7-10 novembre 2013, Bari

12° Congresso Nazionale AME
6th Joint Meeting with AACE

Update in Endocrinologia Clinica

Iposurrenalismo
Inquadramento clinico ed epidemiologico

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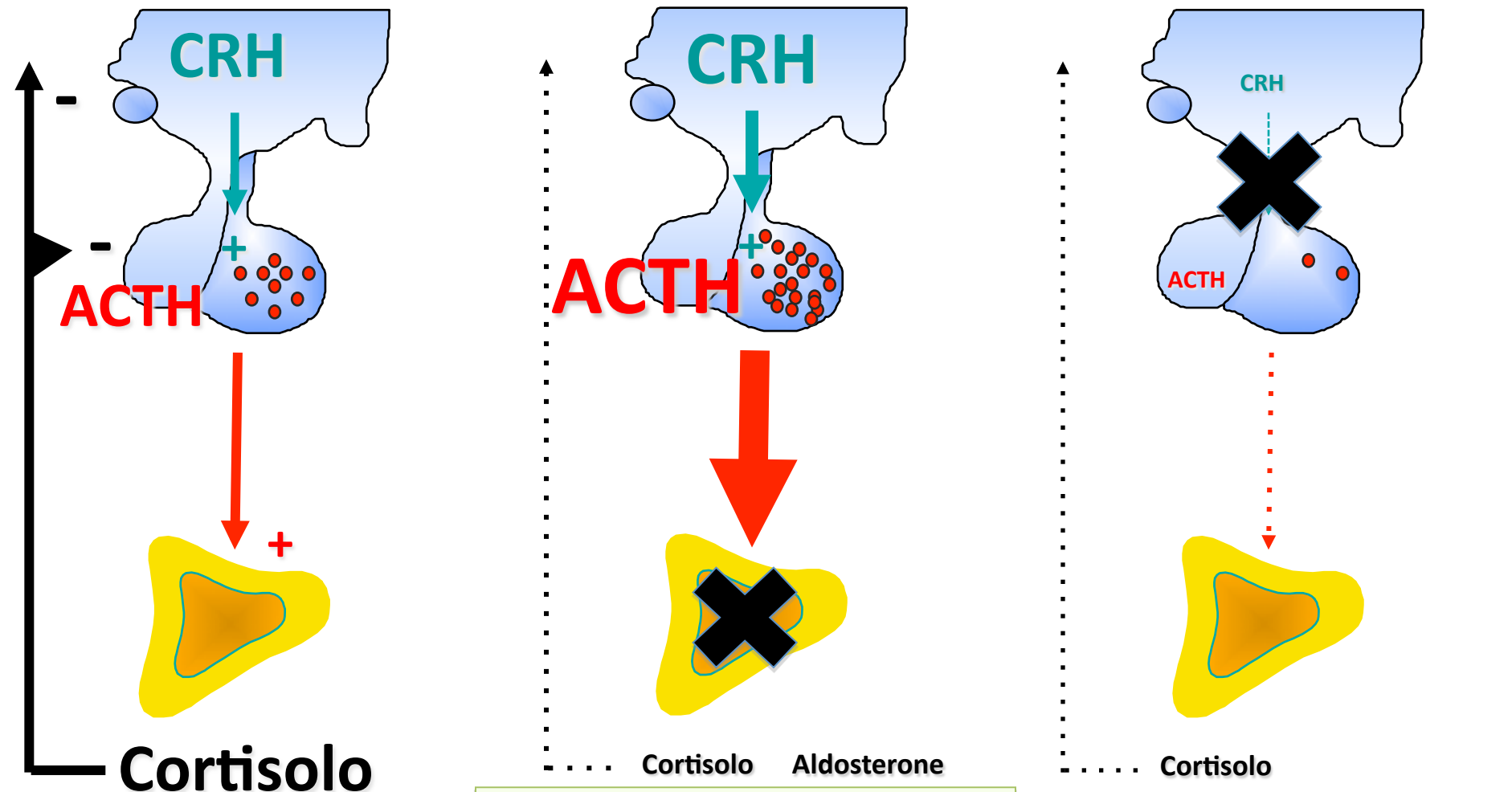
Asse Ipotalamo - Ipofisi - Surrene



EPIDEMIOLOGIA

Insufficienza surrenalica primaria

Prevalenza: 93-140 casi / milione

- Italia (stimato):
  - 6.000-7.000 casi
  - 300 nuovi casi/anno

SOTTOSTIMATA

Insufficienza surrenalica secondaria

Prevalenza: 125-280 casi /milione


sie
Registro Italiano
dell'Insufficienza
Surrenalica
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avanti
Cos'è
Come registrarsi
Enti Partecipanti
Privacy
SIE

Eziologia
Iposurrenalismo Primitivo

Primitivo (Morbo di Addison)	
Autoimmune	Adrenalite autoimmune
Tubercolare	Adrenaliti infettive
Infezioni sistemiche fungine	
Cytomegalovirus	
HIV	
Metastasi e linfomi	
Granulomatosi ed amiloidosi	
Emorragie bilaterali massive	
Adrenoleucodistrofia	Forme genetiche
Deficit enzimatici steroidogenesi	
Ipoplasia surrenalica congenita	
Insensibilità all'ACTH	
Bisurrenalectomia chirurgica	

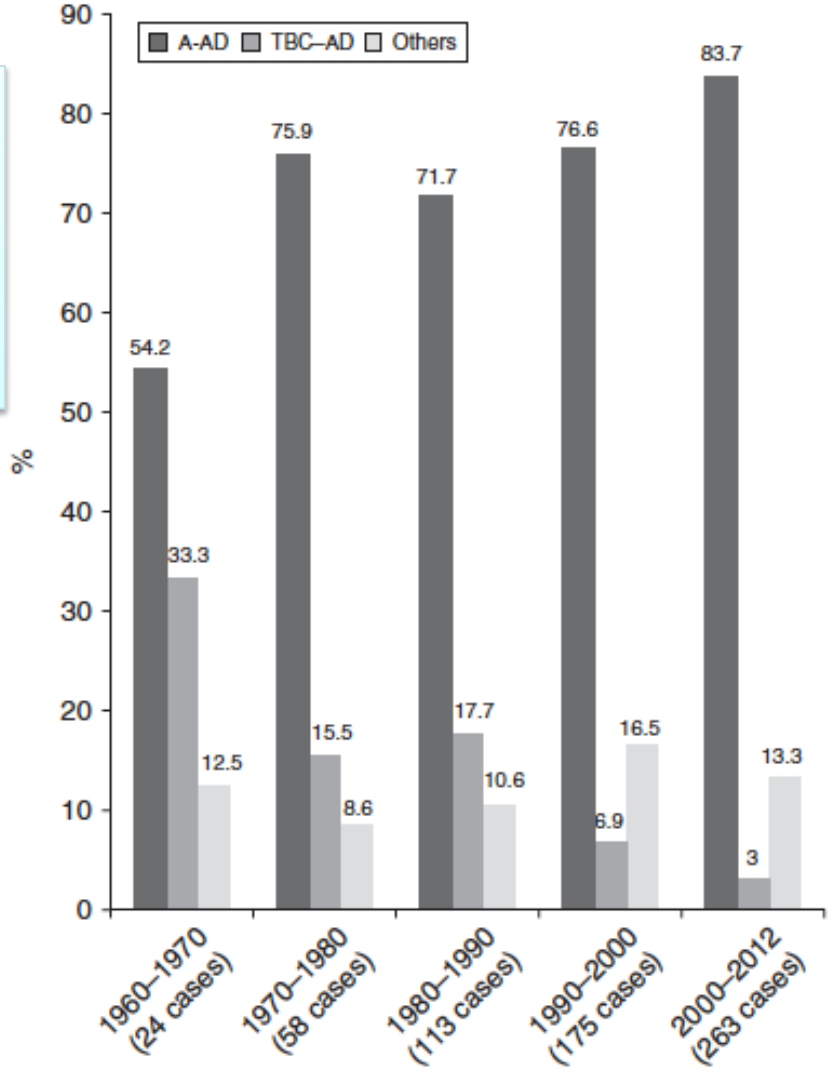
European Journal of Endocrinology (2013) 169 773–784 ISSN 0804-4643

