CONVEGNO MACROREGIONALE

AME DAY

20/21
MAGGIO 2016

- IPOTIROIDISMO
  - ALFREDO CRESCENZI
  - U.O. Medicina interna - Foligno
    - UMBRIA

Sir William Withey Gull, 1st Baronet of Brook Street
(31 December 1816 – 29 January 1890)

Gull è famoso per avere apportato un significativo contributo, alla scienza Medica, per lo studio e la comprensione di alcune malattie tra cui il Mixedema, il M. di Bright, la Paraplegia e la Anoressia Nervosa

Jacques-Louis Reverdin
(28 August 1842 – 9 January 1929)

Nel 1882, con il cugino e assistente Auguste Reverdin (1848-1908), osservava il verificarsi del mixedema quale complicanza tardiva della asportazione chirurgica della ghiandola tiroidea. Documentava le sue scoperte in un articolo intitolato Note sur vinat-deux opérations de goitre. Il **13 settembre 1882** presentava le sue osservazioni alla Società Medica di Ginevra.

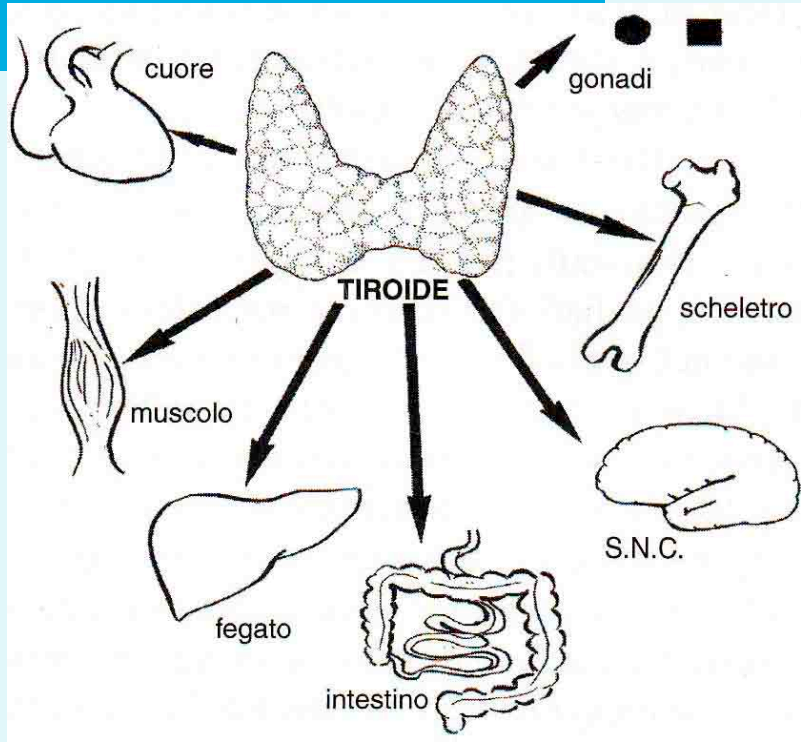
IPOTIROIDISMO

SINDROME CARATTERIZZATA DA RIDUZIONE DEGLI ORMONI TIROIDEI A LIVELLO DELLE CELLULE BERSAGLIO E GENERALMENTE NEL TORRENTE CIRCOLATORIO

DETERMINANTE UNA SINTOMATOLOGIA UBIQUITARIA CARATTERIZZATA DA UNA RIDUZIONE DELLE FUNZIONI DI QUASI TUTTI I SISTEMI

- CARDIOVASCOLARE
- GASTROINTESTINALE
- NERVOSO

-CUTANEO
-MUSCOLARE
-SCHELETRICO



MIXEDEMA

IPOTIROIDISMO GRAVE E DI LUNGA DURATA, CON EDEMA DIFFUSO, NON IMPRONTABILE, RISULTANTE DALL'ACCUMULO DI MUCOPOLISACCARIDI NEL TESSUTO SOTTOCUTANEO E INTERSTIZIALE

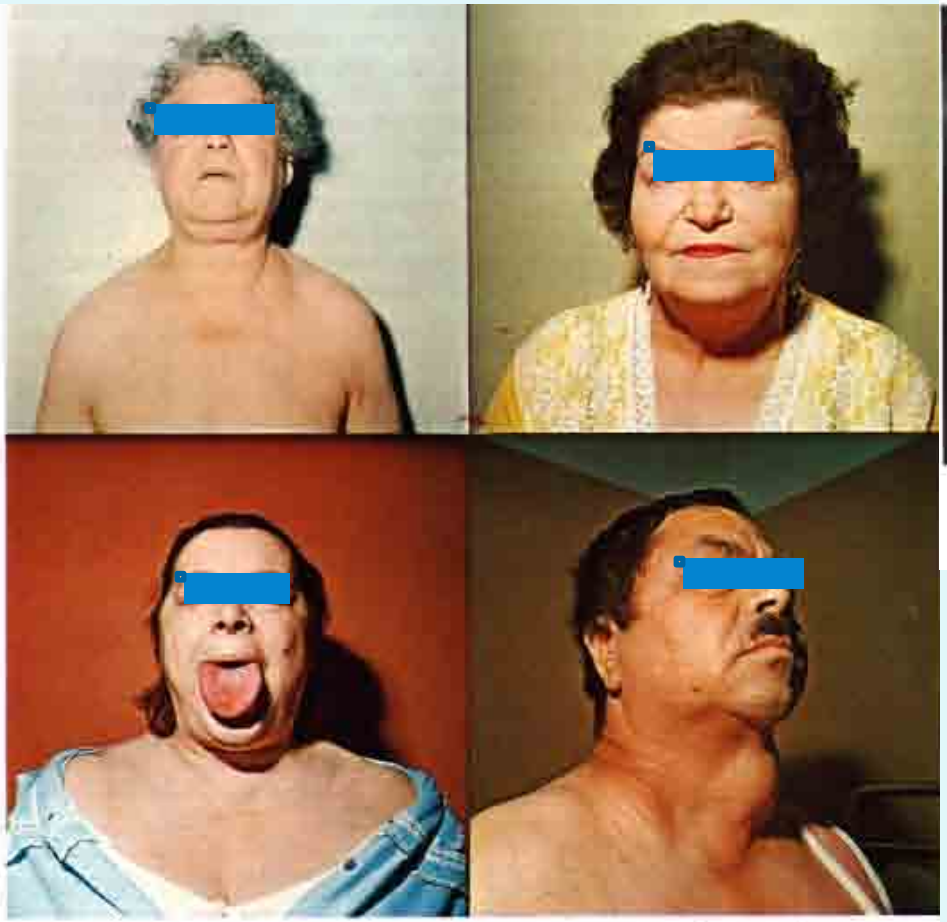
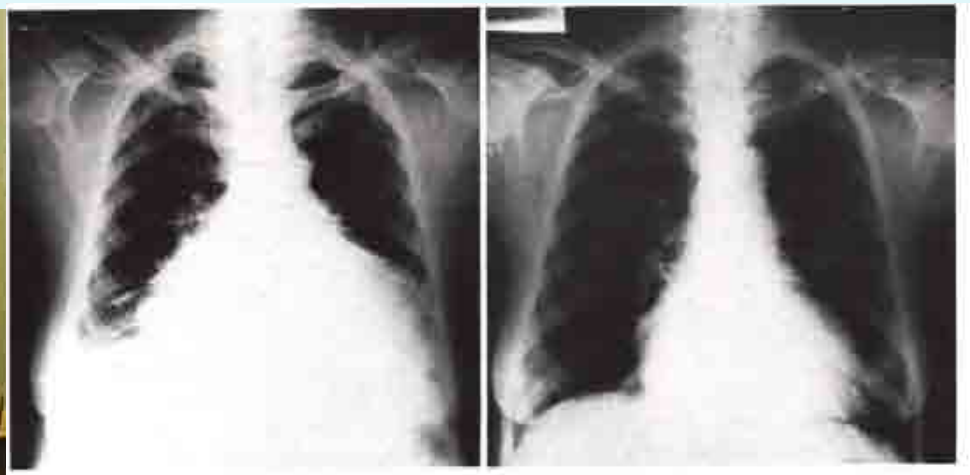


FIG. 22. Alcuni pazienti affetti da mixedema dell'adulto. a) mixedema iatrogeno, da pregresso trattamento con ^{131}I. b) e c) mixedema idiopatico. Si osservi la macroglossia del caso c). d) Mixedema con gozzo.



a) b)

FIG. 23. Aspetto radiologico del cuore del caso « a » (fig. 22), prima a) e dopo b) trattamento tiroideo sostitutivo.

