17:45-19:00 SIMPOSIO 2
L' INSUFFICIENZA SURRENALICA SECONDARIA
Moderatori: Gianluca Aimaretti, Alfredo Scillitani

17:45-18:00 **IL RITMO CIRCADIANO DEL CORTISOLO**
Andrea M. Isidori

18:00-18:15 **L'INSUFFICIENZA SURRENALICA SECONDARIA: RELAZIONE CON I DEFICIT IPOFISARI**
Carolina Di Somma

18:15-18:30 **IL WORK-UP DIAGNOSTICO ACTH-TEST: DOSI STANDARD *VERSUS* BASSE DOSI**
Filippo Ceccato

18:30-18:45 **LA TERAPIA CON GLUCOCORTICOIDI: FARMACI CONVENZIONALI E NUOVE PROSPETTIVE TERAPEUTICHE**
Chiara Simeoli

18:45-19:00 **CONCLUSIONI & DISCUSSIONE**
Alessandro Ciresi

L' INSUFFICIENZA SURRENALICA SECONDARIA: RELAZIONE CON GLI ALTRI DEFICIT IPOFISARI

Carolina Di Somma

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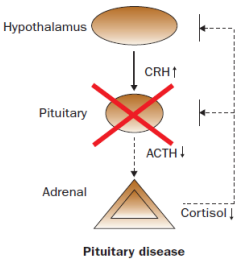
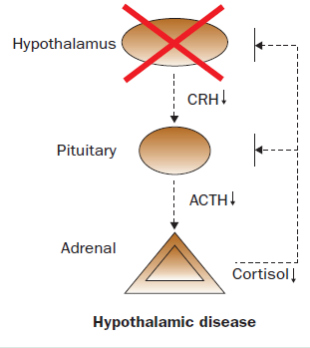
	Pathogenetic mechanisms	Clinical manifestations in addition to adrenal insufficiency
Space-occupying lesions or trauma		
Pituitary tumours (adenomas, cysts, craniopharyngiomas, ependymomas, meningiomas, rarely carcinomas) or trauma (pituitary stalk lesions)	Low corticotropin secretion	Anterior or posterior pituitary hormone deficiencies, or both, and associated symptoms
Pituitary surgery or irradiation for pituitary tumours, tumours outside the HPA axis or leukaemia	Low corticotropin secretion	Anterior or posterior pituitary hormone deficiencies, or both, and primary disease-associated symptoms
Infections or infiltrative processes (lymphocytic hypophysitis, haemochromatosis, tuberculosis, meningitis, sarcoidosis, actinomycosis, histiocytosis X, Wegener's granulomatosis)	Low corticotropin secretion	Anterior or posterior pituitary hormone deficiencies, or both, and primary disease-associated symptoms
Pituitary apoplexy	Low corticotropin secretion	Abrupt onset of severe headache, visual disturbance, nausea, vomiting; anterior or posterior pituitary hormone deficiencies, or both, and primary disease-associated symptoms
Sheehan's syndrome (peripartum pituitary apoplexy and necrosis)	Low corticotropin secretion	Peripartum abrupt onset of severe headache, visual disturbance, nausea, and vomiting; anterior or posterior pituitary hormone deficiencies or both, and primary disease-associated symptoms
Genetic disorders		
Transcription factors involved in pituitary development		
HESX homeobox 1	*HESX1* gene mutations	Panhypopituitarism; short stature, delayed puberty, cognitive changes, septo-optic dysplasia
Orthodentical homeobox 2	Mutations in gene for orthodentical homeobox 2	Panhypopituitarism; neonatal hypoglycaemia, pituitary hypoplasia, ectopic posterior pituitary gland
LIM homeobox 4	Mutations in gene for LIM homeobox 4	Panhypopituitarism; growth hormone, thyrotropin, and corticotropin deficiencies
PROP paired-like homeobox 1	Mutations in gene for PROP paired-like homeobox 1	Panhypopituitarism; late-onset corticotropin deficiency, occasionally enlarged sella turcica
SRY (sex-determining region Y)		
Box 3	Mutations in gene for SRY (sex-determining region Y) box 3	Panhypopituitarism; infundibular hypoplasia, hypopituitarism, mental retardation
T-box 19	Mutations in gene for T-box 19	Congenital isolated corticotropin deficiency
Congenital pro-opiomelanocortin deficiency	Mutations in gene for pro-opiomelanocortin	Early-onset severe obesity, hyperphagia, red hair
Prader-Willi syndrome	Deletion or silencing of genes in imprinting centre for the syndrome	Hypotonia, obesity, mental retardation, hypogonadism