CLINICAL STUDY

Addison's disease: a survey on 633 patients in Padova

1960-1970

Autoimmune 54%
TBC 33%
Altre 12%

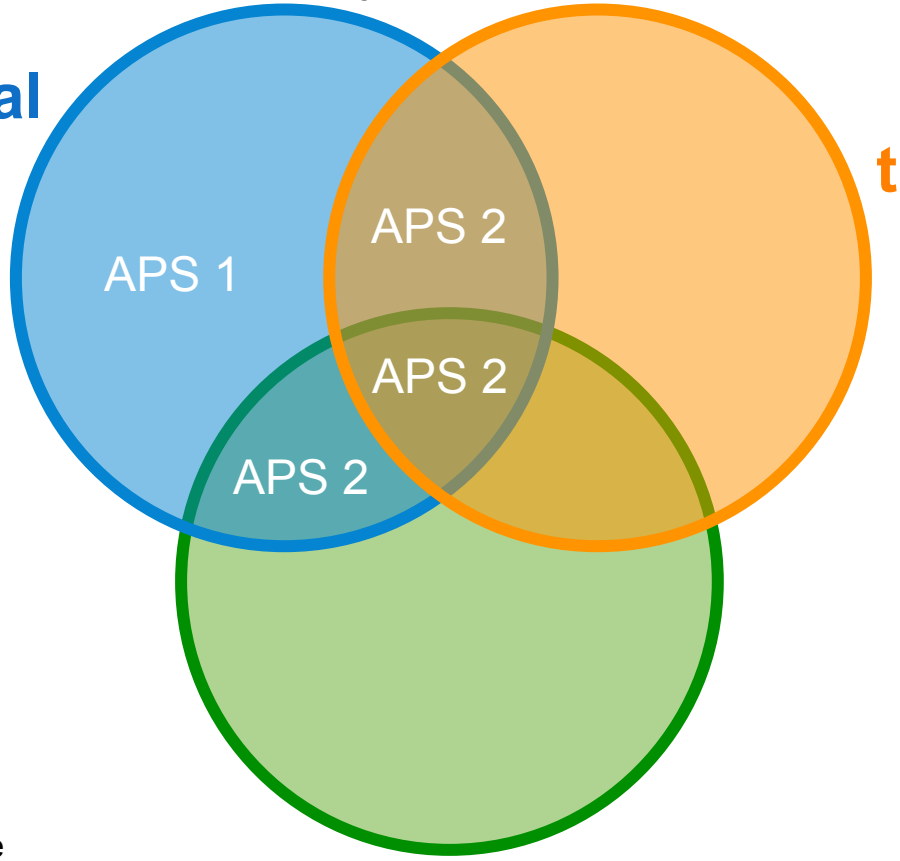


2012

Autoimmune 83%
TBC 3%
Altre 13%

Betterle et al 2013

Primary adrenal insufficiency frequently coexists with autoimmune thyroid disease and type 1 diabetes[1]

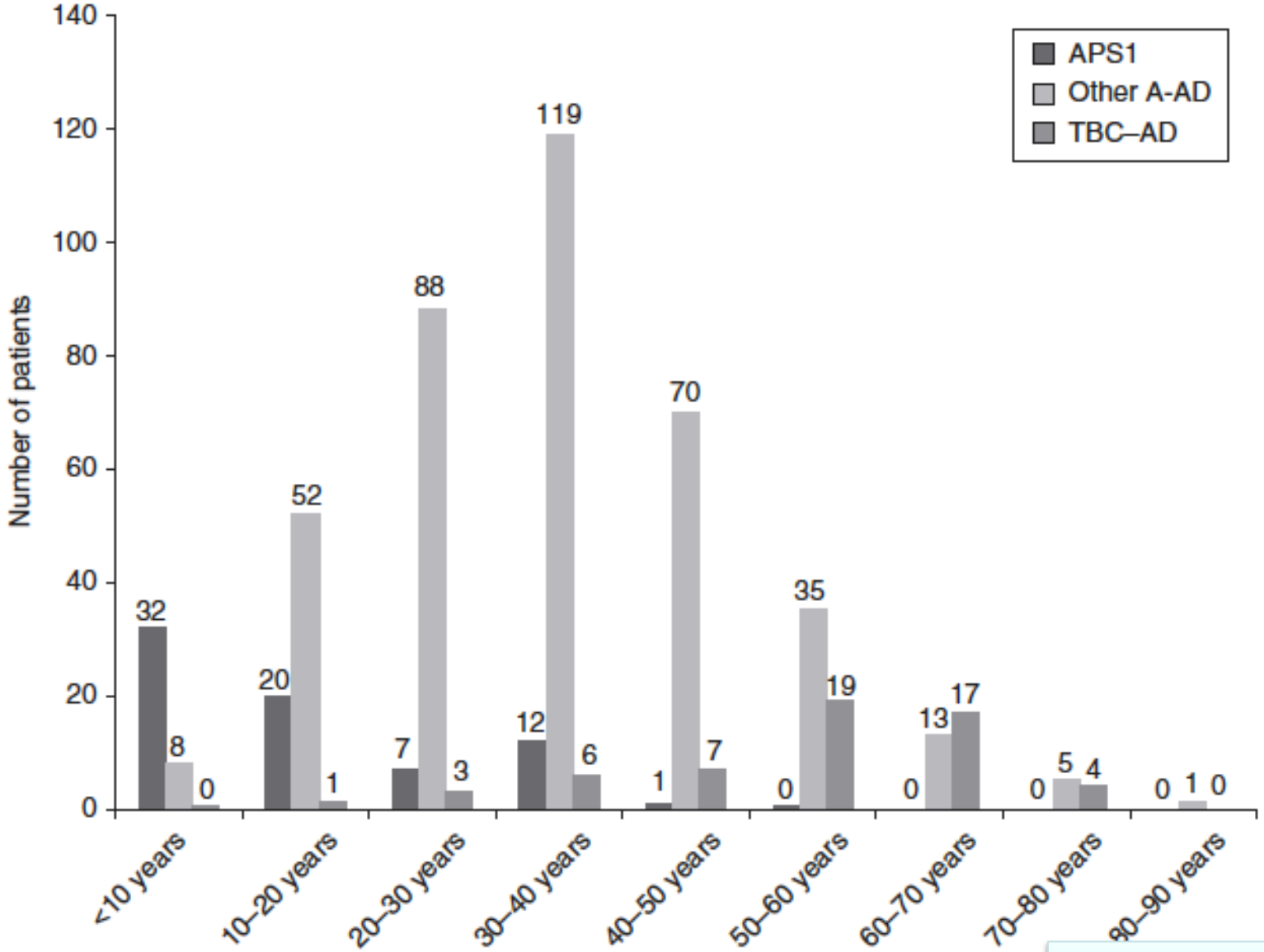


APS: autoimmune polyendocrine syndrome

APS1 : A-AD associated with chronic candidiasis and/or chronic hypoparathyroidism

1. Erichsen MM et al. J Clin Endocrinol Metab 2009;94:4882–4890

Morbo di Addison: età di comparsa



Betterle et al EJE 2013

Morbo di Addison
Insufficienza Cortico-Surrenalica primitiva

Thomas Addison (1793–1860)

1855: prima descrizione del Morbo di Addison

“The leading and characteristic features of the morbid state to which I would direct attention are anaemia, general languor and debility, remarkable feebleness of the heart’s action, irritability of the stomach and a peculiar change of colour in the skin, occurring in connexion with a diseased condition of the ‘supra-renal capsules’ “.