P. Brunetti, F. Santeusanio. Manuale di medicina Interna- Paolo Larizza ; Malattie della tiroide 1979

EPIDEMIOLOGIA IPOTIROIDISMO

- Prevalenza ipotiroidismo spontaneo nella popolazione generale: 1-2 %
  - ↑ Donne
  - ↑ Anziani in comunità
- Incidenza annuale Ipotiroidismo conclamato
  - 3,5 - 5 / 1000 donne
  - 0,6 -1 / 1000 maschi
- Ipotiroidismo subclinico : prevalenza 3 - 9 %
  - Islanda 18 %
  - Ungheria 24 %

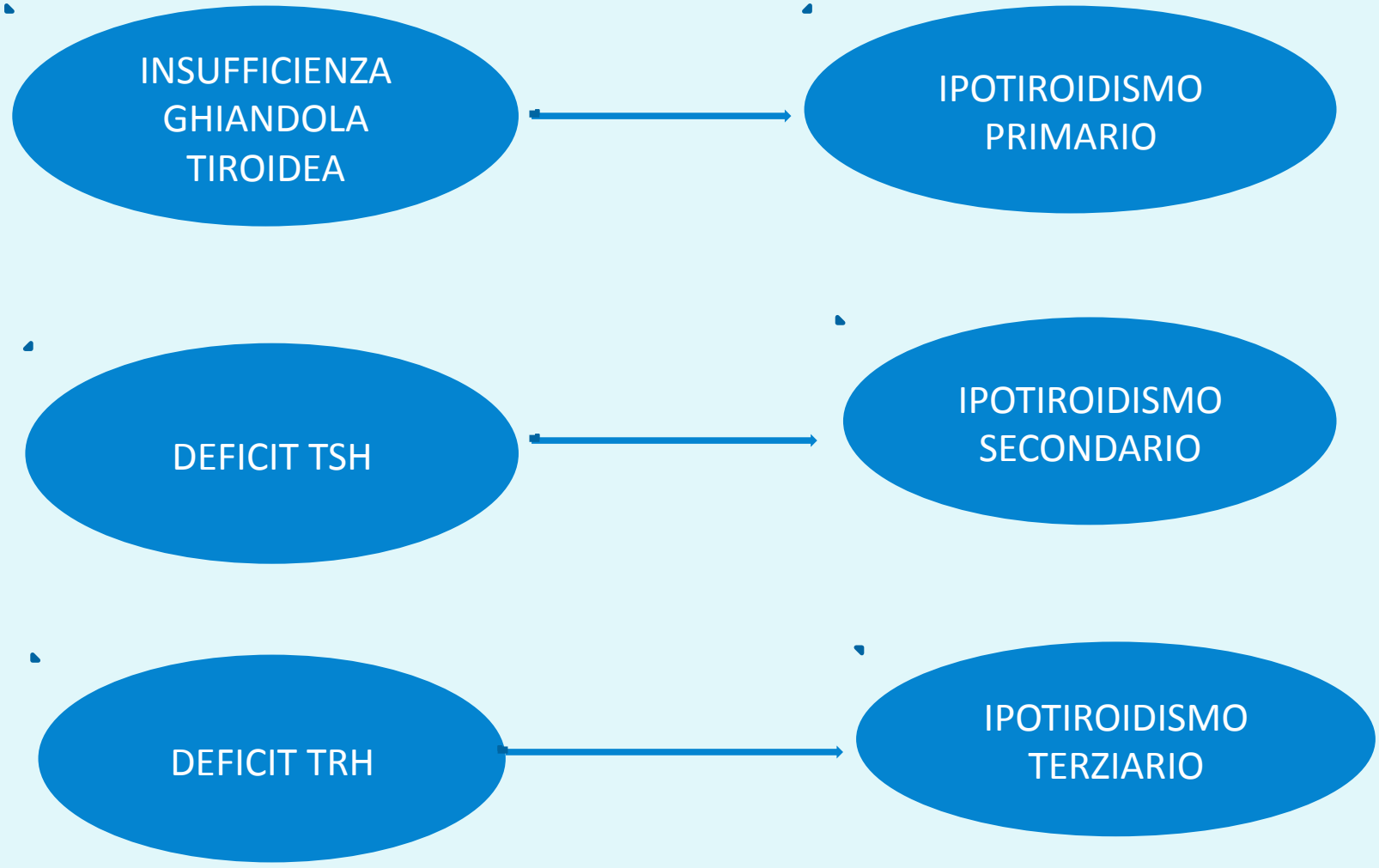
The epidemiology of thyroid disease Mark P. J. Vanderpump **British Medical Bulletin 2011**

Table 1 Prevalence of previously undiagnosed overt hypothyroidism and incidence of overt hypothyroidism in selected epidemiological surveys of thyroid dysfunction.

Study name	*n*	Age (years)	Test	Prevalence (*n*/1000)		Incidence (*n*/1000/year)		
				Men	Women	Follow-up	Men	Women
Whickham, UK[7,22]	2779	18+	TSH, T_4	0	3.3	20 years	0.6 (0.3–1.2)	3.5 (2.8–4.5)
Colorado, USA[3]	25 862	18+	TSH	4.0				
NHANES III, USA[4]	16 533	12+	TSH	2.0				
Pescopagano, Italy[16]	992	15+	TSH, FT_4	0	3.0			
Sapporo, Japan	4110	25+	TSH	2.4	8.5	–	–	–
Copenhagen, Denmark[17]	2656	41–71	TSH, FT_4	2.0	5.0			
Memphis/Pittsburgh, USA[20]	2797	70–79	TSH, FT_4	5.4	13.0			
Leiden, Netherlands[15]	558	85–89	TSH, FT_4	70				
Tayside, UK (1993–1997)[23]	390 000	0+	Treatment for hypothyroidism	–	–	4 years	0.88 (0.80–0.95)	4.98 (4.81–5.17)
Tayside, UK (1997–2001)[24]	390 000	0+	As above			4 years	1.09 (0.95–1.25)	4.75 (4.46–5.07)
Göteborg, Sweden	1283	44–66	TSH	–	6.4	4 years	–	1–2
Birmingham, UK[14]	1210	60+	TSH	7.8	20.5	1 year	11.1	
Gothenburg, Sweden	1148	70+	TSH	–	–	10 years	–	2

†MA, antithyroid microsomal antibodies; TGA, anti-thyroglobulin antibodies (see reference 1 unless stated).

CAUSE DI IPOTIROIDISMO



CAUSES OF HYPOTHYROIDISM

1. Central (hypothalamic/pituitary) hypothyroidism

1. Loss of functional tissue
    1. tumors (pituitary adenoma, craniopharyngioma, meningioma, dysgerminoma, glioma, metastases)
    2. trauma (surgery, irradiation, head injury)
    3. vascular (ischemic necrosis, hemorrhage, stalk interrruption, aneurysm of internal carotid artery)
    4. infections (abcess, tuberculosis, syphilis, toxoplasmosis)
    5. infiltrative (sarcoidosis, histiocytosis, hemochromatosis)
    6. chronic lymphocytic hypophysitis
    7. congenital (pituitary hypoplasia, septooptic dysplasia, basal encephalocele)
2. Functional defects in TSH biosynthesis and release
    1. mutations in genes encoding for TRH receptor, TSHß, pituitary transcription factors (Pit-1, PROP1, LHX3, LHX4, HESX1), or LEPr, IGSF1
    2. drugs: dopamine; glucocorticoids; bexarotene; L-T4 withdrawal

CAUSES OF HYPOTHYROIDISM

2. Primary (thyroidal) hypothyroidism

1. Loss of functional thyroid tissue
    1. chronic autoimmune thyroiditis
    2. reversible autoimmune hypothyroidism (silent and postpartum thyroiditis, cytokine-induced thyroiditis).
    3. surgery and irradiation (131I or external irradiation)
    4. infiltrative and infectious diseases, subacute thyroiditis
    5. thyroid dysgenesis
2. Functional defects in thyroid hormone biosynthesis and release
    1. congenital defects in thyroid hormone biosynthesis
    2. iodine deficiency and iodine excess
    3. drugs: antithyroid agents, lithium, natural and synthetic goitrogenic chemicals, tyrosine kinase inhibitors

CAUSES OF HYPOTHYROIDISM

3. "Peripheral" (extrathyroidal) hypothyroidism

1. Consumptive hypothyroidism (massive infantile hemangioma)
2. Mutations in genes encoding for MCT8, SECISBP2, TRα or TR β (thyroid hormone resistance)

REVERSIBLE CAUSES OF HYPOTHYROIDISM

Table 9-12Reversible causes of hypothyroidism

Etiology	Frequency of reversibility	Clues for potential reversibility
• chronic autoimmune thyroiditis	about 5% [7]	goiter [8]; preserved thyroidal radioiodine uptake [9]; preserved T3 response to TRH during thyroxine treatment [10]
• postpartum thyroiditis	up to 80%	recent delivery; relatively low titers of TPO antibodies
• subacute thyroiditis	almost 100%	recent painful goiter
• postoperative and postradioiodinehypothyroidism	not unusual	thyroidectomy or ^{131}I therapy in previous 6 months
• iodine-induced myxedema	high	exposure to iodine excess; preserved thyroidal radioiodine uptake [11]
• drug-induced hypothyroidism	high	exposure to antithyroid drugs or goitrogenic chemicals

Takasu N, Komiya I, Asawa T, et al.: Test for recovery from hypothyroidism during thyroxine therapy in Hashimoto's thyroiditis. Lancet 1990; 336: 1084-1086.

Comtois R, Faucher L, Laflèche L: Outcome of hypothyroidism caused by Hashimoto's thyroiditis. Arch Int Med 1995; 155: 1404-1408.

Okamura K, Sato K, Ikenoue H, et al.: Reevaluation of thyroidal radioactive iodine uptake test, with special reference to reversible primary hypothyroidism with elevated thyroid radioiodine uptake. J Clin Endocrinol Metab 1988; 67: 720-726.