Table 2: Causes of secondary adrenal insufficiency





	Pathogenetic mechanisms	Clinical manifestations in addition to adrenal insufficiency
Space-occupying lesions or trauma		
Hypothalamic tumours (craniopharyngiomas or metastasis from lung or breast cancer)	Low CRH secretion	Anterior or posterior pituitary hormone deficiencies, or both, and primary disease-associated symptoms
Hypothalamic surgery or irradiation for CNS or nasopharyngeal tumours	Low CRH secretion	Anterior or posterior pituitary hormone deficiencies, or both, and primary disease-associated symptoms
Infections or infiltrative processes (lymphocytic hypophysitis, haemochromatosis, tuberculosis, meningitis, sarcoidosis, actinomycosis, histiocytosis X, Wegener's granulomatosis)	Low CRH secretion	Anterior or posterior pituitary hormone deficiencies, or both, and primary disease-associated symptoms
Trauma, injury (fracture of skull base)	Low CRH secretion	Anterior or posterior pituitary hormone deficiencies, or both, and primary disease-associated symptoms
Drug-induced adrenal insufficiency		
Glucocorticoid therapy (systemic or topical) or endogenous glucocorticoid hypersecretion (Cushing's syndrome)	Low CRH and corticotropin secretion	Primary disease-associated symptoms
Mifepristone	Tissue resistance to glucocorticoids through impairment of glucocorticoid signal transduction	If excessive it can cause severe glucocorticoid deficiency; no other symptoms, unless related to drug
Antipsychotics (chlorpromazine), antidepressants (imipramine)	Inhibition of glucocorticoid-induced gene transcription	None, unless related to drug

HPA=hypothalamic–pituitary–adrenal. CRH=corticotropin-releasing hormone.

Table 3: Causes of tertiary adrenal insufficiency

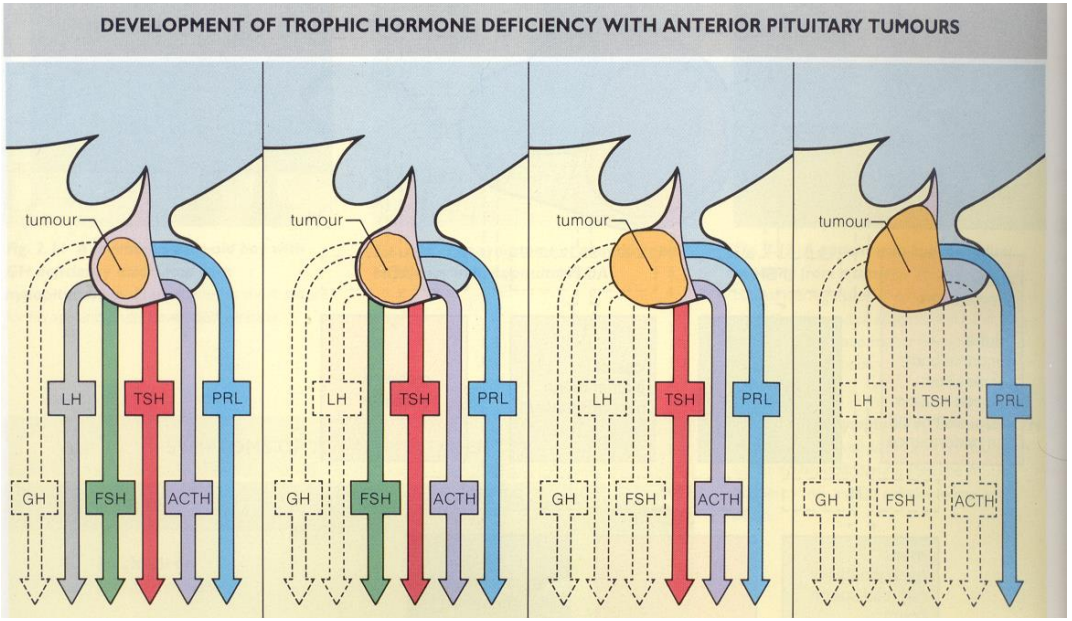
EPIDEMIOLOGY

- **The prevalence of central AI (excluding exogenous steroid use) is 150–280 per million inhabitants.**
- **One-third of the patients with pituitary failure may have AI.**
- **The reported prevalence after pituitary surgery varies with up to 90% after craniopharyngioma surgery**
- **Patients who have undergone cranial radiation for non pituitary tumors have a high prevalence of hypopituitarism.**
- **Adrenal insufficiency was diagnosed in 0–50% of patients with nasopharyngeal tumors and in 3–62% of the patients with intracerebral tumors. ACTH insufficiency occurred after 6 months**