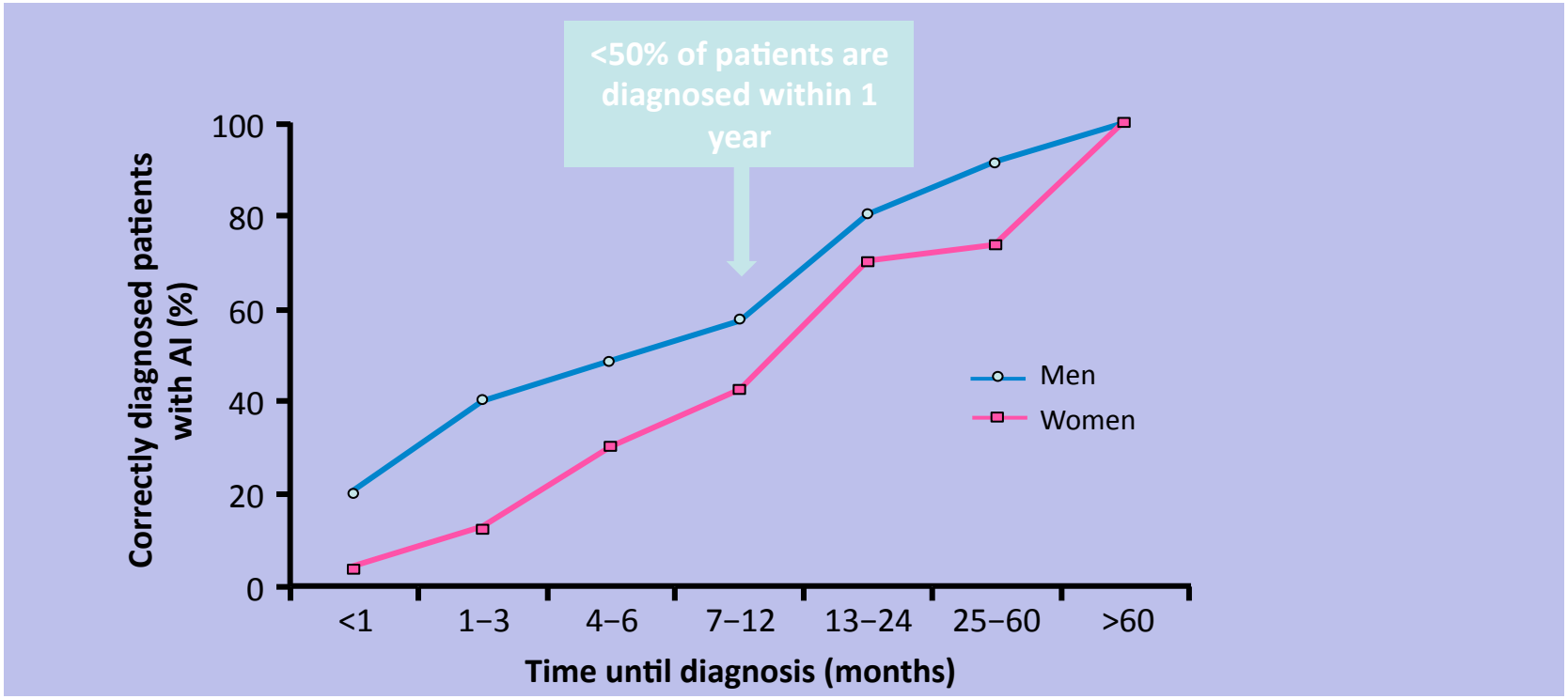
Insufficienza Corticosurrenalica: Clinica

Sintomi
Astenia
Anoressia
Dolori addominali
Mialgie
Turbe neuropsichiche
Vomito
Diarrea
Preferenza cibi salati
Cefalea

Segni
Dimagramento
Iperpigmentazione (solo morbo di Addison)
Ipotensione arteriosa
Amenorrea
Riduzione peli pubici ed ascellari

Laboratorio
Iposodiemia
Iperpotassiemia
Ipoglicemia
Anemia normocromica
Linfocitosi
Eosinofilia

Delayed diagnosis of adrenal insufficiency is common in clinical practice[1]



- 67% of patients consulted ≥3 physicians before being correctly diagnosed
- 68% of patients incorrectly diagnosed initially
  - Psychiatric and gastrointestinal disorders most common incorrect diagnoses

Figure adapted from Bleicken et al. Reproduced bypermission.

1. Bleicken B et al. Am J Med Sci 2010;339:525–531

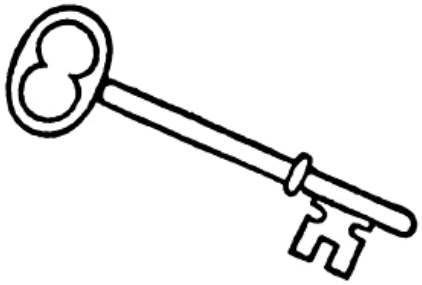
Diagnosi dell'insufficienza surrenalica

Cortisolemia ridotta

< 3 mcg/dl →diagnosi certa

< 18 mcg/dl →necessari test dinamici
ACTH test / CRH / ITT

ACTH elevato (solo nel morbo di Addison)