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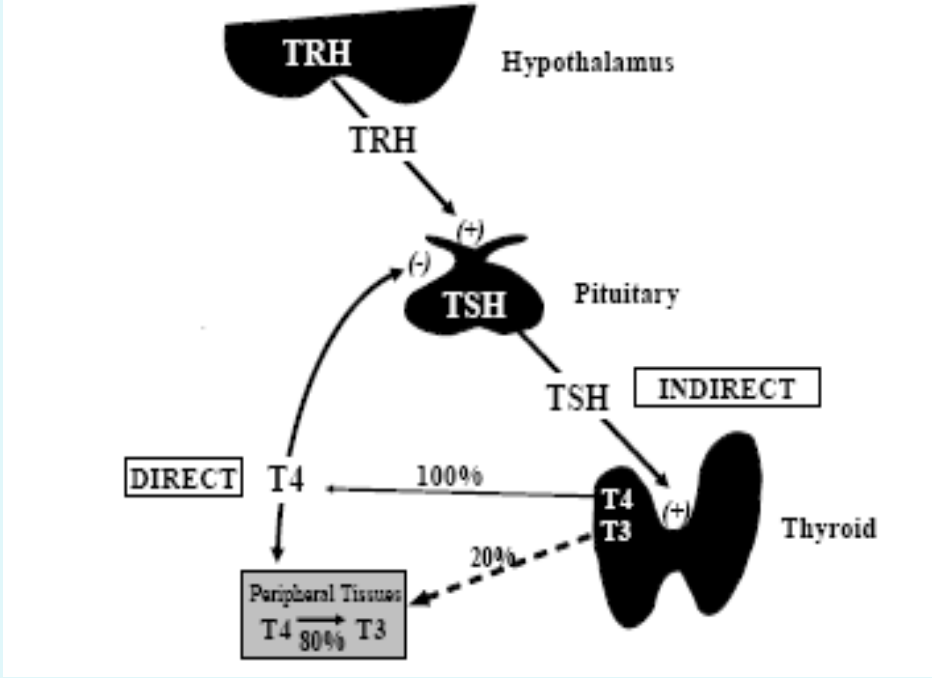
Last Update: March 28, 2014.

IPOTIROIDISMO PRIMITIVO

TSH



IPOTIROIDISMO CENTRALE

TSH

INAPPROPIATAMENTE NORMALE

IPOTIROIDISMO PRIMITIVO 99 %
IPOTIROIDISMO CENTRALE 1 %

TSH

Grades of hypothyroidism

Ipotiroidismo franco → - TSH elevato o > 10
- FT4 ridotto e/o segni e sintomi

Ipotiroidismo sub-clinico → - TSH 4,5-10
- FT4 normale, segni e sintomi assenti o lievi

Grades of hypothyroidism

Grade 1: Subclinical hypothyroidism TSH + FT4 N FT3 N(+)

Grade 2 : Mild hypothyroidism TSH + FT4 – FT3 N

Grade 3 : Overt hypothyroidism TSH + FT4 – FT3 –

+, above upper normal limit; N, within normal reference range; -, below lower normal limit.

L'ipotiroidismo ha una evoluzione graduale, in cui la prima fase di ipotiroidismo subclinico può progredire in un lieve ipotiroidismo e, successivamente, verso un ipotiroidismo manifesto

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Table 1. Proposed grading of hypothyroidism and hyperthyroidism

	TSH	FT_4	FT_3
Hypothyroidism grade IA	increased, >4.0 to <10 mU/l	normal	normal
Hypothyroidism grade IB	increased, ≥10 mU/l	normal	normal
Hypothyroidism grade II	increased	decreased	normal
Hypothyroidism grade III	increased	decreased	decreased
Hyperthyroidism grade IA	decreased, >0.1 to <4.0 mU/l	normal	normal
Hyperthyroidism grade IB	decreased, ≤0.1 mU/l	normal	normal
Hyperthyroidism grade II	decreased	normal	increased
Hyperthyroidism grade III	decreased	increased	increased

Normal, increased, decreased: values within, above, below respective reference intervals.

Grades of hypothyroidism

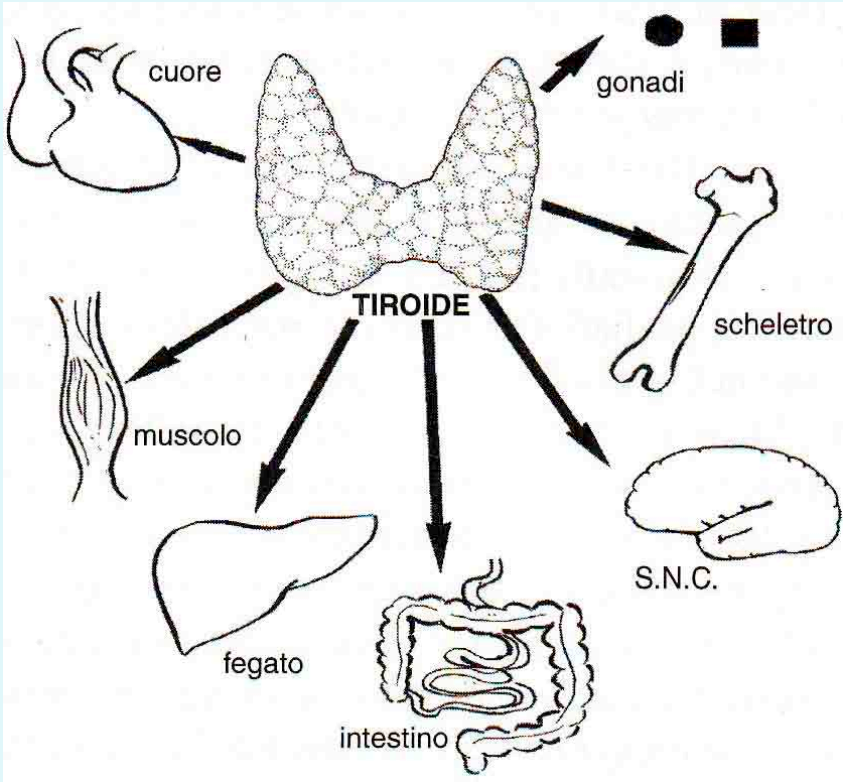
Guidance in Subclinical Hyperthyroidism and Subclinical Hypothyroidism: Are We Making Progress?
W ilmar M. Wiersinga D epartment of Endocrinology and Metabolism, Academic Medical Center, University of Amsterdam, A msterdam, The Netherlands

MANIFESTAZIONI SISTEMICHE DI IPOTIROIDISMO

L'espressione clinica del deficit di ormone tiroideo varia considerevolmente tra i vari individui, a seconda della causa, della durata e della gravità dello stato di ipotiroidismo

Tipicamente, vi è un rallentamento dell'attività fisica e mentale, e di molte funzioni dei vari organi

- Metabolismo e sistema energetico
- Assetto lipidico
- Volto e tegumenti
- Sistema Nervoso
- Sistema gastrointestinale
- Sistema Cardiovascolare, Respiratorio, Muscolo-scheletrico
- Funzione renale ed elettroliti
- Funzione riproduttiva
- Sistema Endocrino ed Emopoietico
- Sistema Emopietico



Manifestazioni Neurologiche e Psichiatriche di Ipotiroidismo

La presenza di recettori per gli ormoni tiroidei ne cervello umano adulto fanno sì che il SNC sia un Sistema Ormorne Tiroideo sensibile e forniscono la base biologica per i sintomi neurologici e neurocomportamentali molto frequente nei pazienti ipotiroidei adulti

compromissione del metabolismo mitocondriale ?

NEUROLOGIC SYMPTOMS AND SIGNS

- Headache
- Paresthesias
- Carpal tunnel syndrome
- Cerebellar ataxia
- Deafness: nerve or conduction type
- Vertigo or tinnitus
- Delayed relaxation of deep tendon reflexes
- Sleep apnea
- EEG: low-amplitude theta and delta waves
- Prolonged evoked potentials
- CSF: elevated protein concentration

COGNITIVE FUNCTIONS

- Reduced attention span
- Memory deficits
- Calculation difficulties

PSYCHIATRIC SYNDROMES

- Myxedema madness (akinetic or agitated schizoid or affective psychoses)
- Depression

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Manifestazioni cardio-vascolari di Ipotiroidismo

Fisiopatologia dei sintomi

- reduced myocardial contractility
- low cardiac output
- increased peripheral vascular resistance
- decreased blood volume
- increased capillary permeability

→

- dyspnea
- decreased exercise tolerance
- angina

Segni

- low pulse rate
- diastolic hypertension
- cardiomegaly
- pericardial effusion
- peripheral (non)pitting edema
- low voltage ECG with conduction disturbances and nonspecific ST-T changes
- prolonged systolic time intervals

Manifestazioni gastro-intestinali di Ipotiroidismo

Sintomi

- anorexia
- gaseous distention
- constipation

Segni

- prolonged gastric emptying
- prolonged intestinal transit time
- slowed intestinal absorption
- rarely ileus or ascites
- gallbladder hypotonia
- elevated liver enzymes and CEA