Table 2. Clinical Manifestations of Hypopituitarism

Symptom/Sign	Pituitary Trophic Hormone Deficiency
General	
Fatigue, weakness	ACTH, TSH, LH/FSH, GH
Weight gain	TSH
Weight loss	ACTH
Decreased exercise capacity	ACTH, TSH, LH/FSH, GH
Impaired sleep quality	TSH, LH/FSH, GH
Depression	TSH, GH, LH/FSH
Cognitive decline	ACTH, TSH, ?GH
Cold intolerance	TSH
Skin	
Pallor	ACTH, LH/FSH
Dry skin	ACTH, TSH
Thinning hair, loss of body hair	ACTH, TSH, LH/FSH
Cardiovascular/metabolic	
Hypertension	TSH, GH
Hypotension, particularly orthostatic	ACTH
Bradycardia	TSH
Decreased lean body mass, increased fat mass	GH
Hyperlipidemia	TSH, GH
Insulin resistance, impaired glucose tolerance	TSH, GH
Hypoglycemia	ACTH
Impaired cardiac function	ACTH, TSH, GH
Premature atherosclerosis	TSH, GH
Pulmonary	
Shortness of breath, dyspnea on exertion	ACTH, TSH
Gastrointestinal	
Anorexia	ACTH
Nausea/vomiting	ACTH
Diarrhea/loose stools	ACTH
Constipation	TSH
Musculoskeletal	
Muscle weakness	ACTH, TSH, LH/FSH, GH
Osteoporosis, fractures	ACTH, TSH, LH/FSH, GH
Renal	
Increased thirst	ADH
Polyuria, nocturia	ADH
Reproductive	
Oligo/amenorrhea	ACTH, TSH, LH/FSH
Erectile dysfunction	LH/FSH
Low libido	LH/FSH
Hot flashes	LH/FSH
Infertility	LH/FSH
Vaginal dryness	LH/FSH

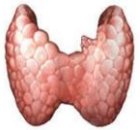
Derived from S. Melmed and J. L. Jameson: Disorders of the anterior pituitary and hypothalamus. In: Jameson JL, ed. *Harrison's Endocrinology*. 2nd ed. Chap 2. New York, NY: McGraw-Hill Professional; 2010:16–49 (65), with permission.



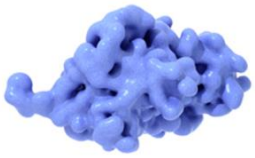
Ordine di sostituzione dei deficit

Interactions between replacement hormones

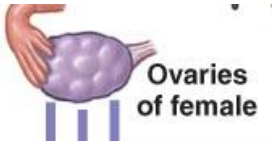
Glucocorticoids and thyroid



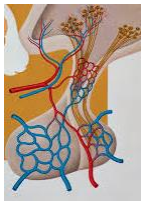
Glucocorticoids and GH



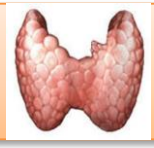
Glucocorticoids and estrogen



Glucocorticoids and diabetes insipidus



Glucocorticoids and thyroid

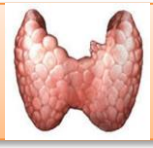


Topliss D J, White E & Stockigt J R (1981): Significance of thyrotropin excess in untreated primary adrenal insufficiency. J Clin Endocrinol Metab 50: 52–56.

Thyroid function in adrenocortical insufficiency during withdrawal and re-administration of glucocorticoid substitution

B. Grubeck-Loebenstein, H. Vierhapper, W. Waldhäusl and P. Nowotny Acta Endocrinologica 1983, 103: 254–258

Glucocorticoids and thyroid



Published in final edited form as:
Best Pract Res Clin Endocrinol Metab. 2009 December ; 23(6): 793–800. doi:10.1016/j.beem.2009.08.003.

DRUGS THAT SUPPRESS TSH OR CAUSE CENTRAL HYPOTHYROIDISM

Bryan R. Haugen, MD [Professor of Medicine and Pathology]

Physiological and pharmacological doses of GC suppress TSH levels

Glucocorticoids

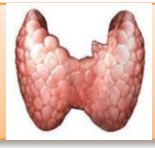
Decreased thyroxine binding globulin levels

TSH suppression

Decrease TSH secretion

Through direct effects on TRH in the hypothalamus

Glucocorticoids and thyroid



Central Hypothyroidism: Pathogenic, Diagnostic, and Therapeutic Challenges

Luca Persani

J Clin Endocrinol Metab, September 2012, 97(9):3068–3078

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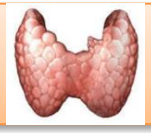
TABLE 4. Recommendations for an adequate LT_4 replacement therapy in patients with CH as derived from the reviewed Refs. 60, 61, 74, 82, 84–89, 94–98 and 101–103

1. Start therapy only after exclusion of adrenal insufficiency or give a prophylactic steroid treatment in cases at risk.