Importanza del contesto clinico
Conoscenza

Natural history of primary adrenal insufficiency

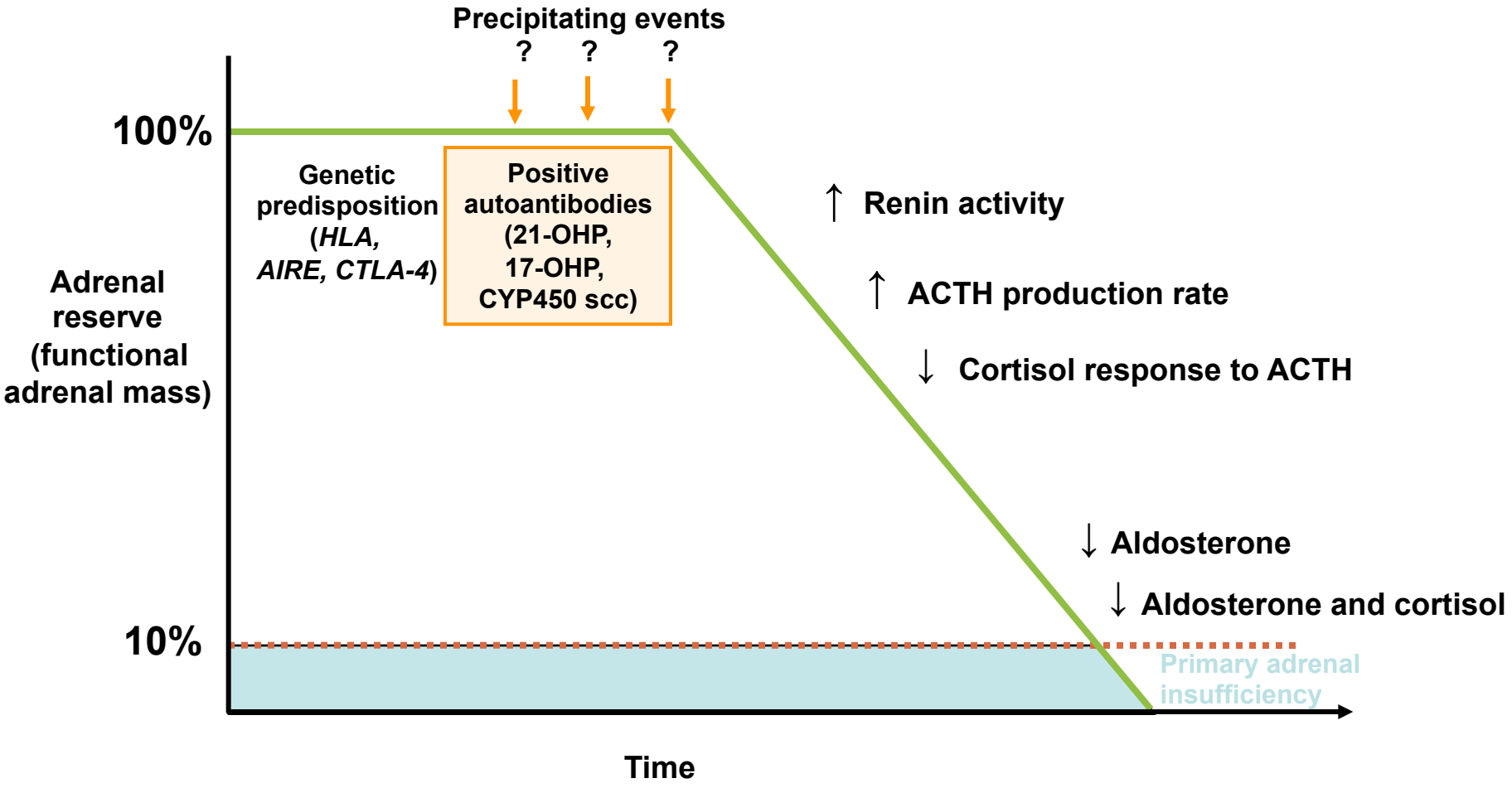


Figure adapted from Ten et al

Ten S et al. J Clin Endocrinol Metab 2001;86:2909–2922

Insufficienza surrenalica
QUADRO CLINICO

ESORDIO CRONICO

NECESSITA' ASSOLUTA di terapia sostitutiva con steroidi

RISCHIO MORTALE

ESORDIO ACUTO

– Grave ipotensione e shock
– Dolori addominali
– Febbre
– Nausea e vomito
– Stato confusionale

L'esordio acuto può essere scatenato da situazioni stressanti come episodi intercorrenti febbrili ed infettivi (vie respiratorie, intestinali etc), interventi chirurgici

Epidemiology of adrenal crisis in chronic adrenal insufficiency: the need for new prevention strategies

EJE 162 597–602, 2010

Stefanie Hahner[1], Melanie Loeffler[1], Benjamin Bleicken[3], Christiane Drechsler[2], Danijela Milovanovic[1], Martin Fassnacht[1], Manfred Ventz[3], Marcus Quinkler[3] and Bruno Allolio[1]

Table 3 Frequency of adrenal crisis (AC) in patients with primary (PAI) and secondary adrenal insufficiency (SAI).

	PAI (n=254)		SAI (n=190)	
Number of AC	n	%	n	%
0	135	53.1	124	65.1
1	58	22.8	32	16.9
2	24	9.4	8	4.2
3	10	3.9	12	6.3
≥4	27	10.6	14	7.4

Table 4 Precipitating factors for adrenal crisis.

	n	Pe
Gastrointestinal infection	59	
Other infectious disease/fever	44	
Surgery	13	
Unknown	12	
Strenous physical activity	14	
Cessation of glucocorticoid substitution by patient	9	
Neglected glucocorticoid intake	9	
Psychic distress	6	
Accident	5	
Cessation of glucocorticoid substitution by attending physician	2	
Other reasons[a]	8	

Table 5 Risk factors for adrenal crisis.

Adrenal crisis with hospital admission	Odds ratio	95% Confidence interval	P
All patients (n=444)			
DHEA replacement	0.88	0.52–1.49	0.63
Glucocorticoid dose/BSA	1.02	0.98–1.07	0.32
Age at diagnosis	0.98	0.96–1.01	0.12
Female sex	1.66	1.00–2.75	0.05
Educational status	1.22	0.70–2.14	0.49
Concomitant disease	**1.81**	**1.13–2.90**	**0.01**
BMI	0.98	0.93–1.03	0.40
SAI versus PAI	**0.51**	**0.27–0.97**	**0.04**
Patients with PAI (n=254)			
DHEA replacement	0.82	0.40–1.72	0.60
Glucocorticoid dose/BSA	1.02	0.96–1.08	0.50
Fludrocortisone dose	0.84	0.38–1.88	0.68
Age at diagnosis[a]	**0.96**	**0.93–0.99**	**0.02**
Female sex	1.60	0.74–3.44	0.23
Educational status	0.90	0.37–2.19	0.82
Concomitant disease	**2.02**	**1.05–3.89**	**0.04**
BMI	0.995	0.91–1.08	0.90
Patients with SAI (n=189)			
DHEA replacement	0.92	0.33–2.55	0.87
Glucocorticoid dose/BSA	1.04	0.96–1.12	0.32
Age at diagnosis	0.98	0.94–1.01	0.21
Female sex	**2.18**	**1.06–4.50**	**0.04**
Diabetes insipidus	**2.71**	**1.22–5.99**	**0.01**
Educational status	1.48	0.62–3.56	0.38
Concomitant disease	1.58	0.66–3.77	0.31
BMI	0.983	0.91–1.06	0.67

	1.1	4	3.6
	4.4	6	5.4

Deficit di ACTH: Cause

Trauma cranico

Emorragia subaracnoidea

Patologie della regione sellare/parasellare

Apoplessia ipofisaria

Adenomi ipofisari

Ipofisiti ed altre infiammazioni

Malattie genetiche

Altri Tumori

Post chirurgia e radioTx

Quali i pazienti a rischio ?
Dove cercarli ?

Hypopituitarism

Seminar

Harald Jörn Schneider, Gianluca Aimaretti, Ilonka Kreitschmann-Andermahr, Günter-Karl Stalla, Ezio Ghigo

Trauma cranico

ACTH deficit 11%

	n	Any degree of hypopituitarism	Multiple deficiencies	GH	LH/FSH	ACTH	TSH	Remarks
Kelly et al, 2000[11]	22	8	3	4	4	1	1	
Lieberman et al, 2001[14]	70	48	12	7	2	32	15	32 patients with low morning cortisol; only 5 patients with cortisol <500 nmol/L after ACTH stimulation
Bondanelli et al, 2004[15]	50	27	6	4	7	0	5	No stimulation test for ACTH
Agha et al, 2004[12]	102	29	6	11	12	13	1	
Popovic et al, 2004[16]	67	23	7	10	6	5	3	
Aimaretti et al, 2005[13]	70	16	7	14	8	4	5	No stimulation test for ACTH
Leal-Cerro et al, 2005[17]	170	42	15	6	29	11	10	Endocrine testing only if clinical suspicion of hypopituitarism (n=99)
Schneider et al, 2006[18]	70	25	3	7	14	6	2	
Tanriverdi et al, 2006[19]	52	26	5	17	4	10	3	
Herrmann et al, 2006[20]	76	18	5	6	13	2	2	
Total (%)	749 (100)	262 (35)	69 (9)	86 (11)	99 (13)	84 (11)	47 (6)	

LH=luteinising hormone. FSH=follicle-stimulating hormone. GH=growth hormone. ACTH=adrenocorticotropic hormone. TSH=thyrotropic hormone.