Incidence of symptoms and signs in hypothyroidism

Symptoms and Signs	Lermans's Series: Percent of 77 Cases of Primary Hypothyroidism	Murray's Series: Percent of 100 Cases of Primary Hypothyroidism	Percent of 15 Cases of Pituitary Hypothyroidism	Percent of 100 Normal Control Subjects
Weakness	99	98	100	21
Dry skin	97	79	47	26
Coarse skin	97	70	7	10
Lethargy	91	85	80	17
Slow speech	91	56	67	7
Edema of eyelids	90	86	40	28
Sensation of cold	89	95	93	39
Decreased sweating	89	68	80	17
Cold skin	83	80	60	33
Thick tongue	82	60	20	17
Edema of face	79	95	53	27
Coarseness of hair	76	75	40	43
Cardiac enlargement (on x-ray film)	6867	—50	—87	—
Pallor of skin	66	65	67	1431
Impaired memory	61	54	33	10
Constipation	59	76	47	36
Gain in weight	57	41	13	21
Loss of hair	57	50	—	—
Pallor of lips	55	72	73	52
Dyspea	55	57	0	2
Peripheral edema	52	74	33	18
Hoarseness	45	40	—	15
Anorexia	35	51	53	42
Nervousness	32	33	—	—
Menorrhagia[a]	30	40	26	15
Deafness	31	23	13	20
Palpitations	30	—	—	—
Poor heart sounds	25	16	7	9
Precordial pain	24	—	—	—
Poor vision	20	—	—	—
Fundus oculi changes	18	—	—	—
Dysmenorrhea	13	9	26	23
Los of Weight	12	—	—	—
Atrophic tongue	11	—	—	—
Emotional instability	9	—	—	—
Choking sensation	9	—	—	—
Fineness of hair	7	—	—	—
Cyanosis	3	—	—	—
Dysphagia	—	41	13	20
Brittle nails	—	60	73	41
Depression	—	61	73	21
Muscle weakness	—	36	13	17
Muscle pain	—	29	26	24
Joint pain	—	56	13	15
Paresthesia	—	2	0	12
Heat intolerance	—	49	67	9
Slow cerebration	—	73	60	14
Slow movements	—	11	0	4
Exophthalmos	—	81	80	58
Sparse eyebrows				

[a]Premenopausal patients

Lerman: 77 pz mixedematosi

Murray : 100 pz ipotiroidismo primario
15 pz ipotiroidismo secondario
100 soggetti controllo

Alcuni dei sintomi elencati sono più indicativi di ipertiroidismo che di ipotiroidismo . Tra i quali: **dispnea, nervosismo, palpitazioni, dolore precordiale, perdita di peso, e instabilità emotiva**. Questi sintomi si trovano anche in soggetti normali di controllo con una frequenza quasi eguale

Molti sintomi tipici di ipotiroidismo primario non si trovano comunemente nell'ipotiroidismo secondario - per esempio: pelle ruvida, macroglossia, grossolanità dei capelli, edema periferico, raucedine e parestesie.

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TSH ELEVATO

SEMPRE IPOTIROIDISMO

?

ETA’

ETNIA

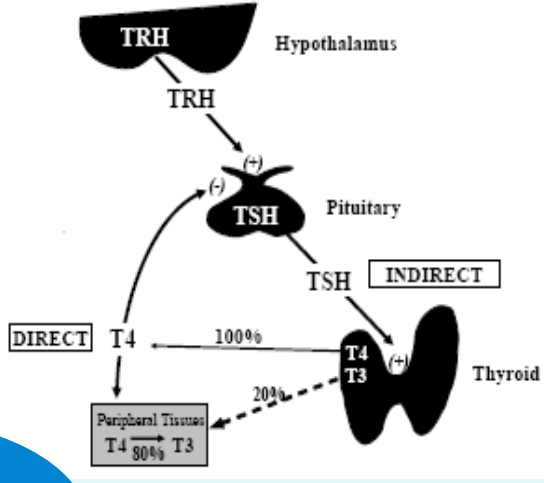
SESSO

SET POINT DEL TSH

MALATTIE SISTEMICHE

FATTORI AMBIENTALI

PRIVAZIONE CALORICA



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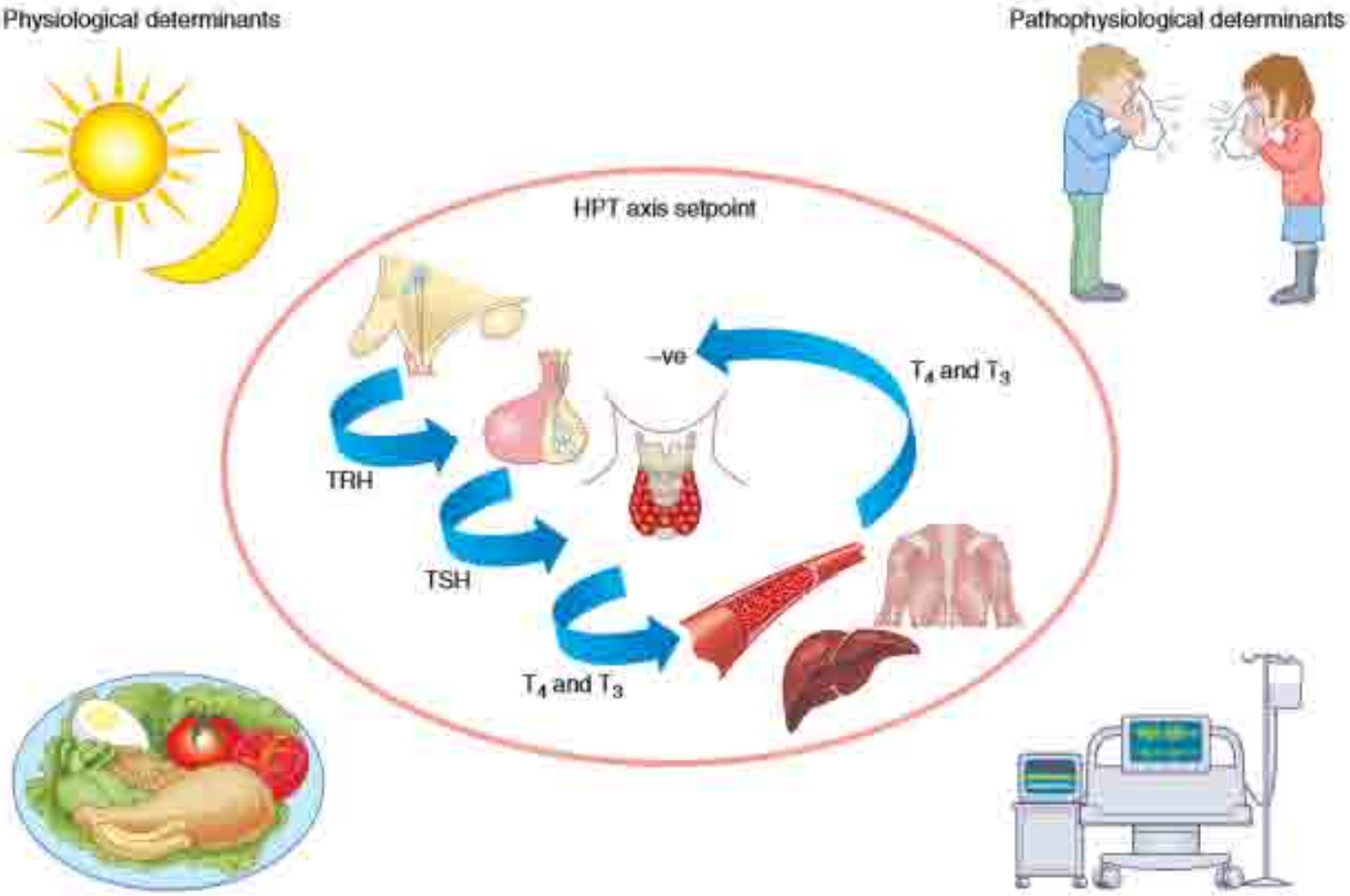
European Journal of Endocrinology



Eric Fliers et al. Beyond the fixed setpoint of the hypotalamus-pituitary-thyroid axis. Europen Journal of Endocrinology 2014

The Relationship Between TSH and Free T4 in a Large Population Is Complex and Nonlinear and Differs by Age and Sex

Narelle C. Hadlow, Karen M. Rothacker, Robert Wardrop, Suzanne J. Brown, Ee Mun Lim, and John P. Walsh

Department of Clinical Biochemistry (N.C.H., K.M.R., R.W., E.M.L.), PathWest Laboratory Medicine, Queen Elizabeth II Medical Centre, Nedlands, Western Australia 6009, Australia; Western Diagnostic Pathology (N.C.H.), Myaree, Western Australia 6154, Australia; School of Pathology and Laboratory Medicine (N.C.H.) and School of Medicine and Pharmacology (J.P.W.), The University of Western Australia, Crawley, Western Australia 6009, Australia; and Department of Endocrinology and Diabetes (K.M.R., S.J.B., E.M.L, J.P.W.), Sir Charles Gairdner Hospital, Nedlands Western Australia 6009, Australia

(J Clin Endocrinol Metab 98: 2936–2943, 2013)

:TheTSH–freeT4 relationship is not inverselog-linear but can be described by 2 overlapping negative sigmoid curves. At physiological free T4 concentrations, TS His higher in men and in older people, whereas the TSH response to hypothyroidism is more robust in younger people.These results advance understanding of the TSH–free T4 relationship, which is central to thyroid pathophysiology and laboratory diagnosis of thyroid disease. (J Clin Endocrinol Metab 98: 2936–2943, 2013)

Pz: 152.261

Per concentrazioni di FT4 fisiologiche, il TSH risulta più alto negli uomini e nelle persone anziane, mentre la risposta all'ipotiroidismo è più forte nella popolazione più giovane

Mediana del TSH in funzione dell'età e del sesso

Table 2. Median TSH in Subjects Not Receiving Thyroxine Treatment with Free T_4 Concentrations Within the Reference Range (10–20 pmol/L)

	Median TSH, mU/L					
	1–19 y	**20–39 y**	**40–59 y**	**60–79 y**	**≥80 y**	***P* Value**
All	2.8 (1.2, 4.5)	2.0 (0.8, 4.3)	3.6 (1.3, 4.9)	3.9 (1.6, 5.0)	4.1 (1.6, 5.4)	<.001[a]
n = 112 037	5817	29 941	40 307	27 875	8097	
Men	3.7 (1.8, 4.7)	2.6 (1.1, 4.5)	3.7 (1.4, 4.9)	4.0 (1.7, 5.1)	4.3 (2.2, 5.6)	<.001[a]
n = 31 207	1823	6172	10 830	9811	2571	
Women	2.3 (1.0, 4.4)	1.9 (0.8, 4.2)	3.6 (1.3, 4.9)	3.9 (1.6, 5.0)	4.0 (1.4, 5.3)	<.001[a]
n = 80 830	3994	23 769	29 477	18 064	5526	

Median TSH (LQ, UQ) are given for each age band in the entire cohort and for men and women separately. Number of subjects (n) for each age band and sex is indicated.