Grossman A et al, European Journal of Endocrinology 2013

Glucocorticoids and thyroid



European Journal of Endocrinology (2004) 150 1–8 ISSN 0804-4643

CLINICAL STUDY

Clinical and hormonal characteristics of central hypothyroidism at diagnosis and during follow-up in adult patients

O Alexopoulou, Cl Beguin[1], Ph De Nayer[2] and D Maiter

CH patients receiving GC therapy do not appear to require L-T4 dose adjustments

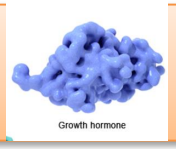
Table 4 Thyroid parameters according other pituitary hormone treatments.

	GH		Estrogens		Cortisone		Testosterone	
	no	yes	no	yes	no	yes	no	yes
T_4 (μg/dl)	9.1±2.4	8.6±1.4	8.7±1.6	10.4±2.7	7.9±2.0*	9.1±2.1	7.6±2.1	8.5±1.8
fT_4 (ng/dl)	1.4±0.4	1.5±0.2	1.4±0.3	1.5±0.3	1.3±0.3	1.4±0.3	1.3±0.4	1.4±0.2
T_3 (ng/dl)	92±32	95±15	82±17	100±28	99±40	89±21	82±12	92±31
fT_3 (pg/ml)	2.9±1.1	3.2±0.7	2.7±0.5	3.1±0.9	3.3±1.4	3.0±0.8	2.7±0.5	3.2±1.1
TSH (μU/ml)	0.2±0.5	0.1±0.2	0.3±0.4	0.2±0.3	0.5±0.8*	0.1±0.3	0.5±0.5***	0.2±0.5
T_4 dose (μg/kg/day)	1.6±0.5*	1.8±0.5	1.3±0.3**	1.8±0.6	1.5±0.5	1.6±0.5	1.4±0.4	1.6±0.5

Values are shown as means±S.D.; *$P < 0.05$, **$P < 0.01$, *** $P < 0.001$ vs respective treated group.

Corticosteroid replacement therapy did not have any influence on the L-T4 dose, but was associated with reduced TSH. This effect may result from the known inhibitory action of glucocorticoids on the basal release of TSH. Higher tT4 levels observed in cortisone treated subjects probably reflect the decreased conversion of T4 to T3 in peripheral tissues

Glucocorticoids and GH



Glucocorticoids and the regulation of growth hormone secretion

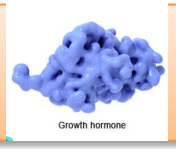
Gherardo Mazziotti and Andrea Giustina

Nat. Rev. Endocrinol. **9**, 265–276 (2013)

Key points

- Glucocorticoids modulate growth hormone (GH) secretion at both the hypothalamic and pituitary level
- Hypoadrenalism might cause GH deficiency that is reversible during glucocorticoid replacement therapy
- Testing for GH deficiency in patients with hypopituitarism should always be performed after adequate periods of cortisol replacement
- Chronic excess of glucocorticoids, either exogenous or endogenous, causes GH deficiency that might be involved in metabolic and cardiovascular complications
- Treatment with recombinant GH could be considered in children and adults with glucocorticoid-induced GH deficiency

Glucocorticoids and GH



European Journal of Endocrinology (2013) **169** R165–R175 ISSN 0804-4643

REVIEW
THERAPY OF ENDOCRINE DISEASE

Perspectives on the management of adrenal insufficiency: clinical insights from across Europe

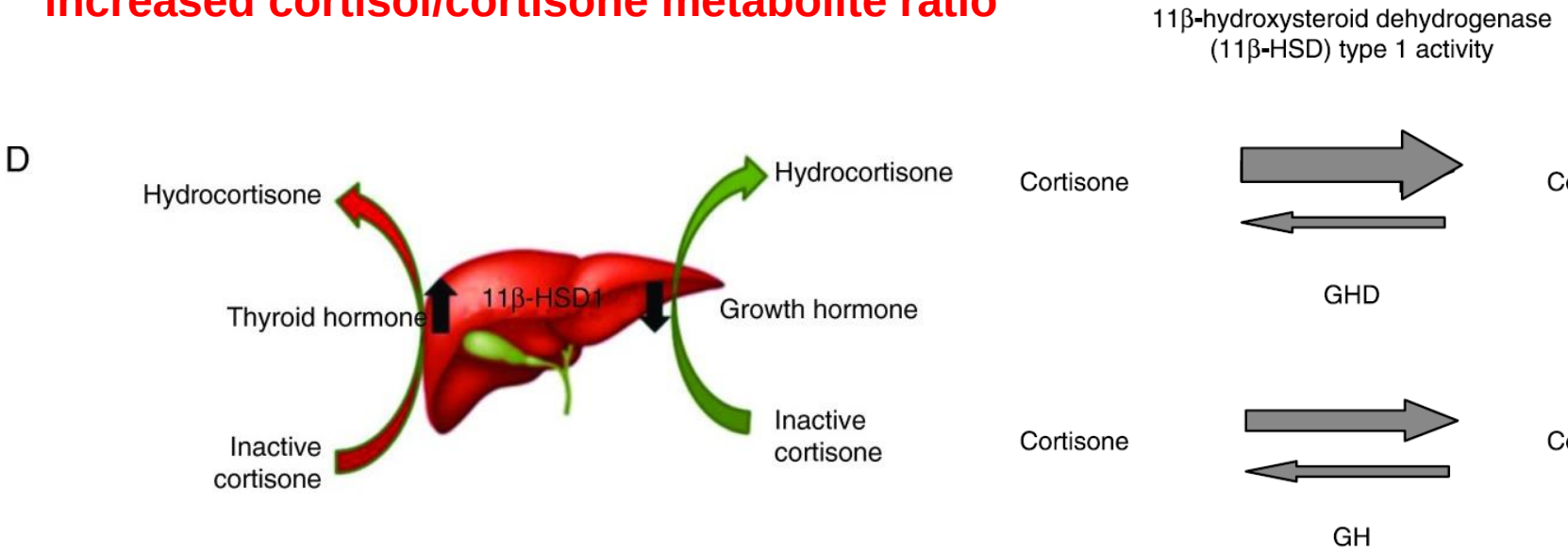
Ashley Grossman, Gudmundur Johannsson[1], Marcus Quinkler[2] and Pierre Zelissen[3]