Table 1: Hypopituitarism in the chronic phase after traumatic brain injury

Lancet 369: 1461, 2007

Hypopituitarism

Seminar

Harald Jörn Schneider, Gianluca Aimaretti, Ilonka Kreitschmann-Andermahr, Günter-Karl Stalla, Ezio Ghigo

Emorragia subaracnoidea

ACTH deficit 16 %

	n	Any degree of hypopituitarism	Multiple deficiencies	GH	LH/FSH	ACTH	TSH	Remarks
Kelly et al, 2000[11]	2	2	0	2	0	0	0	
Brandt et al, 2004[21]	10	5	0	1	4	0	0	
Aimaretti et al, 2004[24]	40	15	4	10	5	1	3	No stimulation test for ACTH
Kreitschmann-Andermahr et al, 2004[23]	40	22	3	8	0	16	1	
Dimopoulou et al, 2004[22]	30	14	4	11	4	3	2	No stimulation test for GH (11 patients low IGF-I)
Total (%)	122 (100)	58 (48)	11 (9)	32 (26)	13 (11)	20 (16)	6 (5)	

LH=luteinising hormone. FSH=follicle-stimulating hormone. GH=growth hormone. ACTH=adrenocorticotropic hormone. TSH=thyrotropic hormone.

Table 2: **Hypopituitarism after subarachnoid haemorrhage**

Lancet 369: 1461, 2007

Pituitary Insufficiency after Infectious Meningitis: A Prospective Study

J Clin Endocrinol Metab, July 2010, 95(7):3277–3281

Aristotelis Tsiakalos,* Ioannis D. Xynos,* Nikolaos V. Sipsas, and Gregory Kaltsas

Department of Pathophysiology, Medical School, National and Kapodistrian University of Athens, 11527 Athens, Greece

30% dei pazienti con ACTH deficit tardivo

TABLE 2. Demographics and evaluation of pituitary function in patients with acute infectious meningitis at the onset of the disease and 12 months later

	Age (yr)	Sex	Meningitis-infectious agent	Endocrine deficits at the acute phase	Endocrine deficits at 12 months
1	23	F	*Cryptococcus neoformans*	Normal	Normal
2	16	M	Unidentified virus	Normal	Corticotropic deficiency
3	40	M	*C. neoformans*	Transient gonadotropic deficiency	Normal
4	18	M	*Neisseria meningitidis*	Low T_3 syndrome	Corticotropic deficiency
5	47	F	Unidentified virus	Normal	Corticotropic and somatotropic deficiency
6	60	F	Unidentified virus	Hyperprolactinaemia	Normal[a]
7	44	M	*N. meningitidis*	Low T_3 syndrome, Transient gonadotropic deficiency	Corticotropic and somatotropic deficiency
8	40	F	Unidentified virus	Low T_3 syndrome	Normal[a]
9	39	F	Unidentified virus	Low T_3 syndrome, Somatotropic deficiency	Somatotropic deficiency
10	67	F	*Listeria monocytogenes*	Low T_3 syndrome, Possible somatotropic deficiency	NA
11	15	F	*Streptococcus pneumoniae*	Normal	Normal
12	32	M	Unidentified virus	Low T_3 syndrome	Normal
13	47	M	*Streptococcus oralis*	Normal	Hashimoto thyroiditis
14	52	F	*S. pneumoniae*	Low T_3 syndrome	Normal
15	40	M	Herpes simplex virus-1	Normal	NA
16	28	M	*N. meningitidis*	Transient somatotropic deficiency	Normal

Paziente oncologico
Complicanze endocrine

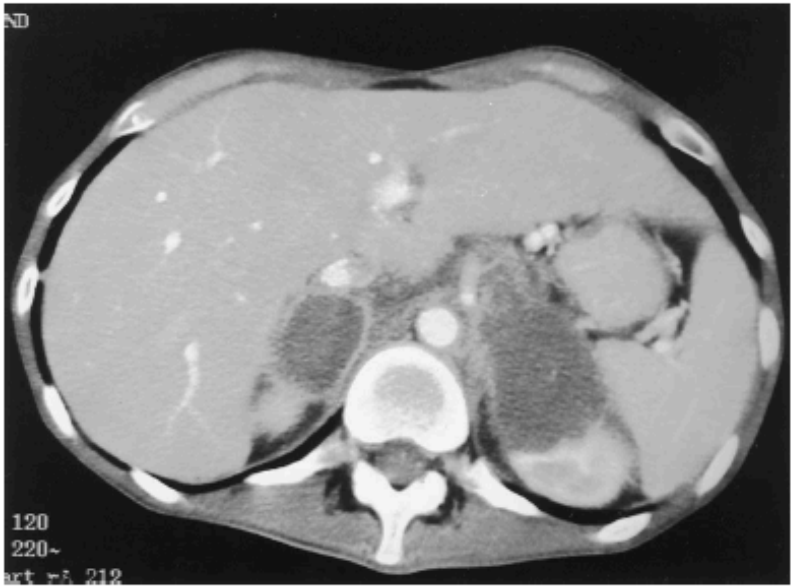
- per azione diretta della neoplasia
- per complicanze della neoplasia
- indotte da terapia

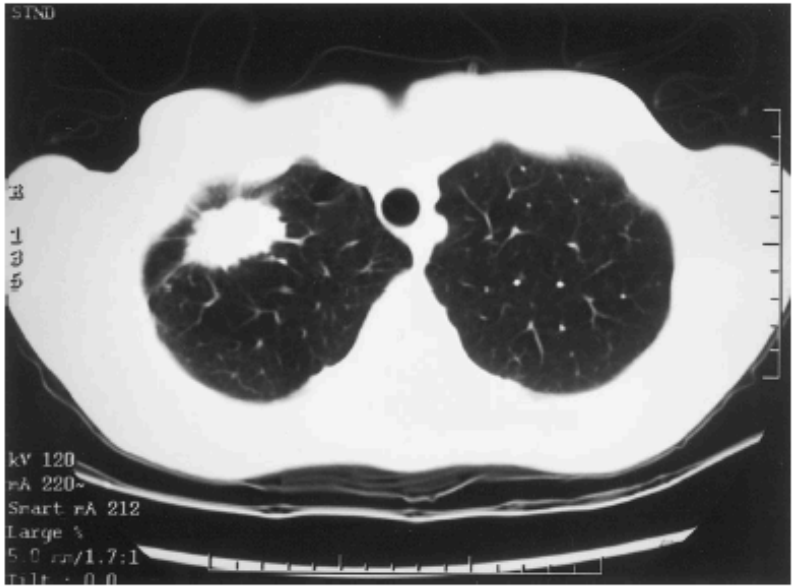
JOURNAL OF CLINICAL ONCOLOGY

Sirachainan and Kalemkerian, 20: 4598, 2002

CASE 2. ADRENAL INSUFFICIENCY AS THE INITIAL MANIFESTATION OF NON–SMALL-CELL LUNG CANCER

A 34-year-old woman presented with back pain, fatigue, anorexia, weight loss, and nausea and vomiting of 8 months' duration. She had smoked one pack of cigarettes per day for 17 years. Her blood pressure was 96/62 mmHg, and the results of her serum electrolyte and liver and thyroid function tests were normal. An abdominal computed tomography (CT) scan showed symmetric, homogenous enlargement of the adrenal glands. A 6 AM plasma cortisol level was 7.5 μg/dL (normal, 6 to 30 μg/dL); it remained unchanged 1 hour after intravenous administration of 0.25 mg of cosyntropin. A repeat adrenocorticotropic hormone (ACTH) stimulation test demonstrated a plasma cortisol level of 2.1 μg/dL at baseline and 4.6 μg/dL 1 hour after cosyntropin. Her plasma ACTH level was 141 pg/mL (normal, 9 to 52 pg/mL). A supine serum aldosterone level on a normal diet was 2 ng/dL (normal, 2 to 9 ng/dL). Her 24-hour urinary free cortisol, 17-ketosteroid, and 17-hydroxycorticosteroid levels were normal. She was initially treated with corticosteroids but was noncompliant. Three months later, she was admitted with orthostatic hypotension, worsening back pain, and persistent nausea and vomiting. She was pale, with no cutaneous hyperpigmentation. Laboratory studies revealed a sodium concentration of 127 mEq/L, a potassium concentration of 5.7 mEq/L, and a bicarbonate concentration of 22 mEq/L. A repeat CT scan showed further enlargement of bilateral adrenal masses (Fig 1), and a chest x-ray showed a vague right upper-lobe opacity. She