[a] *P* value indicates a significant quadratic relationship across age groups ($P < .001$ for both quadratic and linear terms). When the 1- to 19-year age group was excluded from analysis, there was a significant linear trend in median TSH across adult age groups ($P < .001$).

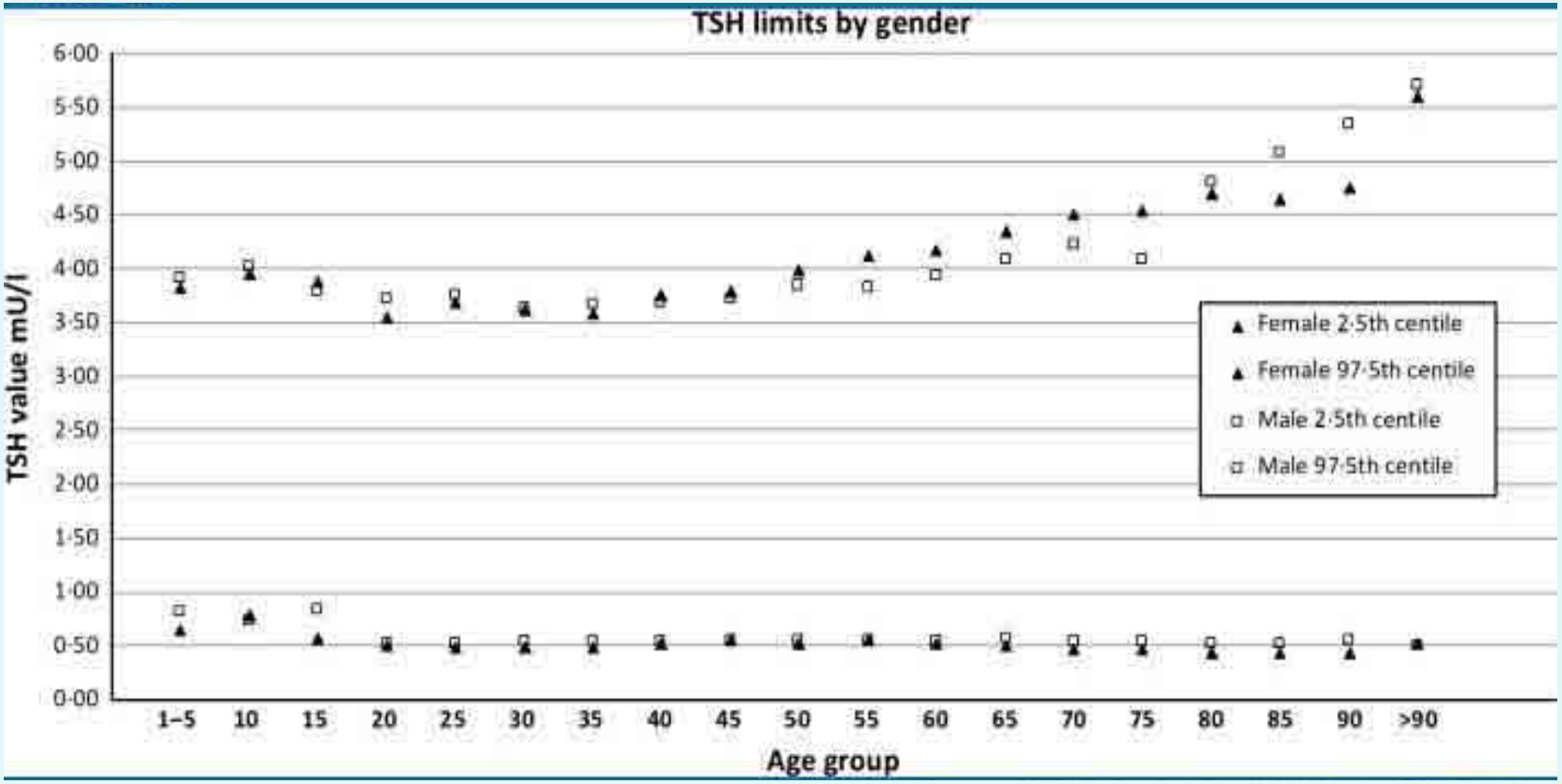
Pediatric Reference Intervals for Serum Thyroxine, Triiodothyronine, Thyrotropin, and Free Thyroxine

, David Zurakowski,1* James Di Canzio,1 and Joseph A. Majzoub2 Departments of Biostatistics and Medicine and 2 Division of Endocrinology, Boston

Clinical Chemistry 45 n° 7 1999

		Females			Males		
Analyte	Age	Mean	Reference interval	*n*	Mean	Reference interval	*n*
T_4, nmol/L[a]	1–11 months	122	82–162	116	120	79–161	135
	1–5 years	120	79–160	471	116	75–158	589
	6–10 years	115	75–154	462	111	69–152	600
	11–15 years	109	69–149	799	106	63–147	614
	16–20 years	104	64–144	565	99	58–142	200
	Total			2413			2138
T_3, nmol/L[b]	1–11 months	2.46	1.52–3.39	70	2.46	1.58–3.35	93
	1–5 years	2.37	1.43–3.30	262	2.38	1.54–3.27	340
	6–10 years	2.20	1.62–3.12	255	2.26	1.37–3.13	362
	11–15 years	2.03	1.09–2.95	483	2.12	1.24–3.00	341
	16–20 years	1.84	0.92–2.78	346	1.98	1.11–2.86	131
	Total			1416			1267
TSH, mIU/L	1–11 months	2.2	0.8–6.3	131	2.2	0.8–6.3	158
	1–5 years	2.0	0.7–5.9	523	2.1	0.7–6.0	659
	6–10 years	1.8	0.6–5.1	562	1.9	0.7–5.4	698
	11–15 years	1.5	0.5–4.4	1057	1.7	0.6–4.9	738
	16–20 years	1.3	0.5–3.9	809	1.6	0.5–4.4	223
	Total			3082			2476
		Females and Males					
Free T_4, pmol/L[c]	1–11 months	19.5	9.5–39.5	47			
	1–5 years	18.4	9.0–37.2	91			
	6–10 years	16.9	8.3–34.1	57			
	11–15 years	15.5	7.6–31.5	88			
	16–20 years	14.1	7.0–28.7	70			
	Total			353			

[a] To convert nmol/L to μg/dL, divide by 12.87.
[b] To convert nmol/L to ng/dL, multiply by 65.1.
[c] To convert pmol/L to ng/dL, divide by 12.87.



Clinical Endocrinology, November, 2012. 10.1111/j.1365-2265.2012.04463.x **ORIGINAL ARTICLE**

Age-specific TSH reference ranges have minimal impact on the diagnosis of thyroid dysfunction Kalani M. Kahapola-Arachchige, Narelle Hadlow, Robert Wardrop, Ee M. Lim, John P. Walsh Australia

LIVELLI SERICI DEL TSH IN RELAZIONE ALL'ETA'

L'INCIDENZA DELL' IPOTIROIDISMO AUMENTA GRADUALMENTE CON L'ETA'

IN RELAZIONE ALL'AUMENTATA INCIDENZA DELLA TIROIDITE DI HASHIMOTO

Dayan CM,Daniels GH,Chronic autoimmune thyroiditis . N Engl J Med 1996. 335(2):99-107

Pinchera A, Mariotti S,Barbesino G et al. Thyroid autoimmunity and ageing. Horm Res 1995;43(1-3):64-8

Diez JJ. Hypothyroidism in patients older than 55 years: an analysis of the etiology and assessment of the effectiveness of therapy. J Gerontol A Biol Sci Med Sci 2002;57(5):315-20

IPOTIROIDISMO NELL'ANZIANO

Prevalenza stimata (entrambi i sessi):

Ipotiroidismo conclamato: 1 % -10 %

Ipotiroidismo sub-clinico: 1 % -15 %

DATI VARIABILI A SECONDA DELLA POPOLAZIONE E DEI CRITERI DI IPOTIROIDISMO

Eur J Epidemiol. 2000;16(1):43-46 Prevalence of hypothyroidism and diabetes mellitus in elderly kubbutz members. Flatau E et al.

JAMA. 2004 Dec 1;292(21):2591-9 **Thyroid status, disability and cognitive function, and survival in old age.** Gussekloo J, et al.

JAMA 2006;295(9):1033-1041. Thyroid status, cardiovascular risk, and mortality in older adults. Cappola AR et al.