European Journal of Endocrinology (2009) **161** S85–S95 ISSN 0804-4643

GH replacement in adults: interactions with other pituitary hormone deficiencies and replacement therapies

Helena Filipsson and Gudmundur Johannsson

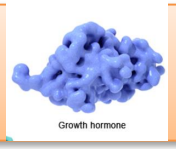
Patients with GHD in the setting of hypopituitarism demonstrate an increased cortisol/cortisone metabolite ratio



Drugs modulating hepatic 11b-hydroxysteroid dehydrogenase type 1 (11b-HSD1) influence HC half-life

Figure 1 The 11β-HSD type 1 enzyme activity is enhanced in GH deficiency (GHD), thus exposing the tissues to more cortisol, whereas GH replacement inhibits the type 1 shuttle.

Glucocorticoids and GH



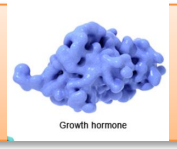
Effect of Recombinant Human Growth Hormone (GH) Replacement on the Hypothalamic-Pituitary-Adrenal Axis in Adult GH-Deficient Patients

CLAUDIA GIAVOLI, ROSSELLA LIBÉ, SABRINA CORBETTA, EMANUELE FERRANTE, ANDREA LANIA, MAURA AROSIO, ANNA SPADA, AND PAOLO BECK-PECCOZ

GH suppresses the conversion of cortisone to cortisol, patients receiving GC replacement may require higher doses once GH is initiated, and those with low adrenal reserve may be rendered hypoadrenal by the GH therapy

The aim of the study was to evaluate the hypothalamus-pituitary-adrenal (HPA) axis in patients (nine males, three females; mean age ± SEM 51 ± 2 yr) with adult-onset GH deficiency (GHD) due to surgically treated pituitary tumors with preserved HPA function and without evidence of tumor recurrence before and during recombinant human (rh) GH replacement therapy (duration 31 ± 6 months). HPA function was assessed by urinary free cortisol and morning serum cortisol levels as well as cortisol responses to 1 μg ACTH test (n = 7 patients) or insulin tolerance test (n = 5 patients) before and during rhGH therapy, the cut-off for the diagnosis of hypoadrenalism being a cortisol peak less than 18 μg/dl (<500 nmol/liter) after stimulatory tests. Serum cortisol and urinary free cortisol levels were significantly lower on therapy than before [7.6 ± 0.8 *vs.* 11.5 ± 0.9 μg/dl (208 ± 22 *vs.* 317 ± 24 nmol/liter), $P < 0.01$, and 19.6 ± 2.5 *vs.* 32.2 ± 3.2 μg per 24 h (54 ± 7 *vs.* 89 ± 9 nmol per 24 h), $P < 0.05$, respectively], whereas no change in cortisol-binding globulin levels was observed. Cortisol peak after either ACTH test or insulin tolerance test was lower on rhGH therapy than before [15.9 ± 1.5 *vs.* 20.2 ± 1.1 μg/dl (437 ± 43 *vs.* 557 ± 31), $P = 0.01$, and 13.1 ± 2.6 *vs.* 20.4 ± 1.4 μg/dl (362 ± 71 *vs.* 564 ± 37 nmol/liter), $P = 0.03$, respectively]. Accordingly, central hypoadrenalism was detected in nine of 11 patients. In conclusion, low GH and IGF-I levels, likely enhancing the conversion of cortisone to cortisol, may mask a condition of central hypoadrenalism. Therefore, the reassessment of HPA function in GHD patients during rhGH therapy is mandatory. (*J Clin Endocrinol Metab* 89: 5397–5401, 2004)