CLINICAL CASE SEMINAR

Tumors Metastatic to the Pituitary Gland: Case Report and Literature Review

JOHN KOMNINOS, VARVARA VLASSOPOULOU, DESPINA PROTOPAPA, STEFANOS KORFIAS, GEORGE KONTOGEORGOS, DAMIANOS E. SAKAS, AND NICOLAS C. THALASSINOS

TABLE 4. Clinical presentation of 190 symptomatic pituitary metastases

Symptom/finding	n	%
Diabetes insipidus	86	45.2
Cranial nerve II deficit	53	27.9
Anterior pituitary insufficiency (partial or total)	45	23.6
Cranial nerve III, IV, VI palsy	41	21.6
Headaches/postocular pain	30	15.8
Fatigue/general malaise	15	7.9
Hyperprolactinemia	12	6.3
Pituitary apoplexy	9	4.7
Nausea/vomiting	7	3.7
Anorexia/weight loss	6	3.1
Altered consciousness	5	2.6

J Clin Endocrinol Metab 2004, 89: 574

CLINICAL CASE SEMINAR

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TABLE 3. Origin of primary tumor metastatic to the pituitary in 380 cases

Tumor origin	n	%	Tumor origin	n	%
Breast	151	39.7	Pancreas	5	1.3
Lung	90	23.7	Pharynx	5	1.3
Gastrointestinal	24	6.3	Endometrium	5	1.3
Colon	9		Leukemia	5	1.3
Stomach	7		Urinary bladder	4	1.1
Ileum	1		Uterine cervix	4	1.1
Prostate	19	5.0	Liver	4	1.1
Unknown	12	3.1	Multiple myeloma	3	0.8
Kidney	10	2.6	Paranasal sinus	3	0.8
Melanoma/skin	9	2.4	Oral cavity	3	0.8
Thyroid	8	2.1	Lymphoma	2	0.5

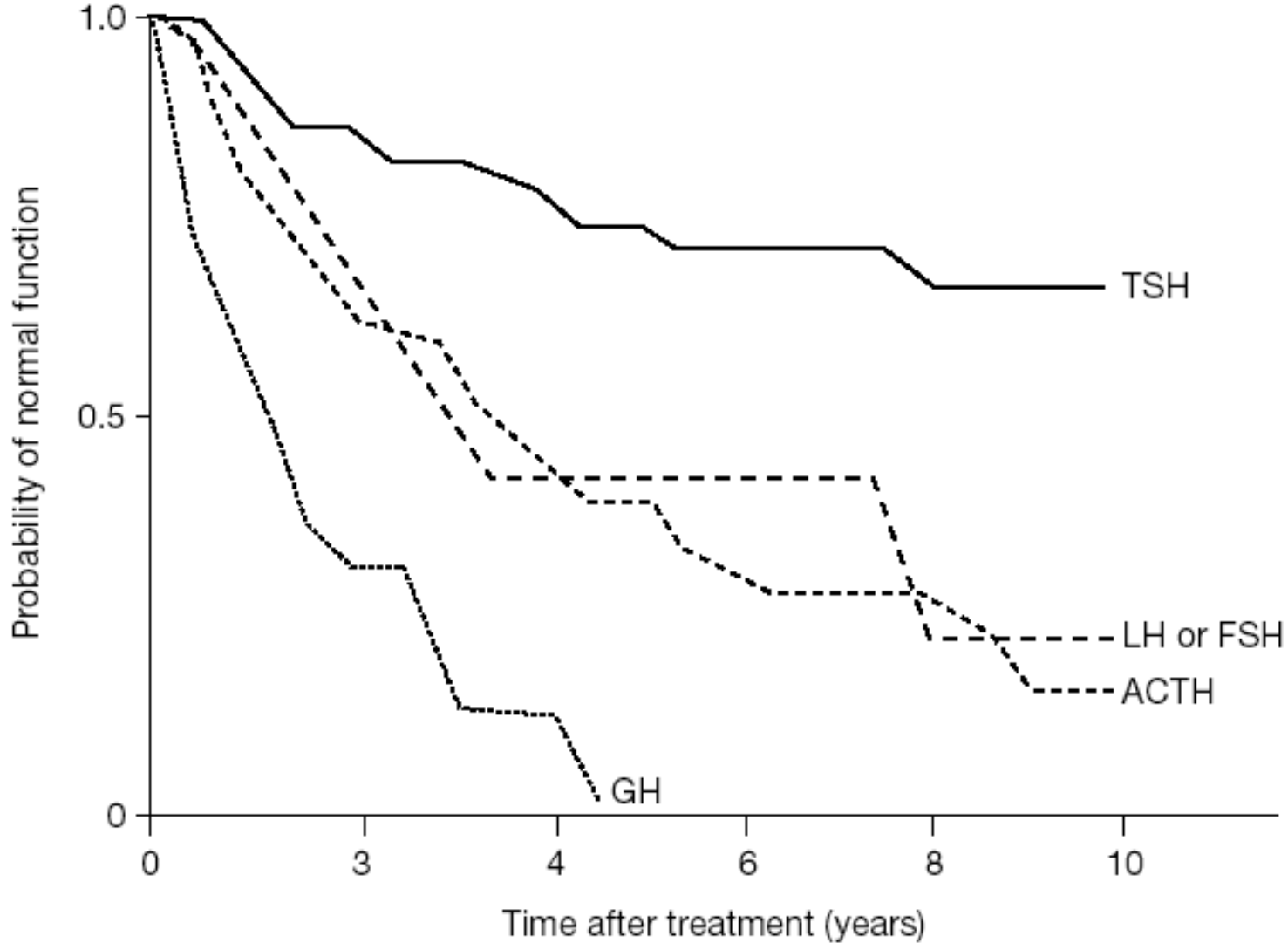
Data are from Refs. 2, 3, 5, 7, 9, 10, 13, 14, 18–26, 30, 35, and 37–51.

J Clin Endocrinol Metab 2004, 89: 574

Paziente oncologico
Complicanze endocrine

- per azione diretta della neoplasia
- per complicanze della neoplasia
- indotte da terapia
  - Radiante

Probability of hypothalamic–pituitary axis dysfunction after conventional radiotherapy for pituitary adenomas.



Littley MD et al. (1989) QJ Med 70: 145–160.

