyroidism

JAMA Intern Med. 2019;179(8):1034-1042.

Cari M. Kitahara, PhD,[1] Amy Berrington de Gonzalez, DPhil,[1] Andre Bouville, PhD (Retired),[1] Aaron B. Brill, MD, PhD,[2] Michele M. Doody, MS,[1] Dunstana R. Melo, PhD,[3] Steven L. Simon, PhD,[4] Julie A. Sosa, MD,[5] Mark Tulchinsky, MD,[6] Daphnée Villoing, PhD,[1] and Dale L. Preston, PhD[7]

Cohort: patients with hyperthyroidism
typical doses to the stomach (150 to 250 mGy)

Results: Lifetime excess of 19 (95% CI, 3-40) to 32 (95% CI, 5-66) solid cancer deaths

Open questions
- Moderate elevation of risk
- No control group
- Some cancers more common in Graves (Chen et al, Thyroid 2013)

Thyroid, Vol. 23, No. 7 | Epidemiology

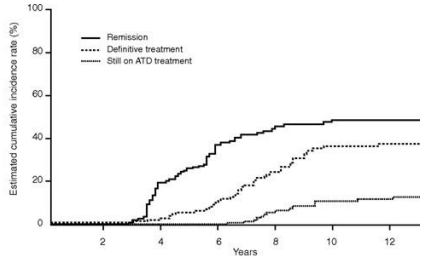
Cancer Risk in Patients with Graves' Disease: A Nationwide Cohort Study

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

Positive Impact of Long-Term Antithyroid Drug Treatment on the Outcome of Children with Graves' Disease: National Long-Term Cohort Study

Juliane Léger, Georges Gelwane, Florentia Kaguelidou, Meriem Benmerad, Corinne Alberti, the French Childhood Graves' Disease Study Group

The Journal of Clinical Endocrinology & Metabolism, Volume 97, Issue 1, 1 January 2012,

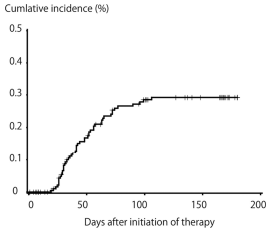


- N=154
- 49% Remission
- Plateau nach 8-10 Jahren

AE:
- Neutropenie n=1
- Allergische Reaktion n=1
- Arthralgie n=1

Thyreostatische Therapie

- Kausale Therapie
  - **Thiamazol** 0,5 (-1mg)/kg in 2 ED
  - PTU – Kontraindiziert <18.Lj
- Symptomatische Therapie:
  - **zB Propranolol**: 1 (-2) mg/kg/d in 3-4 ED po
- Kontrollen:
  - Blutbild! Amylase/Lipase! LFP!
  - Augenarzt (endokrine Orbitopathie?) – Termin in Tagen, NICHT in Monaten!
  - EKG
  - Endo Ambulanz



Watanabe et al JCEM 2012

TABLE 1. Complications of antithyroid drug therapy in more than 500 children (2, 4–6, 37, 38)

Complication	Incidence (%)
Mild increases in liver enzymes	28
Mild leucopenia	25
Skin rash[a]	9
Granulocytopenia[b]	4.5
Arthritis[b]	2.4
Nausea[a]	1.1
Agranulocytosis[b]	0.4
Hepatitis[b]	0.4
Loss of taste	Rare
Hypothrombinemia[b]	Rare
Thrombocytopenia[b]	Rare
Aplastic anemia[b]	Rare
Nephrotic syndrome[b]	Rare
Death	Rare

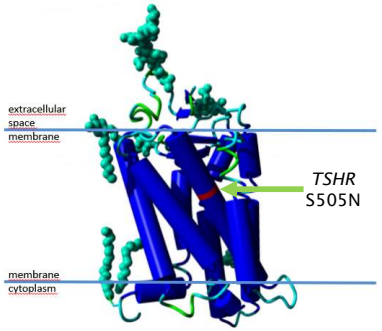
Rivkees et al JCEM 1998

Therapienebenwirkungen

Thiamazol

- Keine Therapie bei Granulozyten unter 500/ml
- Keine Therapie bei LFP über 3 fach normal
- Cave Pankreatitis

- **SOFORT BB Ko** Bei Fieber <3 Mo Therapie!!
  - Und auch danach…
- Cave Amiodaron – Risiko 6-8x!
  (Gershinsky et al Thyroid 2019)



Aktivierende *TSHR*-Mutation

2012 European Thyroid Association Guidelines for the Management of Familial and Persistent Sporadic Non-Autoimmune Hyperthyroidism Caused by Thyroid-Stimulating Hormone Receptor Germline Mutations

Eur Thyroid J 2012;1:142–147
DOI: 10.1159/000342982

R. Paschke[a] M. Niedziela[b] B. Vaidya[c] L. Persani[d] B. Rapoport[e] J. Leclere[f]

***TSHR*- Mutationen**

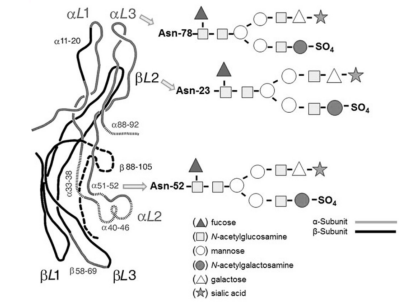
Stand 2012:
27 Familien mit FNAH
15 Fälle mit PSNAH

Empfehlung
Totale Thyroidektomie
Thyreostatische Therapie als „bridging to ablation"
Langzeit TSH-Supression häufig

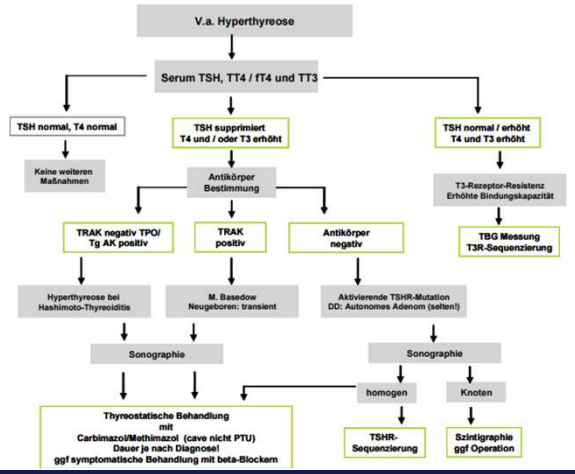
Thyrotropin Isoforms: Implications for Thyrotropin Analysis and Clinical Practice

Joshua M. Estrada,[1] Danielle Soldin,[1] Timothy M. Buckev,[1] Kenneth D. Burman,[2] and Offie P. Soldin[1,3,4,*]

THYROID
Volume 24, Number 3, 2014



- paradoxes TSH bei zentraler Hypothyreose
- Veränderung der Sialinsäuregruppen
- Veränderung der Pulsatilität



AWMF Leitlinie der Deutschen Gesellschaft für Kinderheilkunde und Jugendmedizin (DGKJ)

Take home messages

Hyperthyreose in der Pädiatrie

- Je jünger desto schwieriger
- Seltenes ist selten –
  aber häufiger im Kindesalter
- Maternaler (St.p.) Mb. Basedow =
  TRAK bei Kind
- Cave niedriges TSH - Hypopituarismus