Glucocorticoids and GH



Casi di crisi o insufficienza surrenalica

3 eventi avversi seri,
incluso un caso fatale
3 eventi avversi non seri

3 in soggetti trattati
quotidianamente con rhGH
3 in soggetti trattati con rhGH
depot

Tutti i soggetti avevano una diagnosi precedente di iposurrenalismo secondario ed erano in trattamento sostitutivo con glucocorticoidi

25% (3/12) di tutti gli eventi avversi seri

Hoffman et al, J Clin Endocrinol Metab, 90: 6431, 2005

Glucocorticoids and GH

Hormonal Replacement in Hypopituitarism in Adults: An Endocrine Society Clinical Practice Guideline

Maria Fleseriu (chair), Ibrahim A. Hashim, Niki Karavitaki, Shlomo Melmed, M. Hassan Murad, Roberto Salvatori, and Mary H. Samuels

***J Clin Endocrinol Metab* 2016**

Table 6. Patient Monitoring After Initiating Adult GH Replacement

1. Measure IGF-1 6 weeks after initiating GH replacement, after dose escalations, and every 6 months thereafter.
2. Assess body weight, blood pressure, waist circumference, and BMI every 6 months.
3. Assess thyroid and adrenal function and replace or adjust replacement doses as indicated.
4. Assess metabolic profile including blood sugar and lipids every 6 months.
5. Assess BMD by DXA every 18 months.
6. Periodically assess residual pituitary mass via a pituitary MRI.
7. Assess QOL.

Abbreviation: DXA, dual-energy x-ray absorptiometry. [Derived from S. Melmed: Idiopathic adult growth hormone deficiency. *J Clin Endocrinol Metab*. 2013;98:2187–2197 (167), with permission. ©The Endocrine Society.].

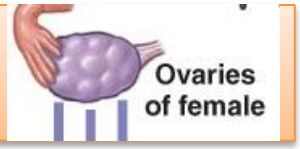
Glucocorticoids and estrogen

1. About 95% of circulating cortisol is bound mainly to CBG and to a lesser extent to albumin, and unbound cortisol is the active fraction.

2. Oral estrogen therapy increases circulating CBG (through a hepatic first-pass effect), leading to increased total cortisol levels.

3. This effect does not occur with transdermal estrogen therapy

Glucocorticoids and estrogen



Menopause. 2007 Nov-Dec;14(6):985-94.

A randomized, open-label, crossover study comparing the effects of oral versus transdermal estrogen therapy on serum androgens, thyroid hormones, and adrenal hormones in naturally menopausal women.

Shifren JL[1], Desindes S, McIlwain M, Doros G, Mazer NA.

To compare the changes induced by oral versus transdermal estrogen therapy on the total and free serum concentrations of testosterone (T), thyroxine (T4), and cortisol (C) and the concentrations of their serum binding globulins sex hormone-binding globulin, thyroxine-binding globulin, and cortisol-binding globulin in naturally menopausal women.

DESIGN:

Randomized, open-label, crossover. Interventions included a 6-week withdrawal from previous hormone therapy (baseline), followed in randomized order by 12 weeks of oral conjugated equine estrogens (CEE) (0.625 mg/d) and 12 weeks of transdermal estradiol (TD E2) (0.05 mg/d), with oral micronized progesterone (100 mg/d) given continuously during both transdermal estrogen therapy regimens.

RESULTS:

Twenty-seven women were enrolled in the study, and 25 completed both treatment periods. The mean(SD) percentage changes from baseline of sex hormone-binding globulin, total T, and free T with oral CEE were +132.1% (74.5%), +16.4% (43.8%), and -32.7% (25.9%), respectively, versus +12.0% (25.1%), +1.2% (43.7%), and +1.0% (45.0%) with TD E2. The mean (SD) percentage changes of thyroxine-binding globulin, total T4, and free T4 with oral CEE were +39.9% (20.1%), +28.4% (29.2%), and -10.4% (22.3%), respectively, versus +0.4% (11.1%), -0.7% (16.5%), and +0.2% (26.6%) with TD E2. The mean (SD) percentage changes of cortisol-binding globulin, total C, and free C with oral CEE were +18.0% (19.5%), +29.2% (46.3%), and +50.4% (126.5%), respectively, versus -2.2% (11.3%), -6.7% (30.8%), and +1.8% (77.1%) with TD E2. Concentrations of all hormones and binding globulins were significantly different (P < or = 0.003) during administration of oral versus transdermal estrogen therapy, except for free T4 and free C.

CONCLUSIONS:

Compared with oral CEE, TD E2 exerts minimal effects on the total and free concentrations of T, T4, and C and their binding proteins.