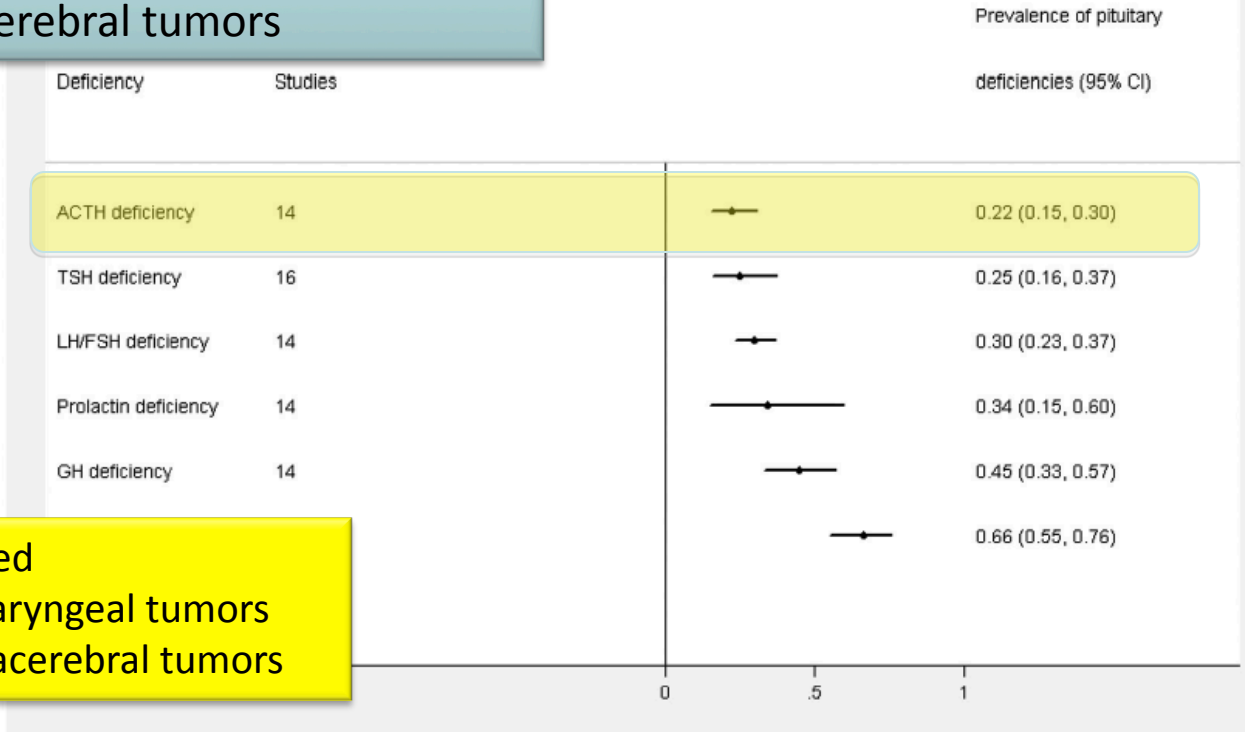
Pituitary Dysfunction in Adult Patients after Cranial Radiotherapy: Systematic Review and Meta-Analysis

Natasha M. Appelman-Dijkstra,* Nieke E. Kokshoorn,* Olaf M. Dekkers, Karen J. Neelis, Nienke R. Biermasz, Johannes A. Romijn, Johannes W. A. Smit, and Alberto M. Pereira

J Clin Endocrinol Metab 96: 2330–2340, 2011

The studies were published between 1975 and 2009. Seventy-five percent of the patients (608 of 813) were treated for nasopharyngeal cancer. The remaining 25% were treated for intracerebral tumors

Circa il 25% dei pazienti sviluppa un deficit di ACTH



Adrenal insufficiency was diagnosed
in 0–50% of patients with nasopharyngeal tumors
in 3–62% of the patients with intracerebral tumors

Paziente oncologico
Complicanze endocrine

- per azione diretta della neoplasia
- per complicanze della neoplasia
- indotte da terapia
  - Radiante
  - Medica

Food and Drug Administration Drug Approval Summary: Sunitinib Malate for the Treatment of Gastrointestinal Stromal Tumor and Advanced Renal Cell Carcinoma

EDWIN P. ROCK,[a] VICKI GOODMAN,[a] JANET X. JIANG,[b] KOOROS MAHJOOB,[b] S. LEIGH VERBOIS,[a] DAVID MORSE,[a] RAMZI DAGHER,[a] ROBERT JUSTICE,[a] RICHARD PAZDUR[c]

ABSTRACT

On January 26, 2006, sunitinib (Sutent) received regular approval as monotherapy for the treatment of patients with gastrointestinal stromal tumor after disease progression on or into

Time-to-tumor

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.0001). Partial

sunitinib-treate

Sunitinib also r

26, 2006, as monotherapy for treatment of advanced renal cell carcinoma (RCC). In two single-arm trials of sunitinib in patients with metastatic RCC, partial responses were observed in 25.5% (95% confidence interval [CI], 17.5, 34.9) and 36.5% (95% CI, 24.7, 49.6) of patients. Median response durations in the two trials were 27.1 weeks (95% CI, 24.4, incalculable) and 54 weeks (95% CI, 34.3, 70.1).

nitinib-treated

abnormalities,

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ction. Cardiac

ing cardiac ab-

onclinical find-

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such as surgery, trauma, or severe infection. Caution should be exercised when administering sunitinib in combination with known CYP3A4 inducers or inhibitors. *The Oncologist* 2007;12:107–113

Based on nonclinical findings, physicians prescribing sunitinib should monitor for adrenal insufficiency in patients who undergo stressors such as surgery, trauma, or severe infection

Sunitinib: rischio surrenalico ?

In studi clinici condotti su 336 pazienti trattati ad uno o più cicli di sunitinib non vi è stata **nessuna** evidenza di necrosi/emorragia surrenalica (TAC/RMN)

Il test all'ACTH eseguito in circa 400 pazienti trattati con sunitinib in trials clinici, ha identificato con certezza **un solo caso** di insufficienza surrenalica
In sette casi si è avuta una risposta parziale del cortisolo (picco compreso tra 12 mcg e 16 mcg)
In nessun caso si è avuta una crisi acuta di insufficienza surrenalica

da Lodish & Stratakis, Endocrine-Related Cancer 17: R233, 2010

Anti-CTLA-4 antibody therapy associated autoimmune hypophysitis: serious immune related adverse events across a spectrum of cancer subtypes

Troy Dillard · Chris G. Yedinak · Joshi Alumkal · Maria Fleseriu

Pituitary (2010) 13:29–38
DOI 10.1007/s11102-009-0193-z

Incidence of autoimmune hypophysitis in clinical trials of anti-CTLA-4 therapy

Percentage	Disease	References
17.0	Metastatic melanoma	Maker et al. [26]
9.0	Metastatic melanoma	Downey et al. [24]
7.1	Metastatic melanoma	Phan et al. [17]
4.9	Metastatic melanoma, renal cell carcinoma	Blansfield et al. [22]
4.0	Metastatic melanoma	Weber et al. [20]
3.3	Renal cell carcinoma	Yang et al. [29]
2.5	Metastatic melanoma	Ribas et al. [18]
1.8	Metastatic melanoma	Attia et al. [10]
0	Metastatic melanoma	Weber et al. [28]
0	Prostate cancer	Small et al. [27]
0	Prostate cancer	Fong et al. [14]
0	Metastatic melanoma	Maker et al. [25]

Here we describe the first 2 cases of hypopituitarism due to presumed autoimmune hypophysitis in subjects undergoing experimental therapy with ipilumumab for **prostate cancer**

Endocrine Side Effects Induced by Immune Checkpoint Inhibitors

Salvatore Maria Corsello, Agnese Barnabei, Paolo Marchetti, Liana De Vecchis, Roberto Salvatori, and Francesco Torino

Evidence Synthesis: The spectrum of endocrine disease experienced by patients treated with ipilimumab includes most commonly hypophysitis, more rarely thyroid disease or abnormalities in thyroid function tests, and occasionally primary adrenal insufficiency. Hypophysitis has emerged as a distinctive side effect of CTLA4-blocking antibodies, establishing a new form of autoimmune pituitary disease. This condition, if not promptly recognized, may be life-threatening (due to secondary hypoadrenalism). Hypopituitarism caused by these agents is rarely reversible, and prolonged or lifelong substitutive hormonal treatment is often required. The precise mechanism of injury to the endocrine system triggered by these drugs is yet to be fully elucidated.