J Clin Endocrinol Metab. 2006 Dec;91(12):4809-16. Epub 2006 Sep 26 **Prevalence of subclinical thyroid dysfunction and its relation to socioeconomic deprivation in the elderly: a community-based cross-sectional survey. Wilson S , et al.**

Sao Paulo Med J. 2010 Jan;128(1):18-23 **Frequency of subclinical thyroid dysfunction and risk factors for cardiovascular disease among women at a workplace. Diaz-Olmos R, et al.**

ETA' E TIROIDITE DI HASHIMOTO

PAZIENTI IPOTIROIDEI
> 55 ANNI

- 47% HASHIMOTO
- 27% CHIRURGICO
- 10 % RADIOIODO
- ALTRE CAUSE 23 %

Med Clin North Am 2012 Mar;96(2):297-310. doi: 10.1016/j.mcna.2012.01.013. Epub 2012 Feb 14. **Approach to and treatment of thyroid disorders in the elderly.**
Papaleontiou M , Haymart MR Division of Metabolism, Endocrinology and Diabetes, Department of Medicine, University of Michigan Health System, Ann Arbor, MI 48105, USA

Diez JJ. Hypothyroidism in patients older than 55 years: an analysis of the etiology and assessment of the effectiveness of therapy. J Gerontol A Biol Sci Med Sci 2002;57(5):315-20

PRINCIPALI SINTOMI E SEGNI

Sintomi

- Astenia
- Adinamia
- *Incremento ponderale*
- *Bradilalia*
- *Iperpolimenorrea*
- *Riduzione libido*
- *Psicosi*
- *Depressione*
- *Letargia*
- *Voce rauca*
- *Perdita memoria*
- *Stipsi*
- *Parestesie*
- *Mialgia*
- *Artralgia*
- *Anoressia*
- *Sordità*

Segni

- Intolleranza al freddo
- Ipotermia
- Capelli fini,secchi
- Cute secca,pallore
- Edema periorbitario
- Rallentameno motorio
- Iporeflessia
- Bradicardia
- Edema non improntabile
- Macroglossia
- Versamento pericardico
- Dispnea
- Gozzo
- Rarefazione III° est sopracc.
- Ipertensione
- S. Tunnel carpale
- Miopatia prossimale

- Astenia
- Facile stancabilità
- Stitichezza
- Cute secca
- Intolleranza al freddo

- Incremento ponderale
- Disturbi cognitivi
- Anoressia
- Dolori muscolari e articolari
- Adinamia

NON E' DETTO CHE I PIU' ANZIANI SIANO SEMPRE IN SPLENDIDA FORMA

pertanto:

Nell'anziano molti dei disturbi determinati da un ipotiroidismo possono essere facilmente interpretati come correlati al processo di invecchiamento dell'individuo

In assenza di segni clinici particolari

In presenza di sintomi generici che possono essere tipici dell’anziano

La diagnosi di ipotiroidismo rimane spesso affidata al laboratorio

TSH NELL'ANZIANO ?

DATI INIZIALMENTE DISCORDANTI IN LETTERATURA CIRCA IL SET-POINT DEL TSH NEGLI ANZIANI

- Alcuni evidenziavano comunque suggerito una alterata funzione ipofisaria nelle fasce di età avanzata

Wiener R, UtigerRD,LewR, EmersonCH1991 Age, sex, and serum thyrotropin concentrations in primary hypothyroidism. Acta Endocrinol (Copenh) 124:364–369

Diversità solo tra fasce estreme < 30 e > 70 anni

Doucet J, Trivalle C, Chassagne P, Perol MB, Vuillermet P, Manchon ND, Menard JF, Bercoff E 1994 Does age play a role in clinical presentation of hypothyroidism? J Am Geriatr Soc 42: 984–986

Non differenze tra pazienti < 30 e > 70 anni

Carle´ A, Laurberg P, Pedersen IB, Perrild H, Ovesen L, Rasmussen LB, Jorgensen T, Knudsen N 2007 Age modifies the pituitary TSH response to thyroid failure. Thyroid 17:139–144

Risposta alla ipotiroxinemia più elevata in pz con T. Hashimoto < 20 anni rispetto a > 80 anni DANIMARCA 2007

ATA/AACE Guidelines 2012

NHANES: National Healt and Nutrition Examination Survey

More recently the NHANES III reference population **was further analyzed** and normal ranges based on age, U.S. Office of Management of Budget ‘‘Race and Ethnicity’’ categories, and sex **were determined**. These indicated the 97.5th percentile TSH values as low as 3.24 for African Americans between the ages of 30 and 39 years and as high as 7.84 for Mexican Americans ‡ 80 years of age. For every 10-year age increase after 30–39 years, the 97.5th percentile of serum TSH increases by 0.3 mIU/L. Body weight, anti-thyroid antibody status, and urinary iodine had no significant impact on these ranges.

Boucai L, Hollowell JG, Surks MI 2011 An approach for development of age-, gender-, and ethnicityspecific thyrotropin reference limits. Thyroid 21:5–11. EL1

TABLE 1. COMPARISON OF DISEASE-FREE AND REFERENCE POPULATIONS ON THYROTROPIN MEDIAN, AND 2.5TH AND 97.5TH CENTILES FOR ALL SUBJECTS, BLACKS, MEXICAN AMERICANS, AND WHITES RACIAL/ETHNIC GROUPS BY DECADES OF AGE

All

	Disease free (n = 15,133)			*Reference population (n = 13,296)*		
Age (years)	*2.5th centile*	*Median*	*97.5th centile*	*2.5th centile*	*Median*	*97.5th centile*
All ages	0.43	1.41	5.04	0.42	1.40	4.30
13–19	0.41	1.30	3.98	0.41	1.30	3.78
20–29	0.40	1.30	3.98	0.40	1.30	3.60
30–39	0.39	1.30	4.17	0.38	1.25	3.60
40–49	0.44	1.41	4.75	0.44	1.40	3.90
50–59	0.50	1.58	5.07	0.49	1.50	4.20
60–69	0.46	1.70	5.56	0.46	1.66	4.70
70–79	0.47	1.83	7.11	0.47	1.74	5.60
80+	0.44	1.99	6.90	0.44	1.90	6.30

Blacks

	Disease free (n = 4430)			*Reference population (n = 4194)*		
Age (years)	*2.5th centile*	*Median*	*97.5th centile*	*2.5th centile*	*Median*	*97.5th centile*
All ages	0.36	1.25	3.90	0.36	1.25	3.70
13–19	0.36	1.20	3.75	0.35	1.20	3.78
20–29	0.36	1.10	3.30	0.36	1.10	3.30
30–39	0.33	1.16	3.39	0.33	1.10	3.24
40–49	0.42	1.30	3.90	0.42	1.30	3.74
50–59	0.43	1.40	4.50	0.44	1.40	3.99
60–69	0.35	1.50	4.64	0.35	1.58	4.20
70–79	0.39	1.50	5.20	0.39	1.50	5.20
80+	0.45	1.60	5.76	0.42	1.50	4.60

Mexican Americans

	Disease free (n = 4410)			*Reference population (n = 3854)*		
Age (years)	*2.5th centile*	*Median*	*97.5th centile*	*2.5th centile*	*Median*	*97.5th centile*
All ages	0.47	1.49	5.20	0.46	1.40	4.37
13–19	0.43	1.40	4.30	0.42	1.33	3.73
20–29	0.47	1.40	4.13	0.47	1.33	3.62
30–39	0.41	1.33	4.68	0.40	1.30	3.75
40–49	0.41	1.50	4.95	0.40	1.49	3.99
50–59	0.56	1.60	5.84	0.55	1.50	4.85
60–69	0.51	1.83	6.13	0.51	1.80	5.54
70–79	0.54	2.10	7.55	0.59	2.13	7.12
80+	0.57	2.10	7.11	0.55	1.91	7.84

Whites

	Disease free (n = 5603)			*Reference population (n = 4671)*		
Age (years)	*2.5th centile*	*Median*	*97.5th centile*	*2.5th centile*	*Median*	*97.5th centile*
All ages	0.50	1.60	5.70	0.49	1.50	4.60
13–19	0.49	1.41	4.10	0.49	1.40	3.93
20–29	0.48	1.30	4.10	0.46	1.30	3.60
30–39	0.47	1.40	5.20	0.46	1.37	3.76
40–49	0.56	1.50	5.37	0.57	1.49	3.95
50–59	0.54	1.60	5.30	0.52	1.58	3.97
60–69	0.51	1.74	5.63	0.56	1.66	4.31
70–79	0.47	1.91	7.32	0.46	1.80	5.60
80+	0.41	2.10	7.02	0.41	1.99	6.56

An Approach for Development of Age-, Gender-, and Ethnicity-Specific Thyrotropin Reference Limits Laura Boucai,1 Joseph G. Hollowell,2,{ and Martin I. Surks1,3
THYROID Volume 21, Number 1, 2011

National Health and Nutrition Examination Survey III

Mediana del TSH tra 2,5 e 97,5 percentile in funzione dell'età, della presenza di Ab-antitiroide (criterio di esclusione) in specifici gruppi raziali / etnici
-Bianchi non ispanici
-Neri non ispanici
- Messicani d'America

Criteri di esclusione: presenza di Ab; TSH > 10 TSH < 0,1

ATA/AACE Guidelines 2012

NHANES III : il valore di TSH nel siero che è stato considerato come limite alto della normalità è di 4,5 mUI/L

Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, Braverman LE **Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to1994): National Health and Nutrition Examination Survey (NHANES III).** J Clin Endocrinol Metab 2002 87:489–499

ATA/AACE Guidelines 2012

In individuals without serologic evidence of AITD, TSH values above 3.0 mIU/L occur with increasing frequency with age, with elderly (> 80 years of age) individuals having a 23.9% prevalence of TSH values between 2.5 and 4.5 mIU/L, and a 12% prevalence of TSH concentrations above 4.5 mIU/L . Thus, very mild TSH elevations in older individuals may not reflect subclinical thyroid dysfunction, but rather be a normal manifestation of aging.

Surks MI, Hollowell JG 2007 Age-specific distribution of serum thyrotropin and antithyroid antibodies in the US population: implications for the prevalence of subclinical hypothyroidism. J Clin Endocrinol Metab 92:4575–4582.