Clinical Endocrinology (2007) 66, 632–635 doi: 10.1111/j.1365-2265.2007.02784.x

ORIGINAL ARTICLE

The influence of the route of oestrogen administration on serum levels of cortisol-binding globulin and total cortisol

Ayesha C. Qureshi, Aman Bahri, Louise A. Breen, Sophie C. Barnes, Jake K. Powrie, Stephen M. Thomas and Paul V. Carroll

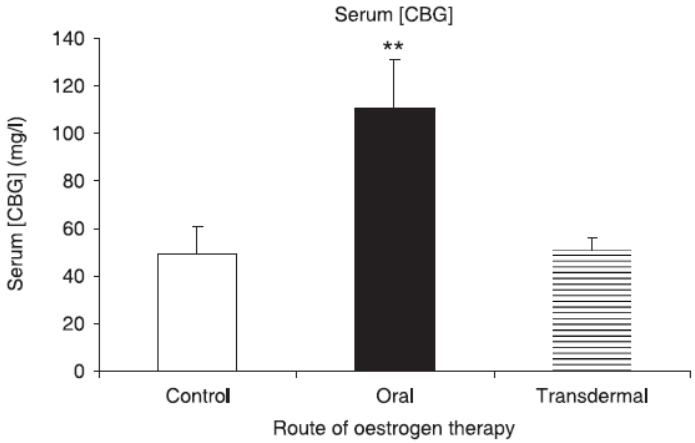
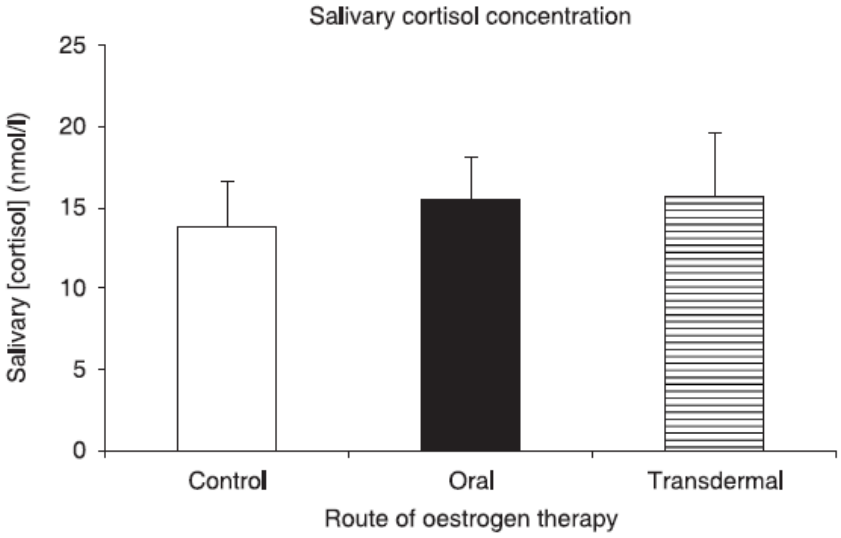
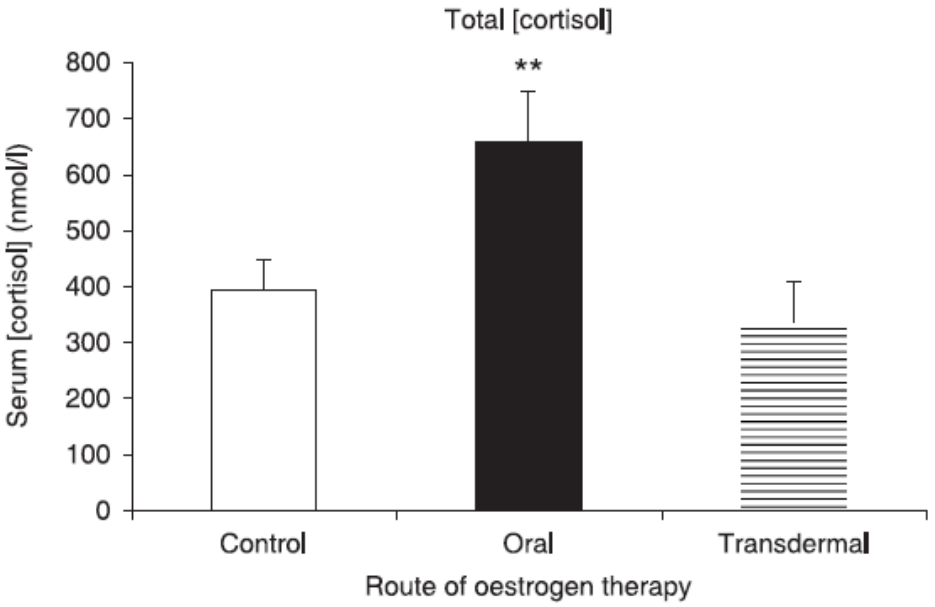


Fig. 2 The mean (± SD) of the serum CBG concentrations (mg/l) grouped according to route of oestrogen therapy. Asterisks denote group values that are significantly different from controls: $^{**}P < 0{\cdot}001$ compared to control group.