Conclusions: Although reports of endocrine side effects caused by cancer immune therapy are abundant, their exact prevalence and mechanism are unclear. Well-designed correlative studies oriented to finding and validating predictive factors of autoimmune toxicity are urgently needed.
(*J Clin Endocrinol Metab* 98: 1361–1375, 2013)

Ipofisiti: incidenza
Studi iniziali: 0-17%
Studi recenti e più numerosi: 5%

Paziente oncologico
Complicanze surrenaliche

- per azione diretta della neoplasia
- per complicanze della neoplasia
- indotte da terapia
  - Radioterapia
  - Medica
    - Inibitori delle tirosinchinasi
    - Inibitori immunitari (anti CTLA-4)
    - Cortisonici

Precedente trattamento con STEROIDI

- **diversa potenza ed emivita**
- **diversa via di somministrazione**
- **durata del trattamento**
- **alte dosi**
- **sensibilità individuale**
- **concomitante uso di inibitori del CYP3A4**
  - Antifungini

5 mg prednisone o equivalente/die per oltre 3 settimane

A pilot study of adrenal suppression after dexamethasone therapy as an antiemetic in cancer patients

Hye-Suk Han · Young Kwang Shim · Jeong Eun Kim · Hyun-Jung Jeon · Sung-nam Lim · Tae-Keun Oh · Ki Hyeong Lee · Seung Taik Kim

Support Care Cancer 2011
DOI 10.1007/s00520-011-1248-z

	Normal adrenal response		Suppressed adrenal response	
	Number	Percentage (%)	Number	Percentage (%)
Overall				
3 or 6 months (n=103)	58	56.3	45	43.7
3 months (n=103)	63	61.2	40	38.8
6 months (n=25)	15	60.0	10	40.0
According to the MA use				
Use of MA (n=58)	28	48.3	30	51.7
No use of MA (n=45)	30	66.7	15	33.3

Patients with normal and suppressed adrenal responses had similar cumulative dexamethasone doses (mean±SD257.9±178.1 vs 243.9± 184.9 mg; P=0.697) and similar total dexamethasone treatment durations (mean±SD, 25.7±15.0 vs 25.3± 15.5 days; P=0.896).

Pituitary-Adrenal Function After Prolonged Glucocorticoid Therapy for Systemic Inflammatory Disorders: An Observational Study

Sacre et al JCEM 2013

Table 2. Cumulative Dose of Glucocorticoid Therapy and Plasma Cortisol Response to SST

Cumulative Dose of Treatment, g	No. of Patients	SST Response, n (%)		
		T0 <100	T60 Response <550	Normal SST
<10	9	0	2 (22)	7 (78)
10–20	25	5 (20)	7 (28)	13 (52)
21–35	10	1 (10)	4 (40)	5 (50)
>35	16	7 (44)	3 (19	
All	60	13	16	

29 pazienti (48.3%)
avevano un deficit surrenalico

Table 3. Duration of Glucocorticoid Therapy and Plasma Cortisol Response to SST

Years of Treatment	No. of Patients	SST Response, n (%)		
		T0 <100	T60 Response <550	Normal SST
<5	30	3 (10)	8 (27)	19 (63)
5–9	11	2 (18)	4 (36)	5 (46)
10–18	15	4 (27)	4 (27)	7 (46)
>18	4	4 (100)	0	0
All	60	13	16	31

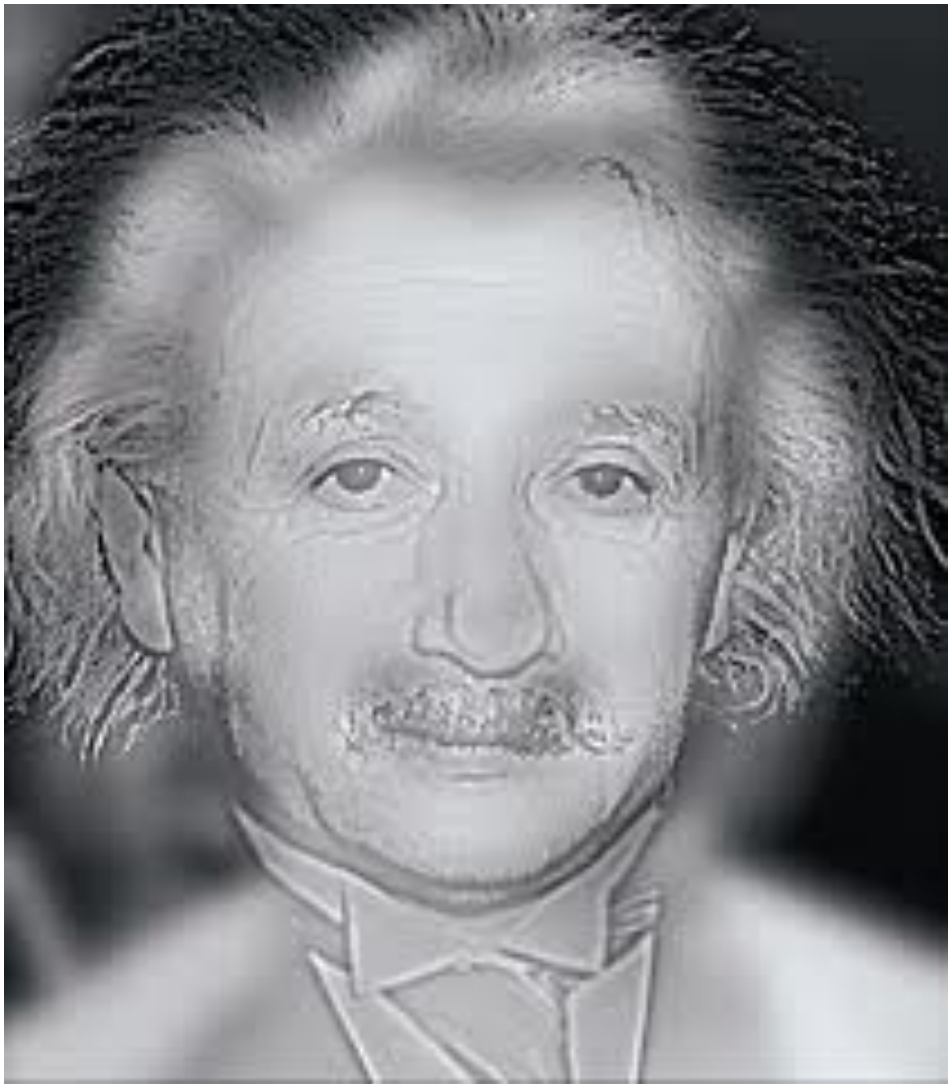
Durata di trattamento
4 mesi-32 a
nni

Dose di prednisone
1 – 132 grammi

Fattori predisponenti e cause di deficit di ACTH

- **Precedente uso di glucocorticoidi**
  - **diversa potenza ed emivita**
  - **diversa via di somministrazione**
  - **concomitante uso di inibitori del CYP3A4**
    - antifungini
- **Trauma cranico + emorragia subaracnoidea**
- **Ipofisite** **(il deficit di ACTH è il deficit più frequente, circa 50%)**
- **Pazienti a rischio, specialmente oncologici**

John Fitzgerald Kennedy
1917 - 1963



Marilyn od Einstein ?

IPOSURRENALISMO

1. SOSPETTO CLINICO

2. DIAGNOSI

3. TERAPIA

Grazie per l'attenzione