TSH NELL'ANZIANO ?

Age modifies the pituitary set point or response to comparably reduced free T4 concentrations,resulting in lesserserum TSHelevation in older individuals. This phenomenon occurs with both spontaneous and iatrogenic hypothyroidism. This may be an adaptive response in normal aging or a pathological alteration of pituitary function with age. **(*J Clin Endocrinol Metab 95: 3675–3683, 2010)***

With iatrogenic hypothyroidism, the mean TSH concentration decreased significantly in each ascending age group (35 yr, 156 mIU/liter; 35–49 yr, 115 mIU/liter; 50–64 yr, 74 mIU/liter; 64 yr, 46 mIU/liter; *P0.001)* despite similar FT4 concentrations.

Pz : 112 affetti da Cr Tiroideo

J Clin Endocrinol Metab. 2010 Aug;95(8):3675-83. doi: 10.1210/jc.2010-0281. Epub 2010 May 19.
Age and the thyrotropin response to hypothyroxinemia.
Over R, Mannan S, Nsouli-Maktabi H, Burman KD, Jonklaas J. Division of Endocrinology, Georgetown University Medical Center, Suite 232, Building D, and Washington Hospital Center,

- Come interpretare un ipotiroidismo sub-clinico nell’anziano ?

- MECCANISMO DI SALVAGUARDIA ?

- PATOLOGIA ?

- NON C’E’ ANCORA CHIAREZZA IN MERITO

- I PAZIENTI ANZIANI CON TSH ELEVATO VIVONO PIU’ A LUNGO E QUELLI CON TSH BASSO VIVONO DI MENO ?

IPOTIROIDISMO E MORTALITA' NEGLI ANZIANI

JAMA. 2004 Dec 1;292(21):2591-9.
Thyroid status, disability and cognitive function, and survival in old age.
Gussekloo J, van Exel E, de Craen AJ, Meinders AE, Frölich M, Westendorp RG. Section of Gerontology and Geriatrics, Department of General Internal Medicine, Leiden University

- MORTALITA' IN PZ ANZIANI CON ELEVAZIONE TSH
- MORTALITA IN PZ ANZIANI CON RIDUZIONE DEL TSH

Pz: 558 > 85 anni seguiti per 3 – 4 anni

(riferimento TSH 0,3 – 4,8)

J Clin Endocrinol Metab. 2014 Jul;99(7):2372-82. doi: 10.1210/jc.2013-4184. Epub 2014 Mar 21.**Subclinical and overt thyroid dysfunction and risk of all-cause mortality and cardiovascular events: a large population study.** Selmer C, Olesen JB, Hansen ML et al.

CONCLUSIONS: Heart failure is the leading cause of an increased cardiovascular mortality in both overt and subclinical hyperthyroidism. Subclinical hypothyroidism with TSH 5-10 mIU/L might be associated with a lower risk of all-cause mortality.

↓ MORTALITA' IN PZ CON IPOTIROIDISMO SUB-CLINICO

Pz: 563.700 studio retrospettivo

A total of 47 327 (8.4%) deaths occurred among 563 700 included subjects [mean age 48.6 (SD ± 18.2) y; 39% males]. All-cause mortality was increased in overt and subclinical hyperthyroidism [age adjusted incidence rates of 16 and 15 per 1000 person-years, respectively; incidence rate ratios (IRRs) 1.25 [95% confidence interval (CI) 1.15-1.36] and 1.23 (95% CI 1.16-1.30)] compared with euthyroid (incidence rate of 12 per 1000 person-years). Risk of MACEs was elevated in overt and subclinical hyperthyroidism [IRRs 1.16 (95% CI 1.05-1.27) and 1.09 (95% CI 1.02-1.16)] driven by heart failure [IRRs 1.14 (95% CI 0.99-1.32) and 1.20 (95% CI 1.10-1.31)]. A reduction of all-cause mortality was observed in subclinical hypothyroidism with TSH of 5-10 mIU/L [IRR 0.92 (95% CI 0.86-0.98)].

Am J Med. 2016 Apr;129(4):423-30. doi: 10.1016/j.amjmed.2015.11.027. Epub 2015 Dec 20. **Subclinical Thyroid Disease and Mortality in the Elderly: A Retrospective Cohort Study.** Grossman A[1], Weiss A[2], Koren-Morag N[3], Shimon I[1], Beloosesky Y[2], Meyerovitch J[4]

Età media: 83 anni

MORTALITA' IPER E IPOTIROIDISMO SUBCLIICO

Both subclinical hypothyroidism and subclinical hyperthyroidism are associated with increased mortality in the elderly. A threshold thyroid-stimulating hormone value (>6.35 mIU/L) exists for increased mortality in subclinical hypothyroidism, but not in subclinical hyperthyroidism.

Pz : 17.440 studio retrospettivo

UN IPOTIROIDISMO SUB-CLINICO SI CORRELA CON AUMENTATA INCIDENZA DI CARDIOPATIA ISCHEMICA NELL'ANZIANO ?

J Clin Endocrinol Metab. 2008 Aug;93(8):2998-3007. doi: 10.1210/jc. 2008-0167. Epub 2008 May 27. **The influence of age on the relationship between subclinical hypothyroidism and ischemic heart disease: a metaanalysis.** Razvi S, Shakoor A, Vanderpump M, Weaver JU, Pearce SH Department of Endocrinology, Queen Elizabeth Hospital, Gateshead

↑ incidenza soltanto < 65 anni

Nessuna differenza con la popolazione sana nei pazienti > 65 anni

Pz : 2.531 ipo sub-cl 2.6491 "sani"

J Clin Endocrinol Meta. 2012 Mar;97(3):852-61. doi: 10.1210/jc.2011-1978. Epub 2012 Jan 11. **Subclinical thyroid dysfunction and the risk of heart failure in older persons at high cardiovascular risk.**

Nanchen D, Gussekloo J, Westendorp RG, Stott DJ, Jukema JW, Trompet S, Ford I, Welsh P, Sattar N, Macfarlane PW, Mooijaart SP, Rodondi N, de Craen AJ; PROSPER Group. Leiden University Medical Center, Department of Gerontology and Geriatrics, Netherlands Consortium for Health Aging, Leiden, The Netherlands.

Pz : 5326 (Pz ipo sub-cl : 199: mortalità e tasso ospedalizzazione)

NON EVIDENZA DI ASSOCIAZIONE TRA EVENTI CARDIOVASCOLARI / MORTALITA' E DISFUNZIONE TIROIDEA SUB-CLINICA

- Ad eccezione dei pz con TSH < 0,1 o > 10

J Clin Endocrinol Metab. 2013 Feb;98(2):533-40. doi: 10.1210/jc.2012-2180. Epub 2012 Nov 16. **Persistent subclinical hypothyroidism and cardiovascular risk in the elderly: the cardiovascular health study.**

Hyland KA, Arnold AM, Lee JS, Cappola AR Sc.M., Division of Endocrinology, Diabetes, and Metabolism, Perelman School of Medicine at the University of Pennsylvania

Pz :4184 (Pz iposubcl: 679) valutazione rischio a 10 anni

- Non evidenza di aumentato rischio di malattia coronarica, insuff. Cardiaca e mortalità cardiovascolare in pazienti anziani > 65 anni

Subclinical hypothyroidism represents an additional risk factor for coronary artery calcification, especially in subjects with intermediate and high cardiovascular risk scores

Nathalie Silva et al.

European Journal of Endocrinology 2014

- Scopo dello studio era valutare la presenza di malattia coronarica (CAD) in pazienti asintomatici con i SCH misurando il punteggio dell'arteria coronarica calcio (CAC).
- Sono stati studiati 222 soggetti di età tra 35 e 65 anni
- È stato dimostrato che SCH rappresenta un fattore di rischio per CAD, in particolare in soggetti ad alto ed intermedio Framingham rischio score (FRS)
- Limitazioni:
  -Studio trasversale non supportato da una valutazione causa-effetto
  - mancanza di informazioni sulla durata della malattia tiroidea
  - non completezza su presenza di altri fattori di rischio (es. alcool)
- Non sono stati valutati pazienti di età superiore ai 65 anni

IPOTIROIDISMO CONCLAMATO NELL'ANZIANO

TERAPIA

MOTIVAZIONI:

- ALLEVIARE I SINTOMI DELL'IPOTIROIDISMO

- EVITARE LA PROGRESSIONE VERSO IL MIXEDEMA E LE SUE COMPLICANZE

OBIETTIVO DELLA TERAPIA SOSTITUTIVA

Raggiungimento di uno stato di eutiroidismo

I pazienti più anziani e quelli coronaropatici o con più fattori di rischio per coronaropatia dovranno essere trattati con molta attenzione

!

Gli ormoni tiroidei aumentano la domanda di ossigeno a livello miocardico e ciò può essere associato ad un, seppur piccolo, rischio di indurre aritmie cardiache, angina pectoris o infarto miocardico nei pazienti più anziani

POSSIBILE SCHEMA DI TRATTAMENTO INIZIALE DELL'IPOTIROIDISMO NELL'ANZIANO

INIZIARE CON UNA BASSA POSOLOGIA DI TIROXINA → Nei cardiopatici ev. 12,5 micgr/die

↓

Es. 25 micgr/die

↓

Monitorizzare il paziente e verificare la tolleranza cardiologica

↓

Aumenti posologici di 12,5-25 micgr ogni 4 settimane fino al raggiungimento dell'eutiroidismo

Possono essere considerati ottimali valori di TSH compresi tra 1.0 e 4.0 mUI/L. ?