Oral oestrogen preparations as routinely used in the clinical setting result in marked increases in total cortisol concentration due to increased CBG levels. Transdermal oestrogen preparations do not appear to alter CBG or cortisol concentrations. Salivary cortisol measurement may be a reliable measure of cortisol, which is independent of the use of an oestrogen-containing product. It is probably not necessary to routinely discontinue transdermal oestrogen products in subjects undergoing assessment of the HPA axis.





Glucocorticoids and diabetes insipidus

Kidney International, Vol. 18 (1980), pp. 58–67

1980

Role of vasopressin in the impaired water excretion of glucocorticoid deficiency

STUART L. LINAS, TOMAS BERL, GARY L. ROBERTSON, GARY A. AISENBREY, ROBERT W. SCHRIER, and ROBERT J. ANDERSON

GC deficiency induces impaired free renal water clearance, resulting in the masking of polyuria in DI

Conclusion. The present results in the rat demonstrate that the impaired water excretion associated with glucocorticoid deficiency is time dependent and is mediated by both vasopressin-dependent and vasopressin-independent pathways rather than by either factor alone. The nonosmotic release of vasopressin is detectable within 24 hours of glucocorticoid deficiency and is associated with known systemic hemodynamic stimuli for vasopressin release. After 2 weeks of glucocorticoid deficiency, a vasopressin-independent defect in water excretion is demonstrable in Brattleboro rats with DI. This vasopressin-independent defect in water excretion is associated with a significant decrease in cardiac output, renal blood flow, and a significant rise in filtration fraction. A decrease in distal fluid delivery rather than an increased water permeability of the collecting duct epithelium thus seems most likely to account for this vasopressin-independent defect in water excretion.

Glucocorticoids and diabetes insipidus

Case Report

Arginine Vasopressin-Independent Mechanism of Impaired Water Excretion in a Patient with Sarcoidosis Complicated by Central Diabetes Insipidus and Glucocorticoid Deficiency

Hindawi Publishing Corporation
Case Reports in Medicine
Volume 2011, Article ID 145856, 5 pages

Katsunobu Yoshioka,[1] Nagaaki Tanaka,[2] Keiko Yamagami,[3] Takeshi Inoue,[4] and Masayuki Hosoi[3]

A 28-year-old man was admitted to our hospital because of reduced livido and increased fatigability. Four months before admission, he noticed polyuria, which was gradually relieved by admission. Magnetic resonance imaging revealed enhancing lesion centrally in the pituitary stalk. Biopsy from the skin revealed noncaseating granuloma composed of epithelioid cells, and a diagnosis of sarcoidosis was made. Although plasma arginine vasopressin (AVP) was undetectable after administration of hypertonic saline, urinary output was within normal range (1.5 to 2.2 L/day). The urine osmolality became above plasma levels during the hypertonic saline test. Hormonal provocative tests revealed partial glucocorticoid deficiency. Soon after the glucocorticoid therapy was begun, moderate polyuria (from 3.5–4.0 liters daily) occurred. At this time, plasma AVP was undetectable, and urine osmolality was consistently below plasma levels during the hypertonic saline test. In conclusion, we showed in human study that masked diabetes insipidus could be mediated by AVP-independent mechanisms.

Glucocorticoids and thyroid hormone

2.20 We suggest evaluating patients with CH for AI before starting L-T4 therapy. If this is not feasible, clinicians should prescribe empiric GC therapy in patients with CH who are starting L-T4 therapy until there is a definitive evaluation for AI. (2|⊕⊕◯◯)

Glucocorticoids and GH

2.19 We suggest testing HPA axis functionality before and after starting GH replacement in patients who are not receiving GC replacement and who have demonstrated apparently normal pituitary-adrenal function. (2|⊕◯◯◯)

Glucocorticoids and estrogen

2.21 We suggest that when clinicians assess adrenal reserve or the adequacy of HC replacement, they take into consideration that total serum cortisol level can be elevated due to the effects of estrogen on corticosteroid-binding globulin (CBG). (2|⊕⊕⊕◯)

Glucocorticoids and diabetes insipidus

2.26 Because AI may mask the presence of partial DI, we suggest monitoring for the development of DI after starting GC replacement. Conversely, patients with improved DI without an AI diagnosis should undergo AI testing. (2|⊕◯◯◯)

Conclusions

Hormonal Replacement in Hypopituitarism in Adults: An Endocrine Society Clinical Practice Guideline

Maria Fleseriu (chair), Ibrahim A. Hashim, Niki Karavitaki, Shlomo Melmed, M. Hassan Murad, Roberto Salvatori, and Mary H. Samuels

***J Clin Endocrinol Metab* 2016**

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