AME Flash gennaio 2012 modificato

Raccomandazione 5. La terapia può essere intrapresa con l'intera dose necessaria alla completa sostituzione della funzione tiroidea mancante. Tuttavia, nei soggetti anziani o fragili e nei pazienti con malattie cardiovascolari o altre comorbilità rilevanti, il trattamento deve essere iniziato con un dosaggio più cauto (25–50 µg/die). L'aumento della dose sostitutiva deve essere effettuato sulla base dei valori di TSH, dei sintomi e degli eventuali effetti indesiderati.

Raccomandazione 6. Il primo controllo clinico e la determinazione del TSH sierico dovrebbero essere effettuati dopo 4–6 settimane di terapia. In corso di gravidanza, nell'infanzia e nei pazienti fragili sono raccomandati una valutazione attenta e un controllo più precoce del TSH.

Raccomandazione 7. Nella scelta terapeutica devono essere considerati importanti non solo il raggiungimento degli obiettivi biochimici di eutiroidismo ma anche il benessere del paziente e i fattori che possono influenzarne l'aderenza alla terapia nel tempo. Per questo motivo, deve essere fornita un'informazione adeguata sulla disponibilità di varie formulazioni di L-T4 e sulla loro assunzione in rapporto ad alimenti o terapie concomitanti, così da personalizzare la gestione di malattia in accordo con lo stile di vita e le preferenze del paziente.

Rinaldo Guglielmi[1] (rinaldo.guglielmi@alice.it), **Andrea Frasoldati**[2], **Michele Zini**[2], **Carlo Cappelli**[3] & **Enrico Papini**[1]

[1]Endocrinologia e Metabolismo, Ospedale Regina Apostolorum, Albano Laziale (RM)
[2]Endocrinologia, Arcispedale S. Maria Nuova IRCCS, Reggio Emilia
[3] Endocrinologia, Università degli Studi, Spedali Civili, Brescia

- Follow up del paziente in trattamento sostitutivo

Controlli periodici clinici e di laboratorio

ANNUALI ?

SEMESTRALI ?

Controlli a 6 mesi e successivamente
a 12 mesi ?

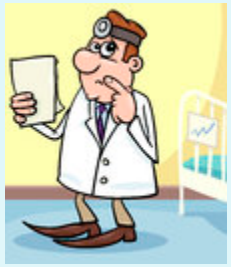
Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association 2012

- Proposta:

- Controlli clinici e di laboratorio semestrali salvo modificazioni del quadro clinico

E L'IPOTIROIDISMO SUB-CLINICO NELL'ANZIANO ?

La prevalenza dell'ipotiroidismo sub-clinico nell'anziano potrebbe essere sovrastimata se non si usano dei range di riferimento del TSH correlati all'età



J Clin Endocrinol Metab, December 2007, 92(12):4575–4582

Age-Specific Distribution of Serum Thyrotropin and Antithyroid Antibodies in the U.S. Population: Implications for the Prevalence of Subclinical Hypothyroidism

Martin I. Surks and Joseph G. Hollowell *Departments of Medicine and Pathology (M.I.S.), Montefiore Medical Center and the Albert Einstein College of Medicine,Bronx, New York 10467; and Department of Pediatrics (J.G.H.), University of Kansas Medical Center, Kansas City*

Quali motivi per trattare un ipotiroidismo sub-clinico ?

- Alleviare i sintomi

- Miglioramento dei sintomi non evidenziato in diversi studi

Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC. L-Thyroxine therapy in subclinical hypothyroidism. A double-blind placebo-controlled trial. *Ann Intern Med. 1984;101(1):18–24.*

Nyström E, Caidahl K, Fager G, Wikkelsö C, Lundberg PA, Lindstedt G. A double-blind crossover 12-month study of L-thyroxine treatment of women with “subclinical” hypothyroidism. *Clin Endocrinol (Oxf).* 1988;29(1):63–75.

Meier C, Staub JJ, Roth CB, et al. TSH-controlled L-thyroxine therapy reduces cholesterol levels and clinical symptoms in subclinical hypothyroidism: a double blind, placebo-controlled trial (Basel Thyroid Study). *J Clin Endocrinol Metab. 2001;86(10):4860–4866.*

Parle J, Roberts L, Wilson S, et al. A randomized controlled trial of the effect of thyroxine replacement on cognitive function in community-living elderly subjects with subclinical hypothyroidism: the Birmingham Elderly Thyroid Study. *J Clin Endocrinol Metab.* 2010;95(8):3623–3632.

Razvi S, Ingoe L, Keeka G, Oates C, McMillan C, Weaver JU. The beneficial effect of L-thyroxine on cardiovascular risk factors, endothelial function, and quality of life in subclinical hypothyroidism: randomized, crossover trial. *J Clin Endocrinol Metab. 2007;92(5):* 1715–1721.

→ Miglioramento dell’astenia dopo terapia

Quali motivi per trattare un ipotiroidismo sub-clinico ?

Prevenire la mortalità per cause cardio-vascolari e per tutte le altre cause

Non sufficienti evidenze che un ipotiroidismo sub-clinico si associ ad un aumentato rischio di mortalità per cause cardiovascolari o per tutte le cause

Rodondi N, Newman AB, Vittinghoff E, et al. Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. *Arch Intern Med. 2005;165(21):2460–2466.*

→ ↑ Rischio scompenso cardiaco congestizio

Sgarbi JA, Matsumura LK, Kasamatsu TS, et al. Subclinical thyroid dysfunctions are independent risk factors for mortality in a 7.5-year follow-up: the Japanese-Brazilian thyroid study. *Eur J Endocrinol.* 2010;162(3):569–577

→ ↑ Rischio mortalità per tutte le cause

Quali motivi per trattare un ipotiroidismo sub-clinico ?

Evitare la progressione in ipotiroidismo conclamato

Valutare i fattori di rischio di progressione:

- Valore del TSH
- Presenza Ab-antitiroide
- Obesità ?
- Sesso femminile ?

TRATTAMENTO O FOLLOW-UP ?

Vanderpump MP, Tunbridge WM, French JM, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol. 1995;43(1):55–68.*

Parle J, Roberts L, Wilson S, et al. A randomized controlled trial of the effect of thyroxine replacement on cognitive function in community-living elderly subjects with subclinical hypothyroidism: the Birmingham Elderly Thyroid Study. *J Clin Endocrinol Metab.* 2010;95(8):3623–3632.

Gopinath B, Wang JJ, Kifley A, et al. Five-year incidence and progression of thyroid dysfunction in older population. *Intern Med J.* 2010;40(9):642–649.

Progressione annuale
2-5 % dei pz/anno

Drugs. 2012 Jan 1;72(1):17-33. **Overt and subclinical hypothyroidism: who to treat and how.** Khandelwal D, Tandon N

IPOTIROIDISMO SUB-CLINICO NELL'ANZIANO

TRATTAMENTO ?

POTREMO VALUTARE:

- Età
- Stato clinico del paziente
- Sintomi e segni di ipotiroidismo
- Entità del TSH

Comunque univocità di vedute nel trattare con valori di TSH > 10

- Presenza di fattori di rischio per progressione

- Considerare un target diverso per TSH per i pz > 70 anni (es. 4 – 6) ATA 2014

TERAPIA DELL'IPOTIROIDISMO NELL'ANZIANO

CONCLUSIONI

Ipotiroidismo conclamato

- Univocità di vedute sulla necessità del trattamento

- La correzione dell'ipotiroidismo va effettuata gradualmente e lentamente
(valutare età ed eventuali affezioni cardiovascolari concomitanti)

- Porre attenzione nell'evitare la soppressione anche parziale del TSH

- Considerare il target del TSH in base allo stato clinico e all'età del paziente
(> 70 anni (es. 4 – 6) ATA 2014)

TERAPIA DELL'IPOTIROIDISMO NELL'ANZIANO

CONCLUSIONI

Ipotiroidismo sub-clinico

- Non vi sono evidenze certe circa un aumentato rischio di cardiopatia ischemica nei pazienti > 65 anni

- La maggior parte degli studi eseguiti fino ad ora non hanno evidenziato un aumentato rischio di mortalità per cause cardiovascolari o per tutte le altre cause

- Il miglioramento dei sintomi non è stato sempre evidenziato in diversi studi

TERAPIA DELL'IPOTIROIDISMO NELL'ANZIANO

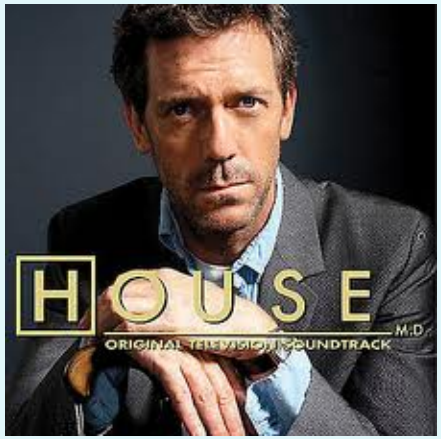
CONCLUSIONI

Ipotiroidismo sub-clinico

- Non essendoci ancora indicazioni chiare sul se trattare un ipotiroidismo sub-clinico:

VALUTARE IL SINGOLO PAZIENTE

- La decisione in merito ad un eventuale trattamento potrebbe essere presa considerando:



- Stato clinico del paziente
- Età
- Sintomi
- Rischio di progressione in ipotiroidismo conclamato

CONVEGNO MACROREGIONALE

AME DAY

20/21
MAGGIO 2016

GRAZIE PER L'ATTENZIONE